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熱帯地域における各種急性肝障害の肝細胞病変を主とした病理組織学的特異性：妊娠中毒症，肝炎ウイルス性劇症肝炎，黄熱，アフラトキシン中毒症の比較検討

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はじめに

熱帯地域の住民にはさまざまな感染症，中毒性疾患，栄養障害などがあるが，それらの多くは肝にも特徴ある病変をきたすことが多い（板倉ら，1984)。それらの中には，急性肝病変を呈する特異的な肝障害がある。本研究では，熱帯地域における妊娠中毒症（および子癇）を主とし，肝炎ウイルス性劇症肝炎，黄熱，アフラトキシン中毒症の各疾患の急性肝障害像を，病理組織学的に比較検討した。

妊娠中毒症は熱帯地域，特に発展途上国においていまだに散見される重要な疾患であり，また各型の肝炎ウイルスによるウイルス性肝炎は熱帯地域では広く高頻度に見られる。黄熱はウイルスによるウイルス性出血熱の代表的疾患で，蚊によって媒介される黄熱ウイルスによる疾患である。アフラトキシン中毒症は，食品寄生真菌類毒性代謝産物（マイコトキシン）によるマイコトキシン中毒症のなかで，最も障害をもたらす疾患の1つであり，ときに熱帯地の食中毒として発生する。

これらの疾患は，何れも病理学的に特徴ある肝障害像を呈する。すなわち肝に急激な障害をきたす場合，肝の主要な実質である肝細胞の障害像と，その修復像に病理学的な差異が見られる。本研究では，赤道東アフリカ・ケニアにおける子癇の症例を中心として，熱帯における上記の各種疾患の病理解剖材料について，急性肝障害像および残存肝細胞の動態像を病理組織学に把握し，病変の発生機序を推察した。

材料と方法

材料：以下の疾患の病理解剖材料を検索した。疾患は妊娠中毒症もしくは子癇（7例），亜広範性肝壊死を示すB型肝炎ウイルス性劇症肝炎（19例），および同じく非A非B型ウイルス性劇症肝炎（4例），黄熱（3例），アフラトキシン中毒症（3例）である。これらは赤道東アフリカ・ケニア，および西アフリカ・ガーナの国立総合病院，国立大学病院などにおける症例である。妊娠中毒症およびウイルス性劇症肝炎の材料については，旧東京都立駒込病院，昭和大学医学部第一病理学教室，長崎大学熱帯医学研究所病理学部門など，各施設における病理解剖材料を補助的に加えて検索した。

方法：病理組織学的ならびに組織化学的検索：肝の組織片をホルマリン固定後，パラフィン包埋切片を用い，hematoxylin-eosin染色を全般的な

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病理組織学的観察に，鍍銀染色，Mallory の膠原線維染色，弾力線維染色の各染色を組織構造の観察に，periodic acid-Schiff（PAS）反応を肝細胞の個々の病変の観察に用いた。

結　果

急性肝障害を呈する各疾患の肝病変の病理組織学的所見をもとに，以下の点を病理形態学的指標として比較検討した。すなわち，1）肝小葉における障害部位（site of lesion in hepatic lobule），2）肝小葉における肝実質の壊死の形状（shape of lesions），3）出血性病変の部位と強弱(hemorrhage)，4）肝細胞の個々の病変：肝細胞の変性・壊死（liver cell degeneration and necrosis)と多形性および大小不同性，5）肝構築像：肝細胞索の配列の乱れ，6）残存肝細胞の動態像：結節性の再生•増殖像（nodular liver cell regeneration），7）肝細胞の異型度：核の多形性と大小不同性，核の異常染色性，異常あるいは高頻度の核分裂像など，8）肝組織内の血栓形成（intrahepatic thrombus formation），9）炎症性細胞浸潤（inflammatory cell infiltration），10）間質における線維組織の増生（fibrous tissue）などである。

これらの指標に基づいた各疾患の病変は，下記のごとくである。また各疾患について比較した結果を表1に示す。

妊娠中毒症および子癇：肝小葉中間帯および周辺部における肝細胞の変性，および壊死が見られる。肝小葉中心部には壊死はほとんど見られない。ときには肝小葉全葉にわたって変性・壊死がおよぶことがあるが，その場合でも門脈域周辺の肝細胞のいわゆる限界板は保たれている。壊死病巣の形状は帯状のこともあるが，不規則で地図状のことが多い。肝実質内各所に比較的新鮮な出血が見られるが，症例によって軽度から強度までその程度はまちまちである。肝細胞の腫大が著しいこともある。肝細胞の大小不同性が見られる。肝細胞索は萎縮性で，不規則な配列を示す。肝細網線維を鍍銀染色で見ると，壊死による肝実質構造の部分的な破壊が見られる。残存肝細胞の結節性再生像は，ほとんど見られない。肝細胞核の大小不同性が見られる。肝細胞の異型性はほとんどない。ごく小さなフィブリン様あるいは血栓様形成物が部分的に見られたが，全般的には明らかなものは見られなかった。肝全体に浮腫が見られる。肝類洞が全般的に拡張し，Kupffer 細胞の動員と

Table 1　Histopathology of acute liver diseases

Disease	Site of lesion in hepatic lobule	Liver cell degeneration and necrosis	Hemorrhage	Shape of lesions	Nodular liver cell regeneration	Intrahepatic thrombus formation	Inflammatory cell infiltration
eclampsia	intermediate and perilobular	++	++	irregular and partially zonal	not clear	−〜+	+
fulminant viral hepatitis	panlobular and partial	+++++	+〜+++	irregular	+++++	−〜++	+++
yellow fever (viral hemorrahgic fever)	intermediate and periportal	+++	+〜+++++	zonal	not clear	not clear	++
aflatoxicosis	centrilobular	+++	− or +	regular	not clear	−	− or +

(−); negative〜(+++++); strongest

軽度のび漫性炎症性細胞浸潤が見られる。肝小葉の門脈域の炎症性細胞浸潤は，比較的軽度である。線維組織の形成は，ほとんど見られなかった（図1-7）。

妊娠中毒症および子癇の各症例と，剖検所見を示すと以下のようである。

症例1（ODKOM1641）： 40F 妊娠中毒症，妊娠腎，心嚢液多量，肺浮腫，肺炎，全身貧血，内臓鬱血，肝小葉周辺性壊死

症例2（ODKOM1711）： 33F 妊娠中毒症，大白腎，心肥大，両側肺浮腫，全身性皮下浮腫，腹水

症例3（ODKOM1870）： 28F 妊娠中毒症，大白腎，心筋混濁変性，胎盤剝離，肝腫大および混濁腫張

症例4（ODKOM1904）： 28F 妊娠中毒症，肝混濁腫張，両腎灰白色混濁，心筋混濁腫張，両側副腎皮質出血，全身性浮腫，出血性傾向，肝病変として肝小葉周辺性変性お

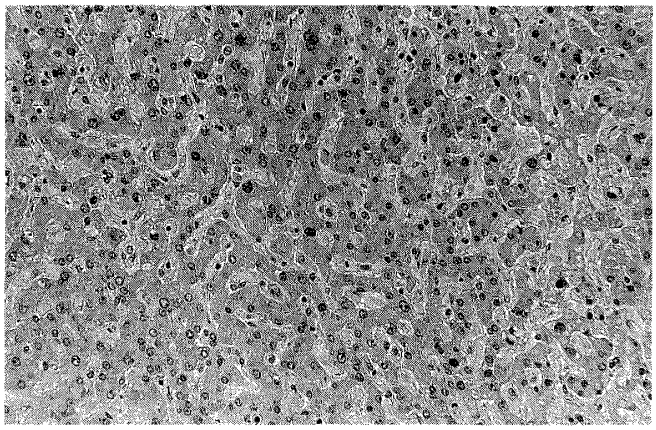

Figure 1 Eclampsia. Edema of liver tissue. Sinusoidal dilatation and inflammatory exudate with Kupffer cell mobilization are seen. Liver cell cords are atrophic and show irregular structures and pleomorphism of liver cell nuclei. (Case 6) (Hematoxylin and eosin stain. Original magnification; ×100)

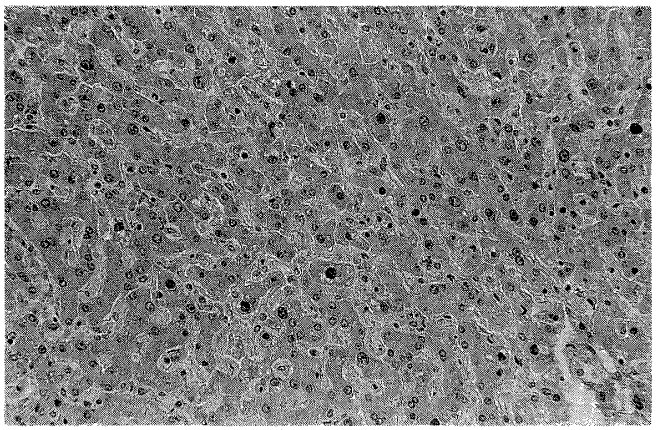

Figure 2 Eclampisa. Sinusoidal dilatation and inflammatory exudate with Kupffer cell mobilization are seen. Atrophic and irregular structures with pleomorphism of liver cell nuclei are marked. Centrilobular areas (on right lower part) are intact. (Case 6) (Hematoxylin and eosin stain. Original magnification; ×100)

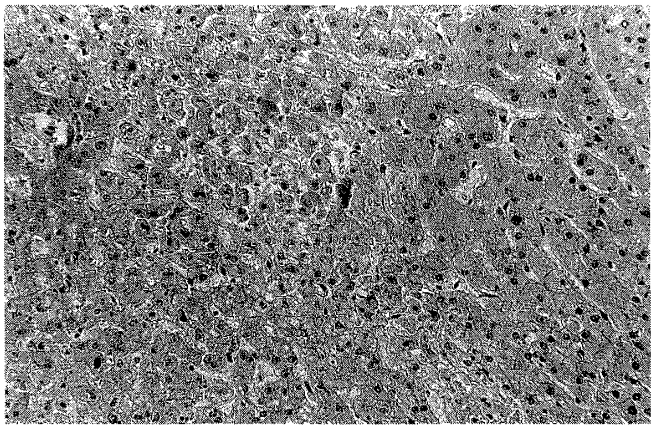

Figure 3 Eclampsia. Complicated and irregular pattern of degenerative or necrotic liver parenchyma in intermediate zones of hepatic lobules. (Case 4) (Hematoxylin and eosin stain. Original magnification; ×100)

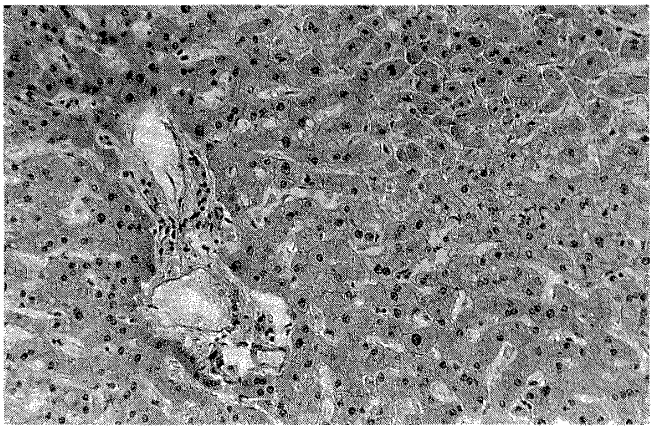

Figure 4 Eclampsia. Degeneration and necrosis of liver cells are irregular and zonal in intermediate zones of hepatic lobules. Inflammatory exudate is rather sparse in periportal areas (on left side). (Case 4) (Hematoxylin and eosin stain. Original magnification; ×100)

よび壊死，肝内の軽度の出血

症例5 (NAK130)： 24F 子癇，大白腎，心点状出血，肺鬱血および部分出血，子宮拡張，肝のび漫性出血壊死，脂肪変性

症例6 (NAK150)： 30F 子癇，心肥大，両下肢浮腫，両側気管支肺炎，両側腎腫大，腹水，肝小葉周辺性の鬱血と出血，肝実質黄疸

症例7 (SHO1428)： 26F 子癇

肝炎ウイルス性劇症肝炎： B型肝炎ウイルスによる劇症肝炎の症例群，および非A非B型肝炎ウイルスによる劇症肝炎の症例群を検索した。何れも亜広範性肝壊死を示す症例である。本研究では，両症例群の間で肝障害像に明確な差異を見ることができなかったので，全例をまとめて記載する。肝小葉の部分的，あるいは全葉にわたる肝細胞の変性・壊死が基本的組織像である。肝小葉周辺領域の肝細胞の限界板が，破壊されている。病変は不整形である。出血は部分的で軽度，時には中程度である。肝細胞には軽度ではあるが，結節性の再生性変化が見られる。しかしそれらの肝細胞には，異型性はほとんどない。門脈域周辺部に偽胆管の増生が見られる。血栓の形成は症例によ

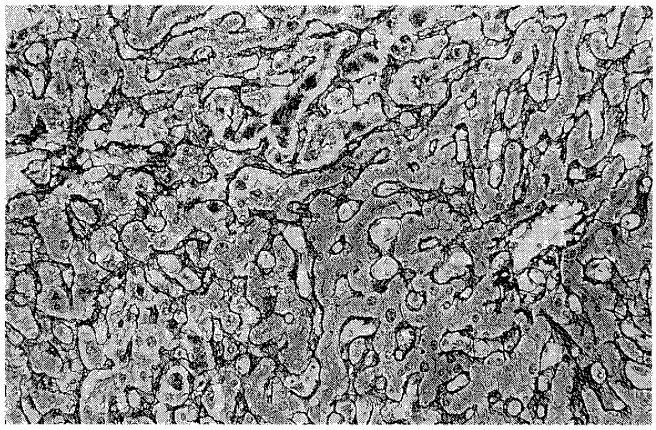

Figure 5 Eclampsia. Silver impregnation of liver parenchyma. Liver cell cords in intermediate zone and periportal area (on left side) of hepatic lobule are irregular and collapsed, while centrilobular area (on right side) is intact. (Case 4) (Original magnification; ×100)

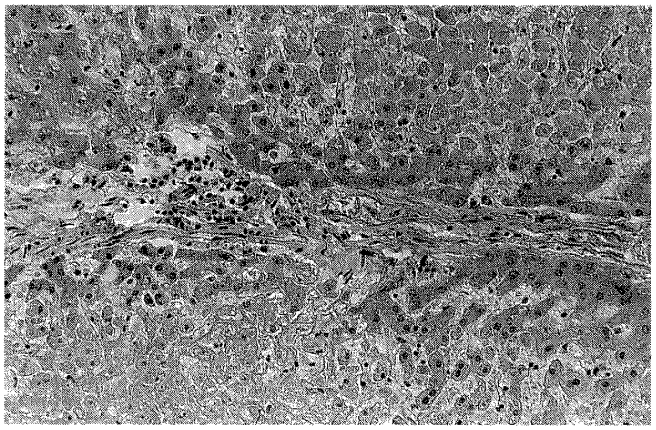

Figure 6 Eclampsia. Lobular necrosis and degeneration of hepatic parenchyma. (Case 5) (Hematoxylin and eosin stain. Original magnification; ×100)

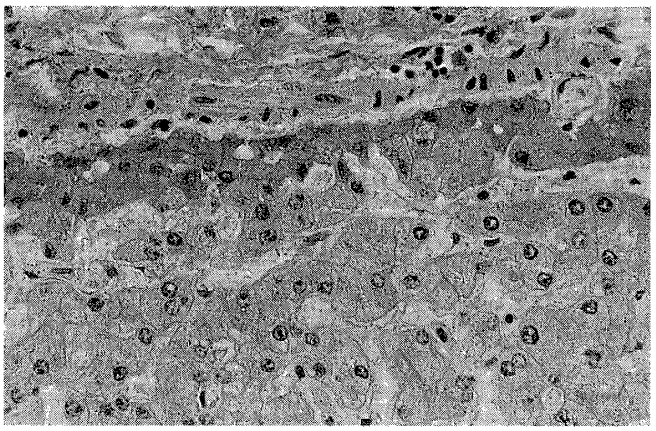

Figure 7 Eclampsia. Higher magnification of the same case of Figure 6. Relatively intact liver cells at the periphery portion of hepatic lobule are observed. (Case 5) (Hematoxylin and eosin stain. Original magnification; ×400)

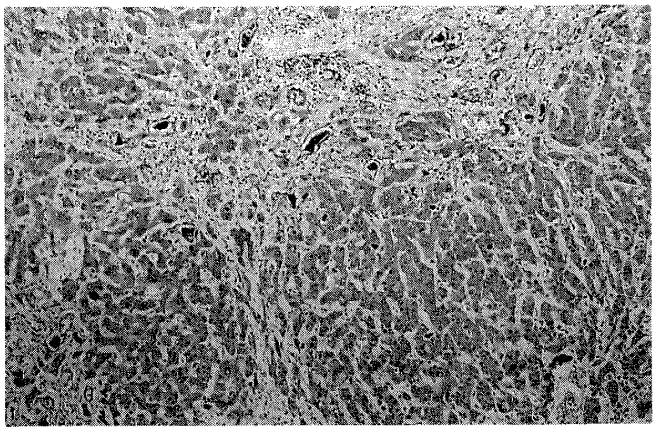

Figure 8 Fulminant viral hepatitis. Irregular necrosis of liver parenchyma with inflammatory exudate and regenerative nodular proliferation with scattered bile stasis of liver cells are seen. In contrast to eclampsia, lobular regenerative arrangements of liver cell cords surrounded by necrotic or collapsed parenchyma are characteristic. (Hematoxylin and eosin stain. Original magnification; ×40)

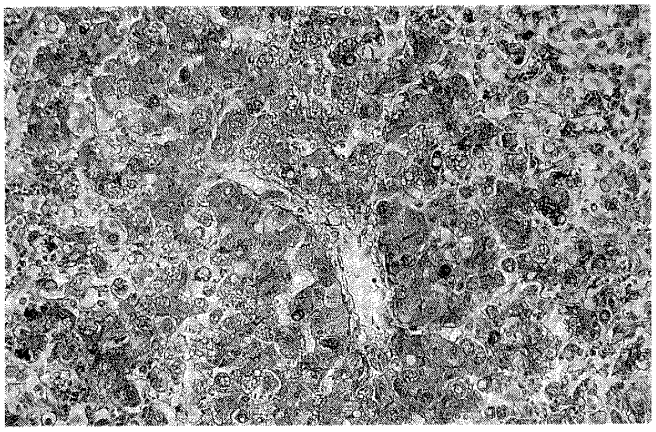

Figure 9 Yellow fever. Zonal necrosis of hepatic parenchyma is seen in intermediate zones of hepatic lobules. Centrilobular areas are relatively intact. Scattered acidophilic bodies of unicellular necrosis of liver cells are also seen in inconspicuous sinusoids. Inflammatory reaction of polymorphonuclear leukocytes is relatively slight. (Hematoxylin and eosin stain. Original magnification; ×200)

り異なり，軽度からないものまでさまざまである。炎症性細胞浸潤が強度で，リンパ球，形質細胞を主とし，一部好中球が見られる。門脈域周辺部から肝細胞の壊死，脱落部分へ膠原線維の増生が見られる（図8）。

黄熱：肝小葉中間帯から周辺部にかけて，肝細胞の強度の変性，壊死が見られる。病変は肝小葉中間帯で帯状を呈する場合もあるが，不整形もある。症例によって異なるが，軽度から強度の不規則な出血が見られる。単一肝細胞の特徴的な好酸性壊死が見られる。残存肝細胞の脂肪変性が見られることもある。肝小葉周辺部の肝細胞の限界板の破壊が見られる症例もあるが，これは壊死性病変の波及による二次的な変化であると思われる。通常，肝細胞の結節性の再生性変化は見られない。また残存肝細胞の異型性はない。血栓形成につい

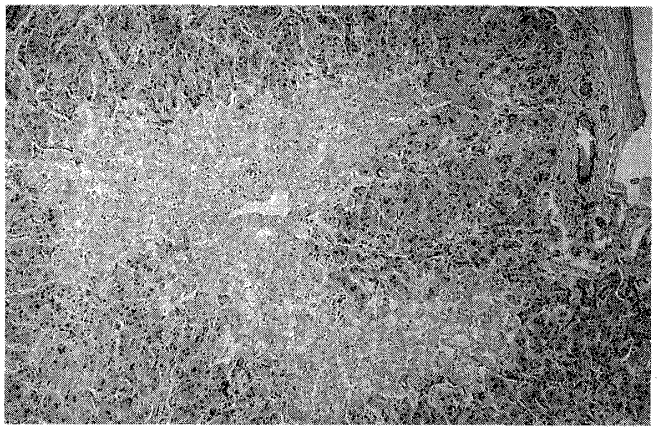

Figure 10 Aflatoxicosis. Centrilobular necrosis of liver cells showing clear zone of hepatocellular parenchyma is prominent. Inflammatory exudate is slight. (Hematoxylin and eosin stain. Original magnification; ×40)

ては，肝の壊死性の変化が強く，ほとんど確認できなかった。リンパ球，好中球，形質細胞などからなる，軽度のび漫性炎症性細胞の浸潤が見られた。線維組織の増生はない（図9）。

アフラトキシン中毒症：肝小葉中心性壊死が，中等度から強度に見られる。形状は不規則ながらも，概して肝小葉中心部を中心とした同心円状である。境界は鮮明である。肝小葉の他の部位は，組織学的には変化は軽度である。出血はほとんど見られない。肝細胞の壊死は凝固壊死である。肝細胞の再生像も，また異型性もない。血栓形成は見られない。炎症性細胞浸潤はほとんどない。線維組織の増生はない（図10）。

考案と総括

各種の病因により，肝小葉単位における肝実質細胞の障害像のあり方として，1）巣状壊死，2）帯状壊死，3）広範性壊死などがある。これらの障害の発生機序として，病原体や毒物などの原因が，肝細胞を直接侵襲して障害する，免疫学的機序が働く，循環障害による，栄養や内分泌障害を含む代謝障害などが考えられる。また肝障害像の修飾要素として，標的細胞の種類，すなわち肝細胞か，胆管上皮細胞か，Kupffer細胞か，または間葉系組織かにより，また肝小葉内における位置的条件，すなわち肝内循環系における部位，肝細胞の老若，肝細胞の酵素活性の差異などが考えられる。しかし実際には，これら多くの要素が組み合わさって，それぞれの疾患に特徴的な病態像が表われるのであろう。

妊娠中毒症は，妊娠後半期に高血圧，salt retention，蛋白尿，および浮腫などの症状が発生する疾患である（鈴木，1975；本多，石井，1983）。胎児発育遅延や胎児死亡をきたし，ときには母体死亡をもきたす，産科学上重要な疾患である。この重症型として，痙攣を伴う子癇が見られる。妊娠中毒症は病態論的には全身性の血管攣縮と，子宮と胎盤との間の血流量の減少という，2つの異常を呈する疾患であるが，その発生原因はまだ完全には明らかではない。妊娠中毒症では電解質の不均衡により，浮腫が生じることもあり，血液が濃縮して血液粘度が高値を示すこともある。子癇ではフィブリン血栓によって肝，腎，脳など各臓器の巣状壊死をきたす。子癇における肝壊死の発生機序としては，全身や局所の循環障害による血流の不均衡，アレルギー，毒性障害などが考えられる。

子癇における肝障害像としては，肝小葉周辺部の壊死像が知られているが，本研究では病変は必ずしも小葉周辺部だけではなかった。肝小葉中心部の障害が強いわけではないので，単に全身性の循環障害によるものだけではない。血栓等による局所の循環障害も考えられるが，それに対応する

明確な所見は得られなかった。肝に毒性に働く，何らかの要因の存在も考えられた。結論として，上記のごとくいくつかの要因が，病変発生の機序として関与することが推定される。肝細胞の結節性の再生性の変化は見られないので，肝病変は一次的な障害によると思われる。

ウイルス性肝炎では，急性障害像として肝細胞の壊死，ならびに再生像と胆管増生像が特徴的である(宇津田，1991)。これはB型肝炎ウイルスによる劇症肝炎でも，非A非B型ウイルス性劇症肝炎でも同様であった。肝炎ウイルスによる劇症肝炎における肝細胞の壊死の機序を考えるに，肝細胞の一様な変性と壊死およびリンパ球の著しい浸潤などにより，肝炎ウイルスの個々の肝細胞への直接の攻撃だけではなく，免疫学的機序もあることが推定される。このように残存肝細胞の再生結節が強い場合は，肝細胞は部分によって異なった異型度を示しながら，増殖しうることを示唆している。また肝細胞の結節性再生が強く長引くと，線維組織の増生と相まって，肝硬変になる可能性がある。

黄熱では，肝は主要な病変の場で，発症後数日は広範な肝細胞の脂肪変性をきたし，それ以後は肝細胞は，び漫性好酸性の変性および壊死に陥る(宇津田，1984)。肝細胞の障害が，ウイルスの直接的攻撃によることが推定される。ただし帯状の壊死が何を意味するのか，その発生機序は不明である。肝構築の破壊が見られるが，肝細胞の再生性の変化は見られない。やはり一次的障害機序によるものと考えられる。熱帯性食中毒の1つとして，アフラトキシンに代表されるマイコトキシンが，ヒト肝癌の原因となりうるか否かについて従来から論議されているが，その実態は不明である(Itakura，1982)。

アフラトキシン中毒症では病変が特徴的で，四塩化炭素による実験的障害に類似している。検索症例が剖検材料だけであるので，その後の推移が把握できないが，回復すればおそらく肝小葉中心性の線維症と，瘢痕化をきたすことであろう。肝小葉中心性の壊死は，循環障害よりも代謝毒性機序の問題であることも考えられる。肝小葉中心静脈の拡張が軽度で，しかも炎症性細胞浸潤が軽度であることは，間接的ではあるがこのことの推定の根拠となる。

本研究のまとめは以下のようである。1）熱帯地域に多い妊娠中毒症をはじめとした，急性肝障害をきたす各疾患の肝病変を病理形態学的に比較検討し，それらの特徴を把握した。2）特に妊娠中毒症は，熱帯地における発展途上国において，肝障害を惹起する重要な疾患であると考えられた。3）子癇では肝細胞の不規則な変性・壊死，ウイルス性肝炎では肝細胞の壊死と再生，黄熱では肝細胞の肝小葉における帯状壊死，アフラトキシン中毒症では肝小葉中心部の肝細胞の壊死という，それぞれ特徴ある肝障害像が見られた。すなわち，それらの惹起された肝小葉単位における障害像が，各種の病因によってそれぞれ特徴があることを明確にした。4）それら各種の急性の肝障害の形態像を病理学的に考察することにより，これらおのおのの急性肝障害をきたす要因は，病原体の直接の攻撃，免疫学的機序，毒性代謝障害，全身および肝内局所の循環障害など諸要因の単独，または組合せによるものであることを推定した。5）急性肝疾患の発生状況として，地理病理学的には興味ある点である。熱帯地におけるそれらの肝障害の直接的原因はそれぞれ存在するが，疾患発症の背景として多くの感染症，栄養状態，社会経済状態などの関与も考えられる。熱帯地域住民のこれらの諸条件が，肝障害の発生にどのように関与しているかは，今後の問題である。

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LIVER LESIONS AND STRUCTUAL ARRANGEMENT OF REMAINING HEPATIC CELL CORDS IN ECLAMPSIA AND OTHER ACUTE LIVER LESIONS IN THE TROPICS

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Histopathological findings of tropical acute liver diseases such as eclampsia, fulminant viral hepatitis, yellow fever, and aflatoxicosis are characteristic. In eclampsia, edema of liver tissue, sinusoidal dilatation and inflammatory exudate with Kupffer cell mobilization were seen. Liver cell cords were atrophic and showed irregular structures and pleomorphism of liver cell nuclei. Complicated and irregular pattern of degenerative or necrotic liver parenchyma in intermediate and outer zones of hepatic lobules were observed, while centrilobular areas were intact. Fulminant viral hepatitis showed irregular necrosis of liver parenchyma with inflammatory exudate and periportal bile duct proliferation. In contrast to other three diseases, lobular regenerative arrangements of remaining liver cell cords surrounded by necrotic or collapsed parenchyma were distinctive feature. Yellow fever showed zonal necrosis in intermediate zones of hepatic lobules. Centrilobular areas were relatively intact. Scattered acidophilic bodies of unicellular necrosis of liver cell were also seen in inconspicuous sinusoids. Inflammatory reaction of polymorphonuclear leukocytes was relatively slight. In aflatoxicosis, centrilobular necrotic changes of liver cells were prominent. Inflammatory exudate was slight. These results suggest that there are different kinds of etiological factors and mechanism to cause characteristic histological features of acute liver lesions in the tropics. Regenerative change is specific in viral hepatitis, while in other three diseases parenchymal lesions are primary changes.

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上気道におけるpyogenic granulomaの血管増生性病変：東アフリカ・ケニアにおける異型血管組織を示した症例を中心として

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はじめに

Pyogenic granuloma (granuloma pyogenicum, hemangioma of granulation tissue type) (PG) は，皮膚や粘膜の毛細血管腫のポリープ状の病変であると考えられており，径数mmから数cmに達する。PGは歯齦，指，口唇，顔面，舌などに多く，しばしば潰瘍を形成し，炎症性細胞浸潤や基質の浮腫を伴う肉芽組織を生じる。PGを構成する血管内皮細胞や，基質の線維芽細胞のmitosisが見られることがある。またPGの毛細血管の増生像は，それに伴う感染性病変によって修飾され，しばしば複雑な組織像を呈することがある。さらに増生する血管組織が，多少の異型性を帯びることもある。

本研究では，口腔および上気道におけるPGの血管組織増生像に着目し，増生した血管成分の異型性について病理組織学的に検討した。特に赤道東アフリカで見られた上気道のPG類似の病変で，病巣の表層部における炎症による肉芽性毛細血管の増生と，深層部における異型性を帯びた血管組織の増生を併せ持った症例を中心に検索した。また参考症例として，軟部組織におけるほかの血管増生性病変，すなわち血管肉腫(angiosarcoma)や非特異的肉芽組織 (non-specific granulation tissue)などと比較検討した。さらに赤道アフリカで散見される風土病の1つである，Kaposi肉腫 (Kaposi's sarcoma) の血管増生性の病変も予備的に参考症例として用いた。

材料と方法

症例：東アフリカ・ケニアにおいて見られた咽頭部に生じた限局的血管増生性の病変の2例(Case 1およびCase 2) (何れも中年男性)，および比較検討材料としておのおの約10例のPG (上気道，口腔粘膜，一部頸部および指の皮膚)，血管肉腫(頭部および軀幹の皮膚)，Kaposi肉腫 (四肢の皮膚)，および非特異的肉芽組織(四肢の皮膚および口腔粘膜) を用いた。PG以下の各症例の患者は何れも中～高年男子で，病理組織材料はアメリカ合衆国および日本において収集したものであるが，Kaposi肉腫はケニア人の症例である。

病理組織学的ならびに組織化学的検索：ヘマトキシリン・エオジン染色，鍍銀染色，Mallory膠原線維染色，periodic acid-Schiff (PAS) 反応を用いた。

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結　果

各疾患の病理組織学的所見，すなわち増殖細胞の増生像（growing pattern），内皮細胞の異型度（atypia），血管組織像の強弱（vascular proliferation），間質における線維組織（fibrous tissue），炎症性細胞浸潤（inflammatory exudate）は表1に示した。

Case 1およびCase 2：この2例は以下の所見により，結果的にはPGの1型と考えられた症例である。病巣は何れも径5 mm～10 mmである。増生する血管組織の異型度（細胞の多形性，大小不同性，核の多形性，核の異常染色性，異常あるいは高頻度の核分裂像など）について注目し，以下のごとくの結果を得た。病巣の表層部は潰瘍化しており，著しい炎症性細胞浸潤とともに，毛細血管の新生や増生が見られる。これらの毛細血管の細胞の異型性はほとんどない。すなわちこの血管組織は，感染に伴う炎症性の肉芽性毛細血管であると考えられる（図1，2）。病巣の中層部では，通常のPGとほぼ同じ程度の異型度を示す血管組織が増生している（図3－5）。病巣の基底部（深層部）では内皮細胞の腫大と増生が著しく，血管内腔に詰まったように増生し，内腔をかなり閉塞したような組織像を呈していることが特徴的である。この部分の血管組織は腫瘍性の毛細血管と考えられる（図6－10）。すなわち本症例群では，血管組織は異型度の点から見て3層に分かれており，表層部は非特異的な肉芽組織における毛細血管より成り，中間層はいわゆるPGと同程度の細胞異型性，ならびに構造異型性を示す血管組織より成り，深層部は細胞異型性および構造異型性がやや強い組織より成り立っていた。

PG：毛細血管腫が基本的組織像であるが，血管内皮細胞にはごく軽度の異型性が見られる（図11－13）。PGの表層部に感染が起これば非特異的

Table 1　Comparative histological findings of vascular and related soft tissue diseases

Disease	Growing pattern	Atypia of endothelial cells	Proliferation of vascular tissue	Fibrous tissue	Inflammatory exudate
granuloma pyogenicum	capillary hemangiomatous, lobular arrangement	+	++++	++	+++
angiosarcoma	highly irregular vascular spaces	+++++	+++++	+	−
Kaposi's sarcoma	irregular vascular spaces	++	+++	++	+
non-specific granulation tissue	regular and irregular	−	++	++++	+++++
Case 1	moderately irregular, lobular arrangement	++	++	++	+++
Case 2	moderately irregular	+	++	++	+

(−); negative～(+++++); strongest

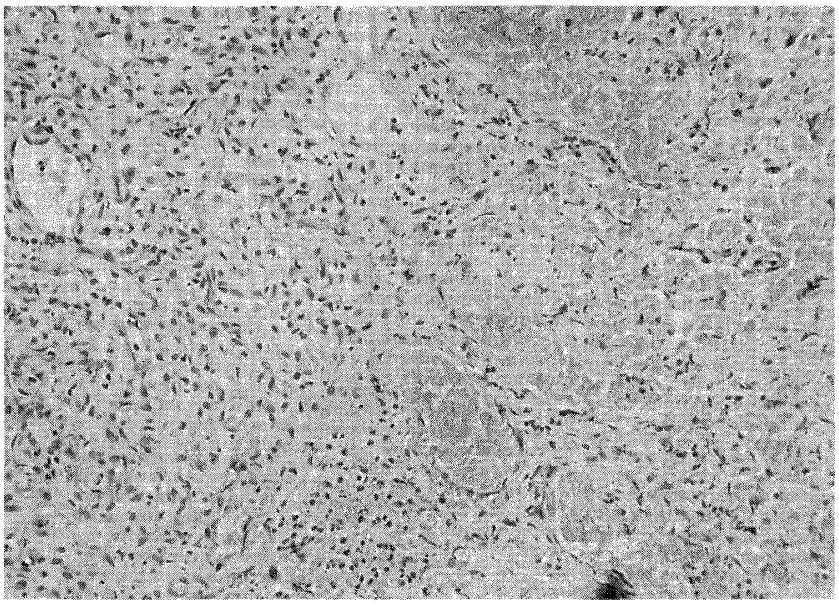

Figure 1 Case 1. Non-specific granulation tissue of overlying surface and superficial part (on the right) of tumorous lesion of the pharynx. Hemangiomatous features (on the left) of deep part of the same lesion. Granulation tissue is consisting of sparse capillary structures with hemorrhage and inflammatory exudate. Hemangiomatous lesions are consisting of irregular vascular structures. (Hematoxylin and eosin stain. Original magnification; ×100)

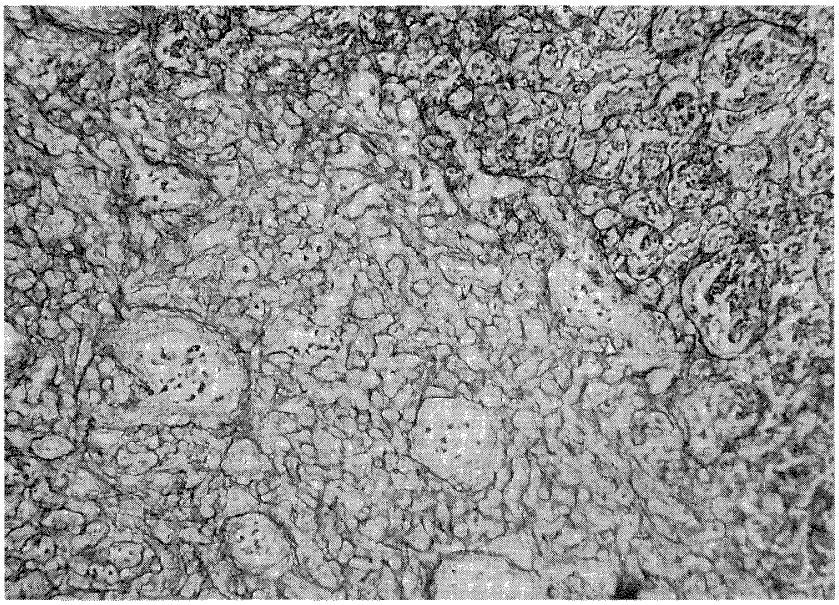

Figure 2 Case 1. Silver impregnation of same area as Figure 1. Simple and rather regular capillary structures with flattened mature endothelium of superficial part of the lesion (on the right). Basement membranes are clear and definite in the granulation tissue. Irregular vascular structures with plump endothelial cells surrounded by basal lamina in hemangiomatous part (on the left). (Original magnification; ×100)

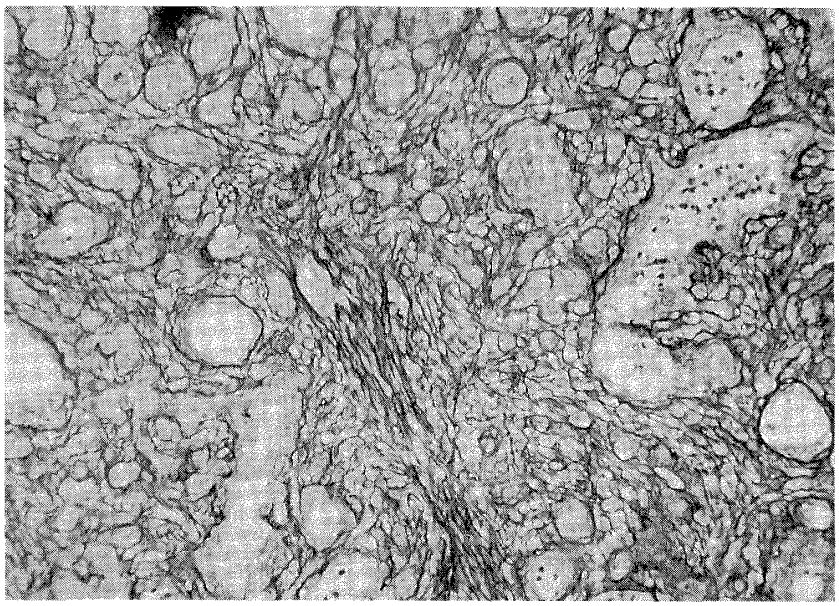

Figure 3 Case 1. Complicated vascular proliferation with mature and immature capillary vessels in hemangiomatous lesions showing structural atypia. (Silver impregnation. Original magnification; ×100)

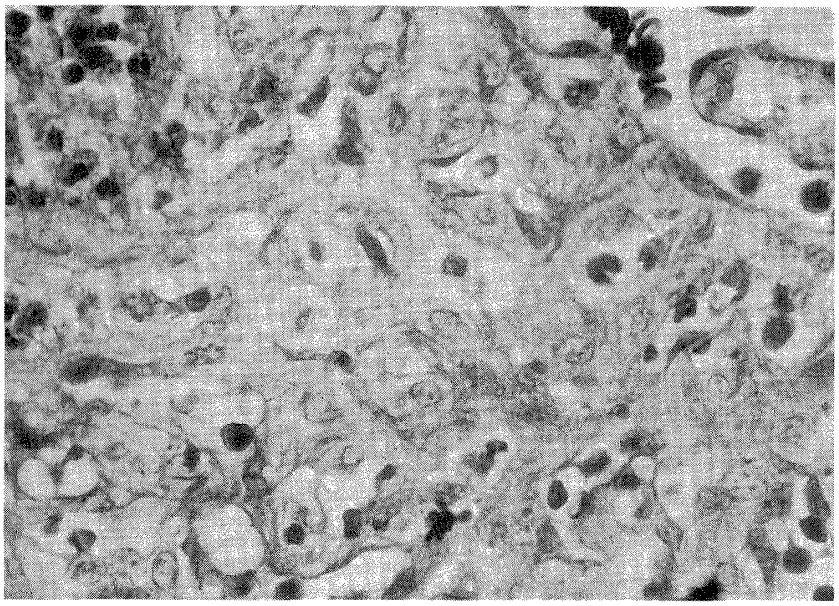

Figure 4 Case 1. Hemangiomatous parts composed of plump endothelial cells. (Hematoxylin and eosin stain. Original magnification; ×400)

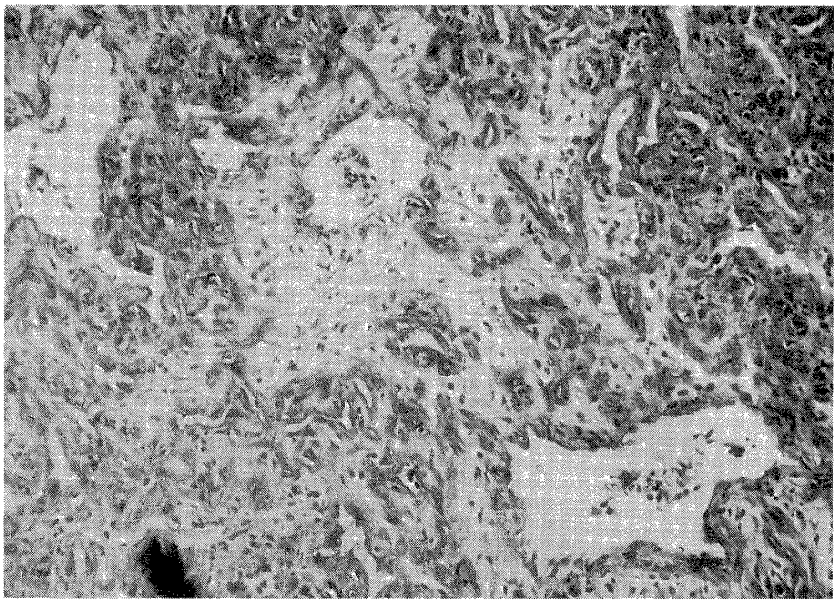

Figure 5 Case 1. Mallory's method for collagen fibers shows sparse fine collagen fibers among vascular lumina. (Original magnification; ×100)

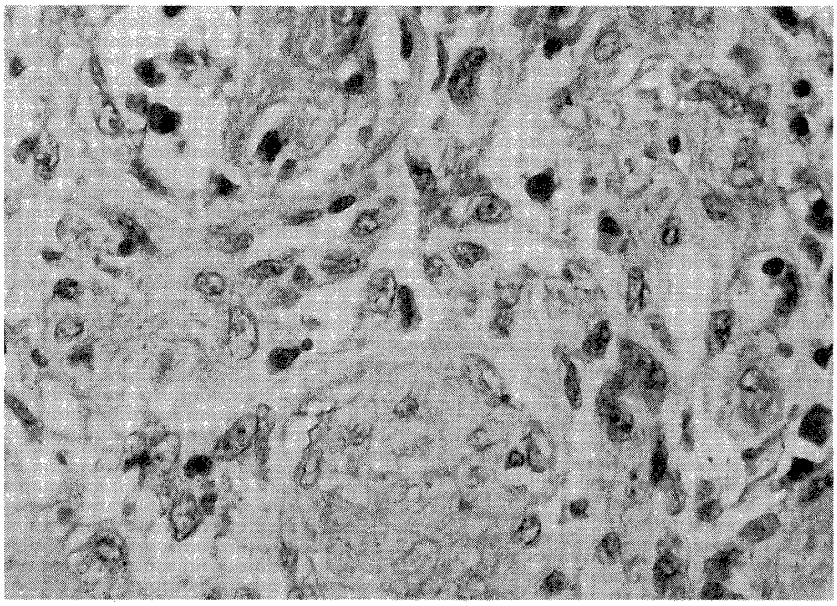

Figure 6 Case 1. Characteristic proliferation of prominent endothelial cells showing glomerular-like formation. (periodic acid-Schiff reaction. Original magnification; ×400)

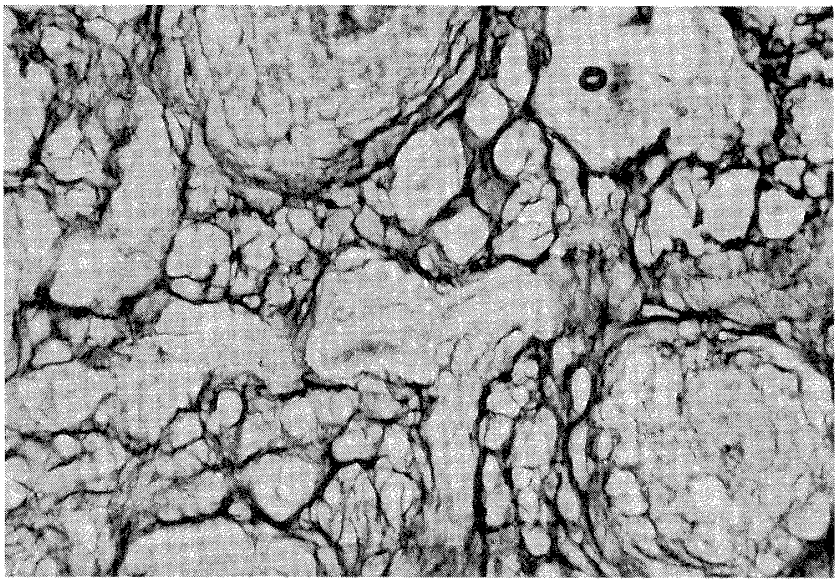

Figure 7 Case 1. Silver impregnation of same area as Figure 4. Glomerular-like formation contained a greater complement of endothelial cells, probably to line vascular lumina and eclipsing lumen. (Original magnification; ×400)

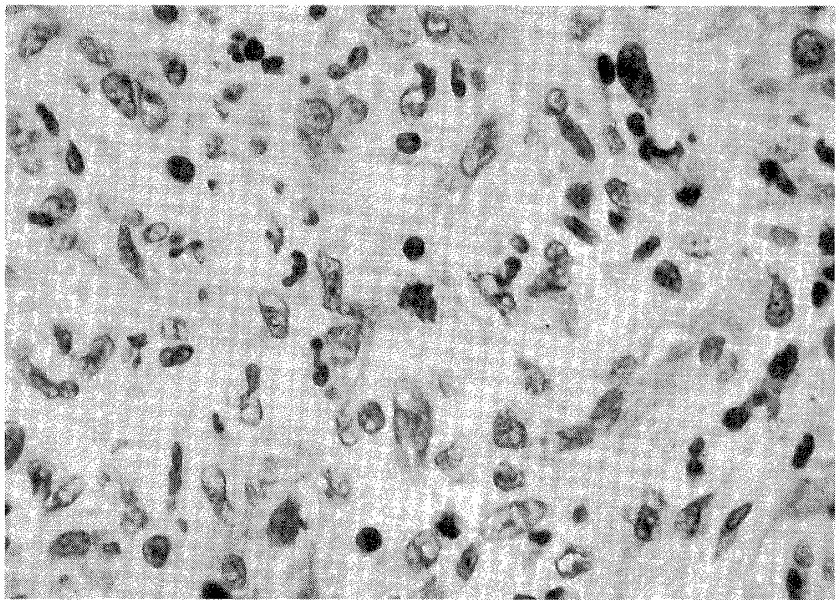

Figure 8 Case 1. Irregular proliferation of endothelial cells with mitosis is characteristic growing pattern in some parts of hemangiomatous lesion. Luminal formation is inconspicuous and suggests atypical proliferation of endothelial cells. (Hematoxylin and eosin stain. Original magnification; ×400)

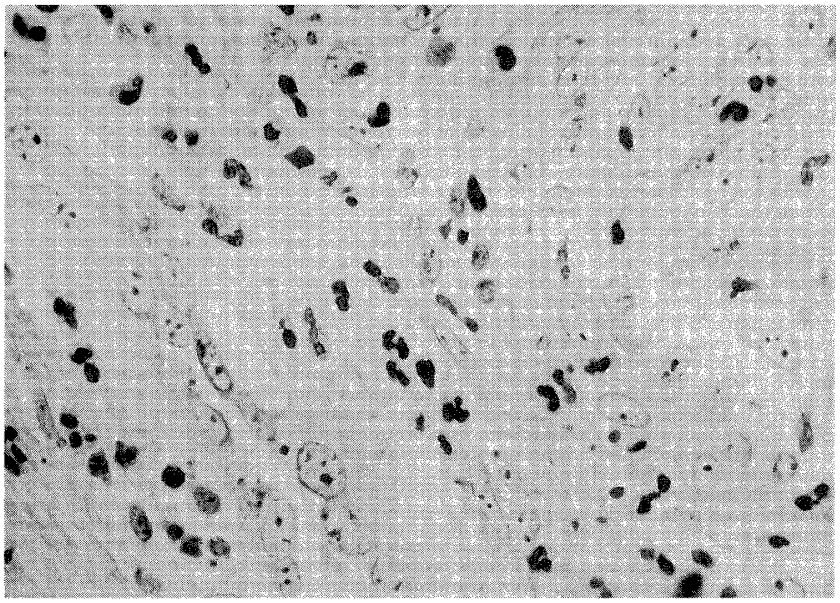

Figure 9 Case 1. Basal lamina are inconspicuous in cleft-like vascular lumina in which a number of irregular shaped endothelial cells. (Hematoxylin and eosin stain. Original magnification; ×400)

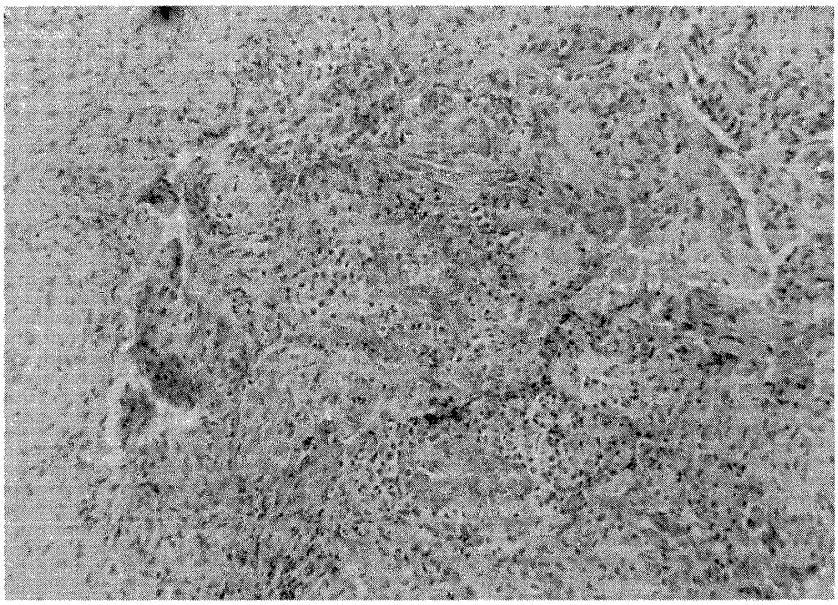

Figure 10 Case 2. Pharyngeal tumor consists of compact proliferation of hemangiomatous vascular tissue and congeries of smaller vessels comprising with fibrous broad septa. Inflammatory reaction of polymorphonuclear leukocytes is relatively slight. (Hematoxylin and eosin stain. Original magnification; ×100)

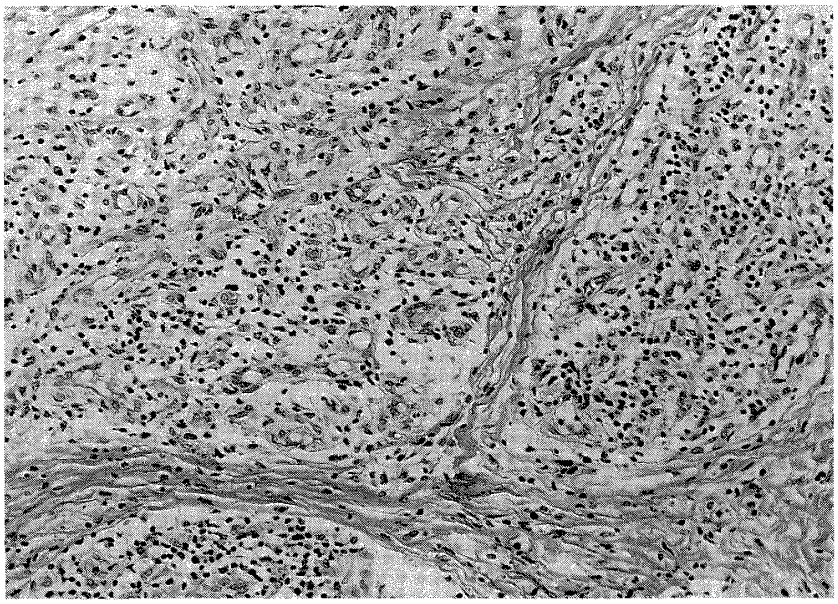

Figure 11 Granuloma pyogenicum. In contrast to Case 1 and 2, lesions show preservation of the vague lobular arrangements of vessels surrounded by loose myxoid zone. (Hematoxylin and eosin stain. Original magnification; ×100)

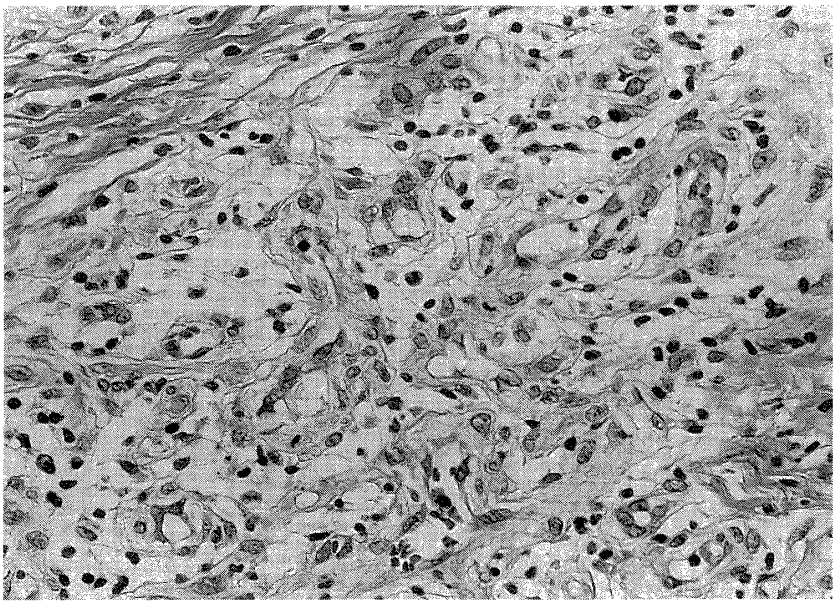

Figure 12 Granuloma pyogenicum. Vascular cavities are relatively sparse. Collagen fibers are admixed with inflammatory elements. (Hematoxylin and eosin stain. Original magnification; ×200)

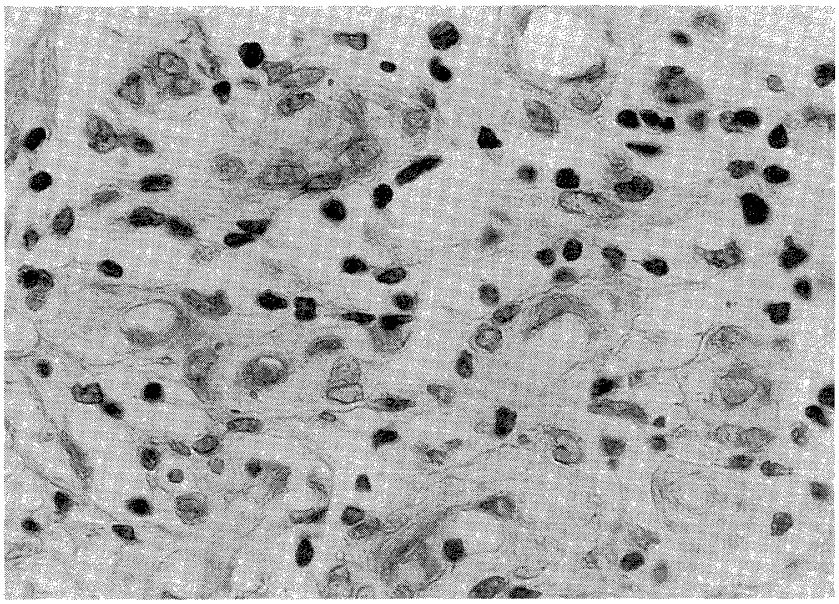

Figure 13 Granuloma pyogenicum. Vascular endothelial cells are plump. However, cellular atypia is less marked than Case 1. Number of mitosis is quite small. (Hematoxylin and eosin stain. Original magnification; ×400)

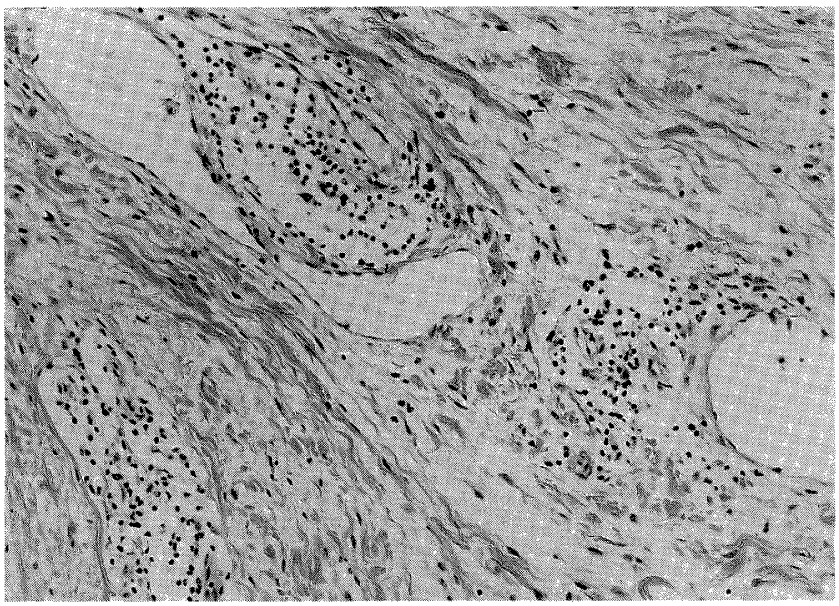

Figure 14 Granuloma pyogenicum. Dilatation of lymphatic vessels adjacent to foci of granuloma pyogenicum suggests lymphostasis in surrounding tissue. (Hematoxylin and eosin stain. Original magnification; ×100)

な肉芽組織が生じるが，その毛細血管には異型性は見られない。周囲組織にはリンパの鬱滞が見られた（図14)。

皮膚の血管肉腫：本研究において検索した疾患群のうちもっとも高度で，しかも種々の異型度を示す血管内皮細胞から成っていた。増殖した腫瘍細胞は結合組織を貫き，不規則な管腔を形成しながら周囲へ浸潤していた。頭皮に生じた症例では肺に転移していた。

皮膚の Kaposi 肉腫：典型例では，毛細血管組織と紡錘形細胞の増生が見られた。血管内皮細胞の異型度は，血管肉腫よりは軽度であるが，PGよりは強かった。

非特異的肉芽組織：肉芽性毛細血管の増生が，主体である。血管組織の構造は通常，一層の血管内皮細胞によって成り立っており，また異型性はない。

考案と総括

軟部組織における，各種血管増殖性病変における毛細血管増生のあり方，特に細胞異型性ならびに構造異型性について，病理組織学的に比較検討した。

PGにおける血管内皮細胞は軽度の異型性を示したが，基本的には毛細血管腫であった。上気道の非上皮性腫瘍に関して臨床病理学的に研究されているが（Fu and Perzin, 1974)，上気道におけるPGの基礎病変としては lobular capillary hemangioma であり，また再発率は低いとされている。しかしPGはよく切除しなかったり，また保存療法後の一部の症例では再発する。ただし浸潤性の病変は見られないので，血管肉腫とは異なる。一方，妊娠中に本病変の1型である granuloma gravidarum が主として歯齦に発生することが知られている。多くは出産とともに消退するので，ホルモン感受性を示唆する。つまり自律性の病変の証拠を欠いているので，腫瘍性の性格がやや希薄である。PGの発生状況として地理病理学的には興味ある点であるが，感染を生じやすい熱帯地域では多いものと思われる。原因論については，本研究の範囲では十分に考察できなかった。なお関連病変として毛細血管腫（単純血管腫）の場合は増生する血管組織が，一ないし数層の血管内皮細胞によって覆われている。異型度はきわめて軽度で，また基底膜は部分的に肥厚しているが概して非薄である。ケニアにおける上気道のPGの症例では，増生した血管組織を観察すると，同一の病巣の中でも部分によってかなり異型度において相異（軽重）が見られた。地理病理学的に地方病として存在する Kaposi 肉腫との鑑別が必要であったが，血管組織の異型度が軽いことと，介在する紡錘形細胞の増生が見られないことから，同疾患とは異なるものであった。本症例の位置付けとしては，基本的にはPG様の病変であり，一方ではより異型性を示す腫瘍病変となり，また一方では感染による非特異的肉芽組織へと生長した病変であると思われた。なお Kaposi 肉腫でも何らかの非特異的感染を起こすと，肉芽組織が生じる可能性もある。

一般に血管肉腫では，腫瘍細胞の異型度は多彩である。脾臓原発の血管内皮腫では，組織学的に増生細胞の異型度が軽く，良性か悪性か不明のこともある（北条ら，1967)。また hemangioendothelioma は異型度が比較的低く，良性と悪性の中間に存在すると考えられている（Weiss and Enzinger, 1986; Enzinger and Weiss, 1988)。鼻腔内血管関連腫瘍では，hemangiopericytoma に類似した腫瘍も報告されている（Compagno and Hyams, 1976)。本研究における検索例では，血管肉腫が他の疾患に比べ最も強い異型度を示した。

通常の感染性肉芽組織，すなわち非特異的肉芽組織では異型性がない毛細血管を生じるので，他の血管増生性病変を見る上での対照群として用いることができる。

以上のことは，1）軟部組織における血管増生病変は，それぞれその疾患に応じた特徴ある異型性を示すものであること，2）上気道におけるPGの病変にも見られるように炎症など繰り返される刺激によって，血管内皮細胞は同一病巣内でも部分によって異なった異型度を示しながら，増殖しうることを示唆している。

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HISTOPATHOLOGY OF ATYPICAL VASULAR PROLIFERATION OF PYOGENIC GRANULOMA OF THE UPPER RESPIRATORY TRACT: KENYAN AND OTHER CASES

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Pyogenic granuloma (PG) is polypoid lesion of cutaneous or mucosal tissue composed of lobular capillary hemangioma. Affected sites of the lesion should be gingiva, fingers, lips, face and tongue in descending order of frequency. Not rarely ulcerous lesions accompany PG. Although cellular atypia is not remarkable, it recur occasionally when the surgical or conservative treatment is not perfect. In this work, we studied cellular atypia of endothelial cells of PG of the upper respiratory tract of Kenyan patients, and histologically compared with other vascular proliferative lesions of soft tissue such as angiosarcoma, Kaposi's sarcoma and non-specific granulation tissue. A wide variety of cellular atypia was observed. The results suggested that there could be atypical transformation of proliferative endothelial cells of PG of the upper respiratory tract of the patients in such areas as repeated infection could occur.

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GEOPATHOLOGY OF ENDEMIC PEDIATRIC LYMPH NODE KAPOSI'S SARCOMA IN WESTERN KENYA

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Abstract: We conducted an epidemiological and histological analysis of the endemic lymph node-type Kaposi's sarcoma (KS) in African children (under 16 years old) in Western Kenya in order to determine the ethno-geographical distribution of the disease and to clarify its histological features and histogenesis during the 12-year period between 1979 to 1990. The age distribution of all endemic type KS in Western Kenya showed two age peaks; one in early childhood and the other in middle to advanced age. Most endemic KS in children initially occurred in the lymph nodes, while that of people of middle to advanced age showed a primary lesion in the skin. The male to female ratio of the endemic KS was 3.1 to 1 (in all pediatric types), 3.4 to 1 (in the pediatric lymph node-type) and 10.8 to 1 (in all adult types). A high incidence of the lymph node-type KS in children was observed in the Luo group ethnically and in Nyanza Province around Lake Victoria geographically. The lymph node-type KS originated at the paracortical areas and gradually grew along the reticulin network originating from the trabeculae. The lesion of KS histologically consisted of several types of cells, especially spindle-shaped cells, macrophage-like cells and immature endothelial cell-like cells and was accompanied by almost normal small blood vessels, lymphatic vessels and postcapillary venules. No abnormal mitoses were observed in any of the cells. There were no primary necroses due to tumor proliferation and also no extracapsular invasions. Immunohistochemically, spindle-shaped cells, immature endothelial cell-like cells and mature endothelial cells were positive for Vimentin, but only mature endothelial cells were positive for Factor-VIIIRa and UEA-1. Macrophage-like cells were positive for Factor-XIIIRa. These findings suggested that: 1) there are certain differences in the etiological co-factors of KS between the endemic lymph node-type KS in children and the endemic cutaneous type KS in adults, 2) KS cells originate from pluripotent mesenchymal cells and 3) KS might not be a malignant tumor, but rather a benign neoplasm, tumor-like lesion or reactive hyperplasia.

INTRODUCTION

Kaposi's sarcoma (KS) was first described by Kaposi in 1872 as an "Idiopathic multiple pigmented sarcoma of the skin". Since then, it has been considered a specific neoplasm which occurs in the skin of elderly men, mainly among people of Jewish origins in Eastern Europe and the inhabitants of the Mediterranean basin. The first patient with KS in African continent was reported by Jojot and Laigret (1922) from Cameroon. It is now a well

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recognized fact that KS is more prevalent in Equatorial Africa than in any other part of the world (Oettle, 1962).

KS can be divided broadly into four types; the classical (European) type, the endemic (African) type, the epidemic (Acquired immunodeficieny syndrome-related) type and the type associated with immunosuppressive therapy. However, there are certain differences among the four types of KS with regard to sex ratio, age distribution, macroscopic findings, histologic findings and biological behavior (Safai, 1985; Gottlieb and Ackerman, 1988).

Pediatric cases of KS are uncommon, except in the African endemic type. According to the published literatures, the majority of pediatric cases of KS in Equatorial Africa initially occurred in the lymph node and often showed a generalized lymphadenopathy (Dutz and Stout, 1960; Davies and Lothe, 1962; Slavin *et al.*, 1970; Olweny *et al.*, 1976; Owor, 1977; Molyneux, 1979; Toriyama *et al.*, 1987a, b). However, no epidemiological and histological analysis of the lymph node-type KS in African children has ever been published.

Previous reports stated that KS is derived from vascular endothelial cell (Rutgers *et al.*, 1986; Hashimoto *et al.*, 1987), lymphatic endothelial cell (Russelljones *et al.*, 1986; Beckstead *et al.*, 1985; Dictor, 1986), Schwann cell (Pepler, 1959), mesenchymal cell (Harrison and Kahn, 1978) or fibroblast (Mottaz and Zelickson, 1966; Nickoloff and Griffiths, 1989). However, the cell origin of KS remains unknown.

Many hypotheses have been raised about the nature of KS, for example that it is a malignant tumor (Master *et al.*, 1970; Taylor *et al.*, 1971), tumor with low-grade malignancy, tumor-like lesion or reversible hyperplasia (Brooks, 1986; Mirra, 1986), but no conclusion has been reached.

We studied the lymph node-type KS in children in Western Kenya to elucidate its ethnogeographical distribution and to determine its histological features and histogenesis.

Table 1 Dilution ratio of primary antibodies

Primary antibodies	Animal	Dilution	Pre-digestion†	Sources
Factor-VIIIRa	rabbit/poly	1:200	+	DAKO
Factor-XIIIRa	rabbit/poly	1:150		BEHRING
Vimentin	mouse/mono	1:25		DAKO
Actin	mouse/mono	1:100	+	S.K.
Desmin	mouse/mono	1:100		DAKO
ACT	rabbit/poly	1:300	+	DAKO
CD35	mouse/mono	1:20	+	DAKO
S-100	rabbit/poly	1:400		DAKO
UEA-1*	rabbit/poly	1:200		E-Y

DAKO: DAKOPATTS, Copenhagen, Denmark. Behring: Behringwerke AG, Marburg, Germany. S.K: Seikagaku Kogyo Co. Ltd., Tokyo, Japan. E-Y: E-Y Laboratories, Inc., San Mateo, CA, USA. Avidin-biotin peroxidase complex were obtained from Vector Laboratories: Vectastain ABC Kit, Burlingame, CA, USA.

* Peroxidase-conjugated rabbit immunoglobulins to UEA-1.

† Incubated with trypsin in phosphate-buffered saline at 37°C for 5 min.

MATERIALS AND METHODS

Twenty-two cases of the lymph node-type KS in children under 16 years old were selected from 185 cases histologically diagnosed as KS. This study was carried out in three provinces, that is, Western, Nyanza and Rift Valley Province, in the Western part of the Republic of Kenya, East Africa during the 12-year period between 1979 and 1990. Clinical data and epidemiological information were recorded as accurately as possible with reference to age, sex, ethnic group and habitant place. The specimens were examined histologically and immunohistochemically. Specimens of the cutaneous type KS and the lymph node-type KS in adults were used as controls.

After fixation in formalin and embedding in paraffin, the specimens were cut in 4 μm-thick slices. In addition to routine staining with hematoxylin and eosin (HE), they were subjected to periodic acid-Schiff (PAS), Azan-Mallory, reticulin, elastica van Gieson (EVG), and mucicarmine stains. For immunohistochemical staining, twelve selected cases of pediatric lymph node-type KS were used and Factor-VIIIRa, Factor-XIIIRa, Vimentin, Actin, Desmin, Alpha-1-antichymotrypsin (ACT), CD-35 and S-100 were used as primary antibodies at the dilution ratio shown in Table 1 and by the avidin biotin peroxidase complex (ABC) technique (Hsu *et al.*, 1981). Lectin binding with Ulex europaeus agglutinin 1 (UEA-1) was also performed.

RESULTS

Epidemiological results:

Figure 1 and Table 2 describe the age distribution of the lymph node-type KS and the cutaneous type KS in Western Kenya. There were two peaks in the age distribution of KS;

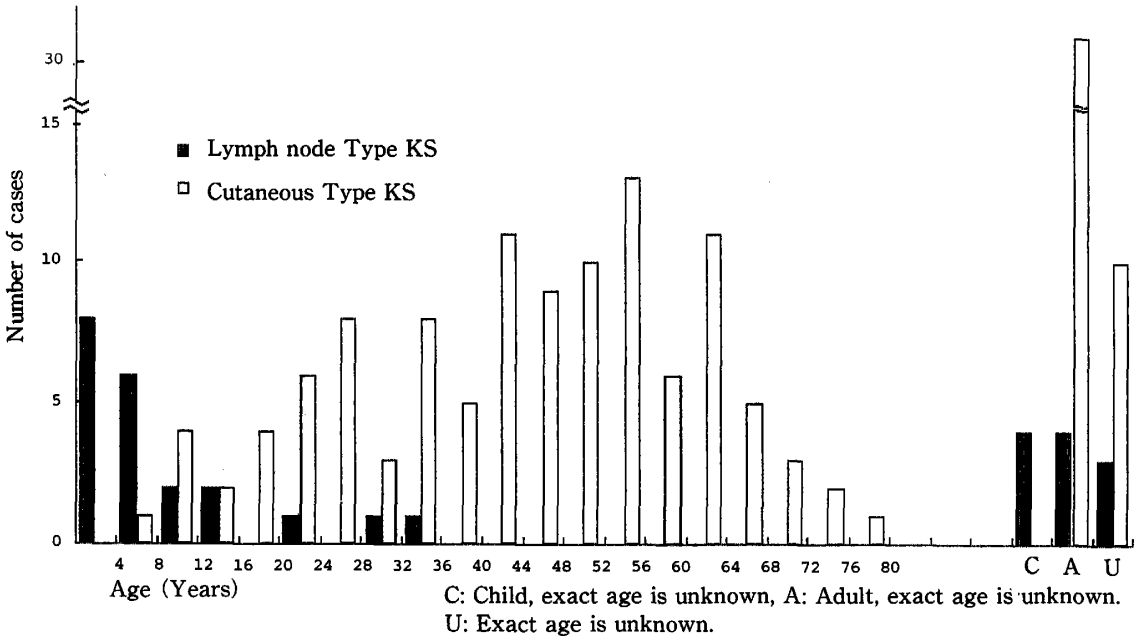

Figure 1 Age distribution of endemic lymph node-type and cutaneous type Kaposi's sarcoma.

Table 2 Lymph node-type Kaposi's sarcoma in children

Case	Age	Sex	Site of lesion	Ethnic group	District	Province
1	1	M	Inguinal lymph node	Luhya	Busia	Western
2	1y6m	M	Generalized lymph nodes	Luo	South Nyanza	Nyanza
3	1y6m	M	Unknown lymph node	Luo	Kisumu	Nyanza
4	1y8m	M	Generalized lymph nodes	Luo	Kisumu	Nyanza
5	1y9m	M	Generalized lymph nodes	Luhya	Kakamega	Western
6	1y9m	M	Generalized lymph nodes	Luo	Siaya	Nyanza
7	2y6m	M	Generalized lymph nodes	Luhya	Kisumu	Nyanza
8	3	M	Generalized lymph nodes	Luhya	Kakamega	Western
9	4	F	Unknown lymph node	Luo	South Nyanza	Nyanza
10	4	M	Generalized lymph nodes	Luo	Nakuru	Rift Valley
11	4	M	Generalized lymph nodes	Luo	?	?
12	5	F	Generalized lymph nodes	Luo	South Nyanza	Nyanza
13	6	M	Generalized lymph nodes	Luo	Kisumu	Nyanza
14	7	M	Generalized lymph nodes	Luo	Kakamega	Western
15	8	M	Elbow lymph node	Kisii	Kisii	Nyanza
16	10	F	Unknown lymph node	Luhya	Kakamega	Western
17	12	M	Generalized lymph nodes	Luo	Kisumu	Nyanza
18	12	M	Cervical lymph node	Luo	Kisumu	Nyanza
19	Child*	M	Generalized lymph nodes	Luo	Kisumu	Nyanza
20	Child*	M	Unknown lymph node	Luo	Kisumu	Nyanza
21	Child*	F	Unknown lymph node	Luo	Kisumu	Nyanza
22	Child*	F	Unknown lymph node	Luo	Kisumu	Nyanza

*Exact age is unknown (under 16 years old).

Table 3 Age and sex distribution of 185 cases of Kaposi's sarcoma

Age group	In lymph node			Other lesions			Total
	Male	Female	Unknown	Male	Female	Unknown	
0-15	15	3	0	5	2	0	25
Child*	2	2	0	0	0	0	4
subtotal	17	5	0	5	2	0	29
Over 16	3	0	0	98	7	0	108
Adult†	4	0	0	24	5	2	35
subtotal	7	0	0	122	12	2	143
Unknown‡	2	1	0	9	1	0	13
Total	26	6	0	136	15	2	185

*Exact age is unknown (under 16 years old).
†Exact age is unknown (over 16 years old).
‡Age is unknown.

childhood and middle to advanced age. Although 17% (32/185) of all KS patients had lymph node lesions, 76% (22/29) of the pediatric type KS showed primary lesions in the lymph nodes and 59% (13/22) of the lymph node-type KS in children showed generalized lymph node involvement without any skin lesions.

Table 3 describes the sex distribution of the endemic KS in Western Kenya. The male to female ratio of KS was 3.1 to 1 (in all pediatric types), 10.8 to 1 (in all adult types) and 3.4 to 1 (in the pediatric lymph node-type).

A high incidence of the lymph node-type KS in children was observed in the Luo group ethnically and Nyanza province around Lake Victoria geographically.

Histological results:

The early stage of KS, that is, initial focus localized in an infinitesimally small part of the lymph node, revealed that KS originated at a site near the paracortical area, gradually growing toward the subcapsular sinus along the reticulin network from the trabeculae (Photo. 1). The center of the lesion consisted mainly of spindle-shaped cells, while the marginal sites consisted of immature blood or lymphatic vessel-like structures. Until the late stage when KS occupied most of the lymph node, lymph follicles remained at the marginal sites and were slightly compressed and atrophic (Photo. 2). Finally, the lymph node was completely replaced by KS cells, but there were no extracapsular invasions. In the medullary area of lymph node, there was only a small number of spindle-shaped cells with marked dilatation of blood and lymphatic vessels. Infiltration of plasma cell was slight (Photo. 3).

Histologically the KS lesions consisted of several types of cells, especially spindle-shaped cells, macrophage-like cells and immature endothelial cell-like cells and were accompanied by almost normal small blood vessels, lymphatic vessels and postcapillary venules.

The spindle-shaped cells in the lymph node-type KS had more round nuclei than those in the cutaneous type KS, and had long, thin, eosinophilic and slightly wavy cytoplasm. They showed an interlacing bundle pattern. There were slit-like structures containing erythrocytes among some spindle-shaped cells, which were indicative of an immature vascular structure. However, the distinct formation of vascular basement membrane and communication with other vascular spaces were obscure. These spindle-shaped cells showed various sized compact nodules, and argyrophil fibers developed extensively around them (Photo. 4). These spindle-shaped cells might have the ability to produce collagen fiber thereafter.

The macrophage-like cells with relatively clear and abundant cytoplasm and round nuclei showed phagocytic activity because of cell debris in the cytoplasm. There were numerous macrophage-like cells interposed among the spindle-shaped cells, creating a starry sky appearance (Photo. 5).

Immature endothelial cell-like cells with hyperchromatic and slightly small plump nuclei showed a hob-nail structure in the slit-like lumens. In several fields, some of the immature endothelial cell-like cells showed a transformation to spindle-shaped cells.

In marginal sites of the lesion, there was a proliferation of blood vessels, lymphatic vessels and postcapillary venules with relatively tall endothelial cells (Photo. 6).

Mitotic figures were observed only in spindle-shaped cells and macrophage-like cells; the number of mitotic figures was 2-5 per each high power field (×200). No abnormal mitoses were observed in any of the KS cells.

Although there were secondary necroses due to hemorrhage from the thin-walled dilated blood vessels in several cases, there were no primary necroses due to tumor proliferation.

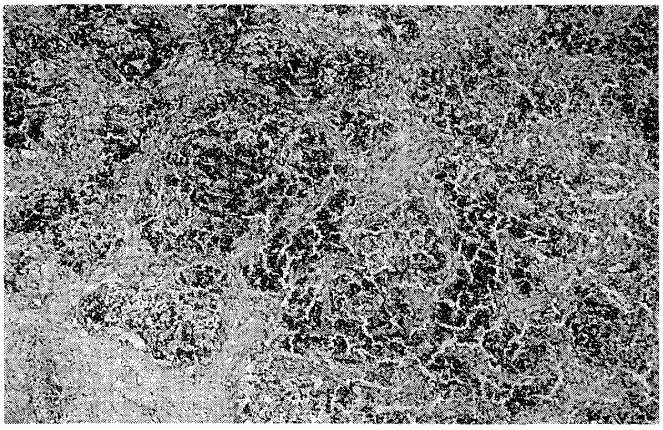

Photo. 1 KS cells proliferate along the reticulin network which originated from the trabeculae of lymph node (H.E. original magnification, ×40).

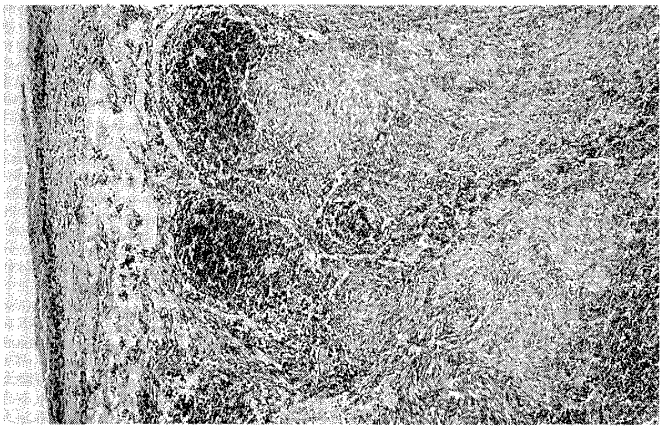

Photo. 2 KS cells proliferate in the paracortical area (in center) and lymph follicles are compressed by KS cells (in left side). (H.E. Original magnification, ×40).

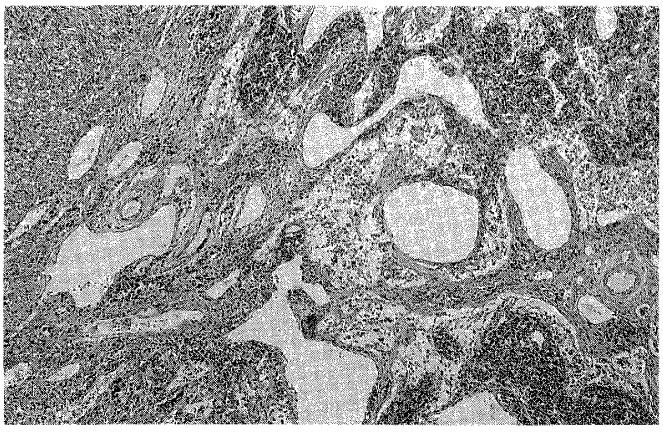

Photo. 3 A small number of spindle-shaped cells in the medullary area with marked dilatation of blood and lymphatic vessels (H.E. original magnification, ×40).

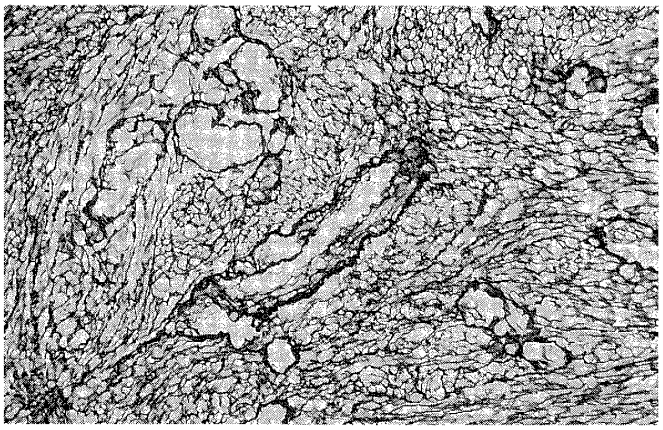

Photo. 4 Argyrophil fibers prolong around spindle-shaped cells, without distinct formation of vascular basement membrane and communication with other vascular spaces (Reticulin stain, original magnification, ×100).

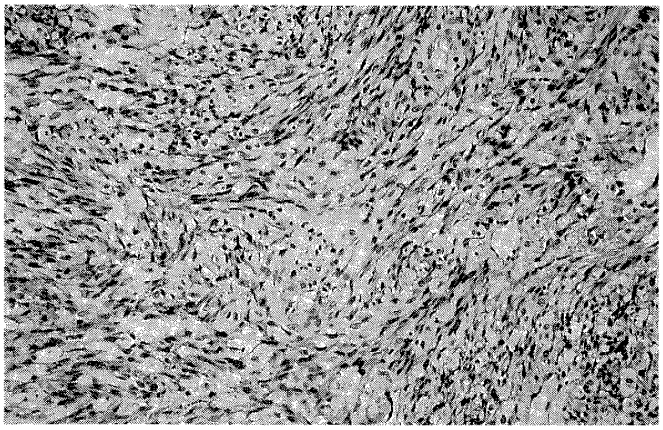

Photo. 5 Macrophage-like cells which having clear and abundant cytoplasms with phagocytic activity interpose among spindle-shaped cells (H.E. original magnification, ×100).

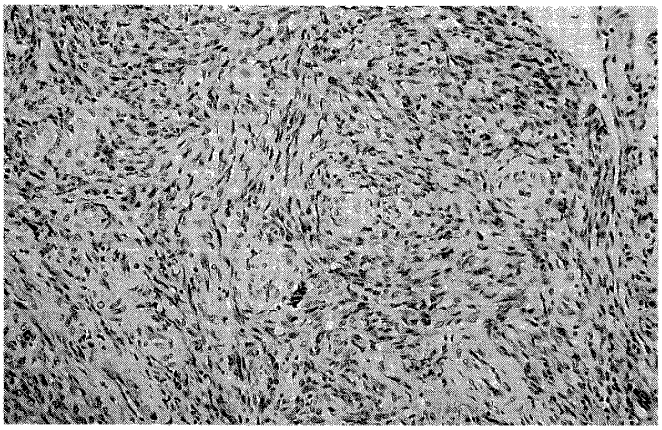

Photo. 6 Postcapillary venules which having relatively tall endothelial cells interpose among spindle-shaped cells (H.E. original magnification, ×100).

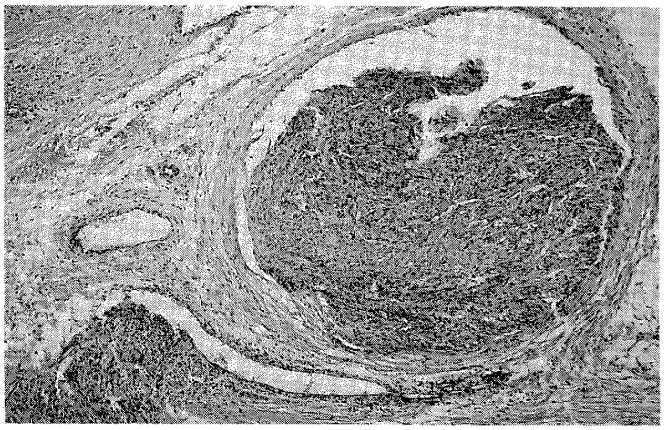

Photo. 7 Marked proliferation of endothelial cells in blood and/or lymphatic vessels adjacent to a lymph node, resembles intravascular papillary endothelial hyperplasia (H.E. original magnification, ×40).

Photo. 8 Vimentin is strongly positive in spindle-shaped cells and endothelial cells but is negative in macrophage-like cells (ABC technique. original magnification, ×100).

The characteristic findings were papillary proliferation of KS cells in the blood vessels and/or lymphatic vessels adjacent to the lymph node (Photo. 7). In the proliferative cells of this lesion, there were no cellular atypia or mitotic figures.

In the immunohistochemical examination, spindle-shaped cells, immature endothelial cell-like cells and mature endothelial cells were positive for Vimentin (Photo. 8), but only mature endothelial cells were positive for Factor-VIIIRa and UEA-1. Macrophage-like cells were positive for Factor-VIIIRa. All types of KS cells were negative for Desmin, Actin, S-100, CD-35 and ACT (Table 4).

Discussion

Our epidemiological results and several reports showed that the African endemic-type KS is characterized by its occurrence in two age peaks; one in early childhood and the other

Table 4 Immunohistochemical results

Primary antibodies	Cell types					
	SC	MLC	IEC	PCV	LV	BV
F-VIIIRa	−	−	−	+	+	+
F-XIIIRa	−	+	−	−	−	−
Vimentin	+	−	+	+	+	+
Actin	−	−	−	−	−	−
Desmin	−	−	−	−	−	−
ACT	−	−	−	−	−	−
CD35	−	−	−	−	−	−
S-100	−	−	−	−	−	−
UEA-1	−	−	−	+	+	+

SC: Spindle-shaped cell. MLC: Macrophage-like cell. IEC: Immature endothelial cell-like cell. PCV: Post-capillary venule. LV: Mature lymphatic vessel. BV: Mature blood vessel.

in middle to advanced age (Oettle, 1962; Lulat, 1989). Most endemic KS cases in children initially occurred in the lymph node, while those of people of middle to advanced age showed primary lesions in the skin. In addition, over half of pediatric cases showed generalized lymphadenopathy. With regard to the male to female ratio, the adult type KS showed a much higher incidence in males than in females. On the other hand, the pediatric type KS showed a higher female incidence than the adult type KS. These findings suggest that there are certain etiological differences between the pediatric type and adult type KS in Western Kenya. It has been postulated that some infections with a transmissible agent in young non-immune children lead to proliferation of KS in the lymph node (Slavin *et al.*, 1969). Both pediatric and adult type KS showed similar ethnic and geographic distribution (Taylor *et al.*, 1971; Schmid, 1973; Toriyama *et al.*, 1987a, b). A high incidence of KS was observed in the Luo ethnic group living around Lake Victoria, which is a relatively moist tropical savanna. However, there were only a few cases in dry areas where other ethnic groups including the Luo group reside. These findings are consistent with those of previous reports (Davies, 1959; Davies and Lothe, 1962) and suggest that climatic conditions such as high temperature and humidity play an important role in the causation of KS. In Colombia, South America, where KS showed histological patterns similar to those of African endemic type KS, there were no pediatric patients with KS and the lymph node-type KS (Garcia *et al.*, 1989). In classical type KS, there were very few pediatric cases and lymph node cases (Bluefarb, 1957; Bisceglia *et al.*, 1988). These reports indicate that genetic factors and environmental factors such as life style, living conditions and aging differ among the various types of KS.

KS cells developed at the paracortical area of the lymph nodes and gradually proliferated along the reticulin network originating from the trabeculae. KS cells were composed of several elements, that is, spindle-shaped cells without any differentiation, spindle-shaped cells with slit-like structures and immature endothelial cell-like cells. Immunohistochemically these cells were only positive for Vimentin, which is a marker for mesenchymal cells, while other markers for differentiated cells were negative. These results suggest that KS cells

originated from pluripotential cells near the reticulin network, that is, mesenchymal cells which become immature and mature endothelial cells, and showed the features of undifferentiated spindle-shaped cells. Although previous reports have expressed different opinions about the histogenesis of KS, such as vascular endothelial cell (Rutgers *et al.*, 1986; Hashimoto *et al.*, 1987), lymphatic endothelial cell (Bechstead *et al.*, 1985; Dictor, 1986; Russelljones *et al.*, 1986), Schwann cell (Pepler, 1959) and fibroblast (Mottaz and Zelickson, 1966), there may be no contradiction if the stage of differentiation from mesenchymal cell to each of the components is regarded as a spectrum of differentiation. It is thought that macrophage-like cells are one of the components of KS lesions, but it is still obscure whether the macrophage-like cells are part of the spectrum of mesenchymal cells, or of the stromal reaction around KS tissues.

From the histological findings of the lymph node-type KS in children, that is, coexistence of spindle-shaped cells, immature endothelial cell-like cells, macrophage-like cells, and relatively well differentiated small blood and lymphatic vessels, KS seems to be an independent disease with histological features differing from those of 1) Castleman's disease, which shows marked hyperplasia and hyalinization of intra- and extrafollicular blood vessels in tumor tissue (Kessler and Beer, 1983); 2) angioimmunoblastic lymphadenopathy with dysproteinemia, which is characterized by bifurcated hyperplasia of PAS-positive, thick-walled small blood vessels and proliferation of immunoblasts and plasma cells (Frizzera *et al.*, 1974); and 3) vascular transformation of lymph node sinuses, which is characterized by hyperplasia of small blood vessels localized in the sinus or trabeculae without any association of spindle-shaped cells (Michal and Koza, 1989).

The histological features of KS also differ from those of 1) spindle cell hemangioendothelioma, which shows the coexistence of cavernous hemangioma with spindle cells (Weiss and Enzinger, 1986); 2) angiosarcoma, which is composed of Factor-VIIIRa positive endothelial cells with atypia (Enzinger and Weiss, 1988a); and 3) fibrosarcoma, which is surrounded by enormous collagen fibers with a herring-bone pattern of spindle cells but no slit-like lumens (Enzinger and Weiss, 1988b).

Several reports have suggested that the pediatric type KS is a malignant or low-grade malignant tumor (Master *et al.*, 1970; Taylor *et al.*, 1971) because of its clinical and histological features, that is, rapid growth and short period leading to death, generalized invasion to organs, necroses, some abnormal mitoses and atypism of proliferating cells. In our histological results, however, there are no abnormal mitoses, primary necroses, cellular atypia or invasive growth. Some cases with poor prognosis showed a potential for misdiagnosis as malignant tumors such as angiosarcoma. In classical KS, KS associated with immunosuppressive therapy and Acquired immunodeficiency syndrome-related KS, some cases showed spontaneous remission, and lesions of the patients who had been treated with steroid therapy appeared or disappeared depending on variation in immunosuppressive status (Zisbrod *et al.*, 1980; Real and Krown, 1985). These results indicate that KS might not be a malignant tumor, but rather a benign neoplasm, tumor-like lesion or reactive hyperplasia.

Our findings indicate that: 1) there are certain differences in the etiological co-factors of KS between the endemic lymph node-type KS in children and the endemic cutaneous type KS in adults, 2) KS cells originate from pluripotent mesenchymal cells, and 3) KS might not be a malignant tumor, but rather a benign neoplasm, tumor-like lesion or reactive hyperplasia.

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西部ケニアにおける小児の風土病型リンパ節型カポシ肉腫

小室　哲・鳥山　寛

風土病型カポシ肉腫（KS）は赤道アフリカに多く見られ，比較的小児にも好発し，また，リンパ節に発生するものも多く認められてきた。今までの我々の調査でも，小児に発生するKSは，主にリンパ節に初発していた。しかし，これらのKSに関する組織学的検討は，ほとんどなされていない。今回我々は，小児KSのうちリンパ節に初発した症例22例を用いて，地理病理学的，組織学的，免疫組織学的な検索を行い，その民族，地理的分布，組織学的形態像，細胞の由来，発生機序に関して検討した。その結果1）風土病型KSの好発年齢には，小児期と中高年齢期の二峰性が見られ，初発部位は小児では主にリンパ節で，多発する傾向が見られ，中高年齢期では四肢の皮膚に多く見られた。2）小児リンパ節型KSは，成人皮膚型KSと同様にLuo族に多く見られ，高温で多湿なビクトリア湖周辺に多く，乾燥した地域にはまれであった。3）KSはリンパ節のpara-cortical areaより発生し，reticulin networkに沿って増生していた。4）KSの病変部はspindle-shaped cell, macrophage-like cell, immature endothelial cell-like cell, mature blood vessel, lymphatic vessel, postcapillary venuleなどの細胞からなっていた。5）悪性を示唆する細胞異型，異型核分裂像，腫瘍による増殖性壊死，リンパ節被膜外への浸潤像などは認められなかった。6）免疫染色およびレクチン染色では，内皮細胞のマーカーであるFactor-VIIIRa, UEA-1はmature blood vesselなどのendothelial cellに陽性で，spindle-shaped cell, macrophage-like cell, immature endothelial cell-like cellは陰性であった。間葉系細胞のマーカーであるVimentinは，spindle-shaped cell, immature endothelial cell-like cell, mature blood vesselなどのendothelial cellに陽性であった。macrophage-like cellはFactor-XIIIRaのみ陽性で，KSの病変部に多く見られたが，KSの構成成分の一種であるか，反応性の増生であるかは不明であった。これらの結果より，KSの発生には自然環境，生活様式などの因子とともに遺伝因子など，いくつかの因子が強い影響を与えていると考えられた。また，KSはparacortical areaのreticulin network近傍の多潜能なmesenchymal cellより発生し，悪性腫瘍というよりは良性腫瘍，あるいは反応性疾患と考えられた。

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A REVISIONARY NOTE ON THE BLACKFLY, HITHERTO CALLED "*SIMULIUM* (*GOMPHOSTILBIA*) *BATOENSE* EDWARDS, 1934" FROM THE RYUKYU ISLANDS, JAPAN (DIPTERA: SIMULIIDAE)

HIROYUKI TAKAOKA

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Abstract: A new species name, *Simulium* (*Gomphostilbia*) *yaeyamaense* sp. nov. is proposed for the blackfly species in the Ryukyu Islands which has been hitherto regarded as *S.* (*G.*) *batoense* Edwards, 1934, originally described from Java. The new species is readily distinguished from *S.* (*G.*) *batoense* by the large basal tooth on the female claws, the characteristic pruinose pattern on the male scutum, and the branching of the pupal gill filaments. Revised descriptions are given for female, male, pupa and mature larva of this new species, and discussed are also taxonomic affinities with related species.

INTRODUCTION

Edwards (1934) described *Simulium* (*Gomphostilbia*) *batoense* from adult and immature specimens collected from East Java. This species has not, since then, been recorded from anywhere else until Ogata (1956) reported it from Ishigaki Island, Yaeyama-island group, situated in the southern part of Ryukyu Islands. This species was also found from Iriomote Island, close to Ishigaki Island (Takaoka, 1972, 1976). However, later surveys on blackfly fauna in Taiwan and the Philippines failed to discover *S.* (*G.*) *batoense,* although several other *Gomphostilbia* species were collected (Takaoka, 1979, 1983).

Recently, the author had an opportunity to examine the lectotype male, two paralectotype females, six pupae and three larvae of *S.* (*G.*) *batoense* preserved in British Museum (Natural History), London (BMNH), and found the clear morphological differences at all stages between specimens from Java and Ryukyu Islands, which are considered to be sufficient for species separation. Most striking is the observation that the Javanese females bear a small subbasal tooth on the claws (Fig. 3e) whereas Ryukyu's specimens show a large basal tooth (Fig. 2d), as in most *Gomphostilbia* species. These differences have been also confirmed by the materials newly collected from Java by the author.

In this paper, a new species name is proposed for the blackfly so far regarded as *S.* (*G.*) *batoense* in Ryukyu Islands. Here given are revised descriptions of this new species although descriptions were previously given under the name of *S.* (*G.*) *batoense* for the adults and pupa by Ogata (1956) and for the larva by Takaoka (1976). The taxonomic affinities with related species including *S.* (*G.*) *batoense* are also discussed.

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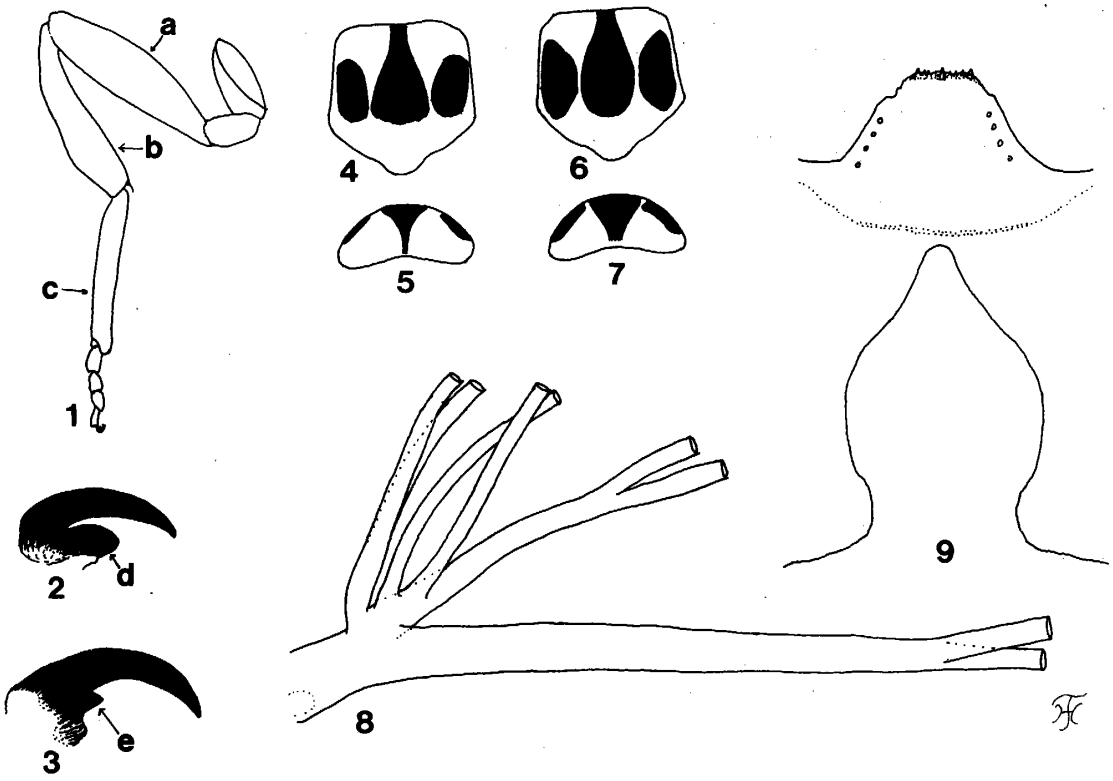


Figs. 1, 2, 4 and 5 *S.* (*G.*) *yaeyamaense* sp. nov.: 1, hind leg of female (a, femur; b, tibia; c, basitarsus); 2, female claw with a large basal tooth (d); 4 and 5, dorsal and front views of male scutum.

Figs. 3, 8 and 9, *S.* (*G.*) *batoense*: 3, female claw with a small subbasal tooth (e); 8, enlargement of basal portion of pupal gill showing branching method; 9, ventral view of larval head capsule showing deep postgenal cleft.

Figs. 6 and 7, *S.* (*G.*) *friederichsi*: 6 and 7, dorsal and front view of male scutum.

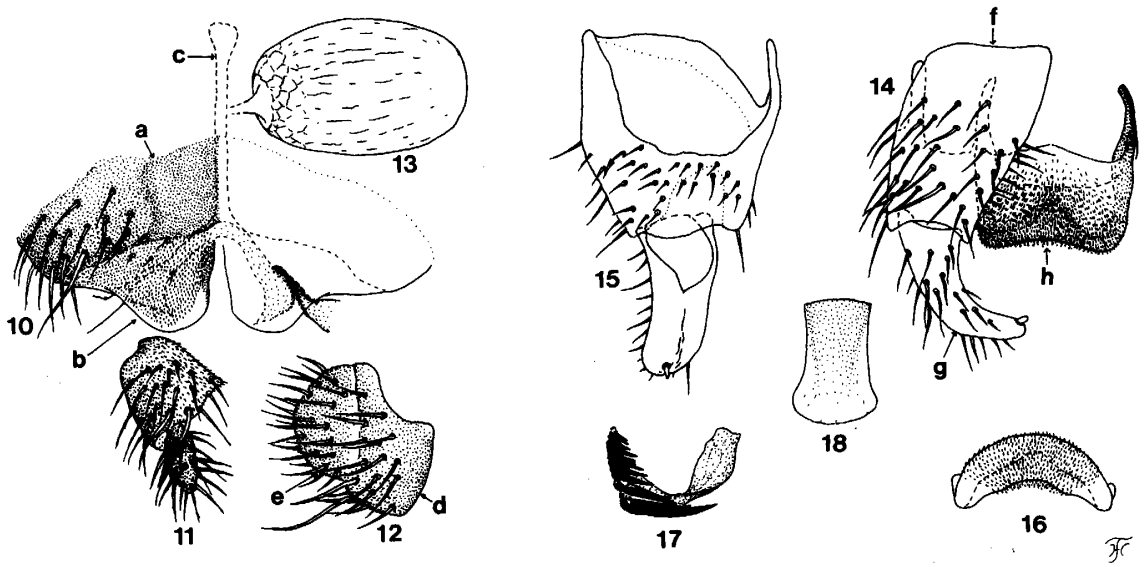
Description

Simulium (*Gomphostilbia*) *yaeyamaense* sp. nov.

Simulium (*Nevermannia*) *batoense* (*nec* by Edwards): Ogata (1956), Jpn. J. M. Sc. Biol., 9, 59-61 (female, male and pupa)

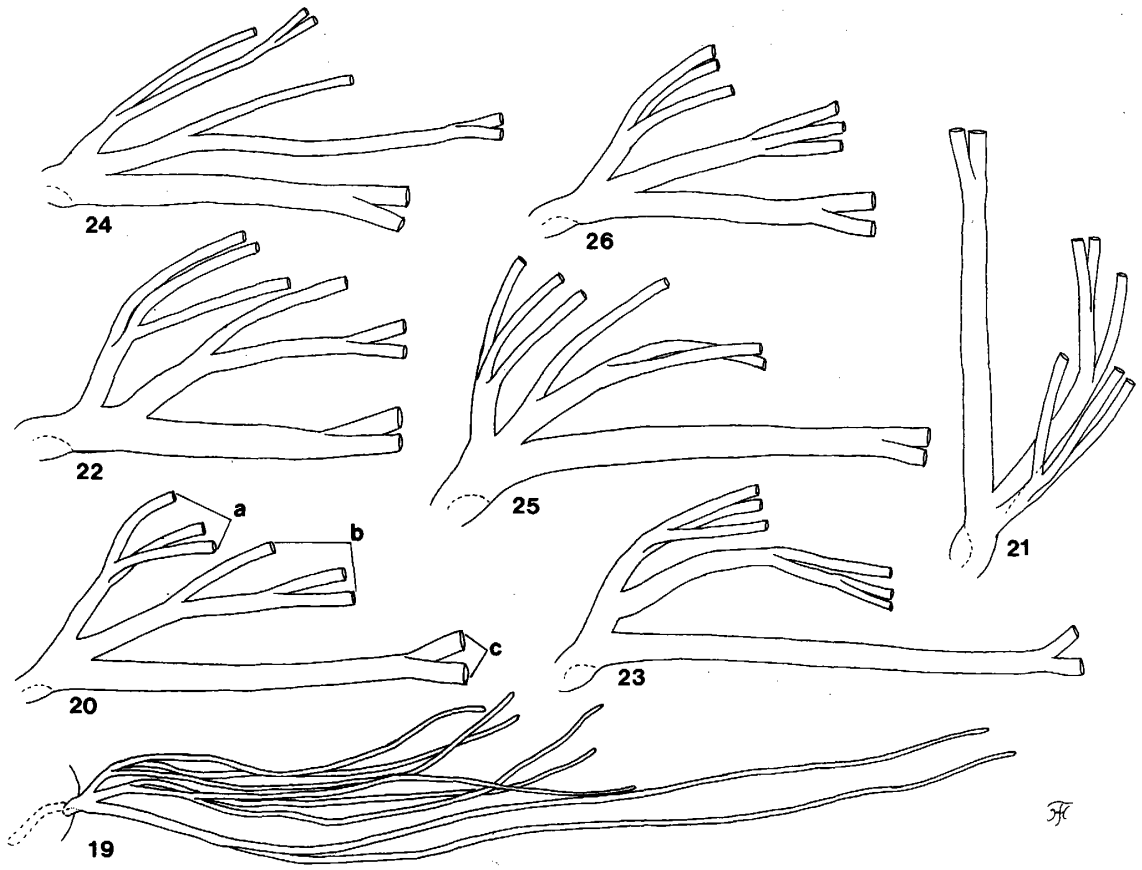
Simulium (*Gomphostilbia*) *batoense* (*nec* by Edwards): Takaoka (1976), Jpn. J. Sanit. Zool., 27, 389 (larva)

Female. A small, blackish species (body length 2.0 mm). *Head* slightly narrower than width of thorax. Frons black, whitish grey pruinose, moderately covered with whitish yellow pubescence as well as a few dark hairs, except middle longitudinal portion narrowly bare; frons shiny and brightly iridescent when viewed in light; frontal ratio (i.e., ratio of the greatest width at vertex, the narrowest near antennal base, and the height of the frons) 1.5:1.0:1.65. Frons-head ratio (i.e., ratio of the greatest width against that of head) 1.0:4.6.



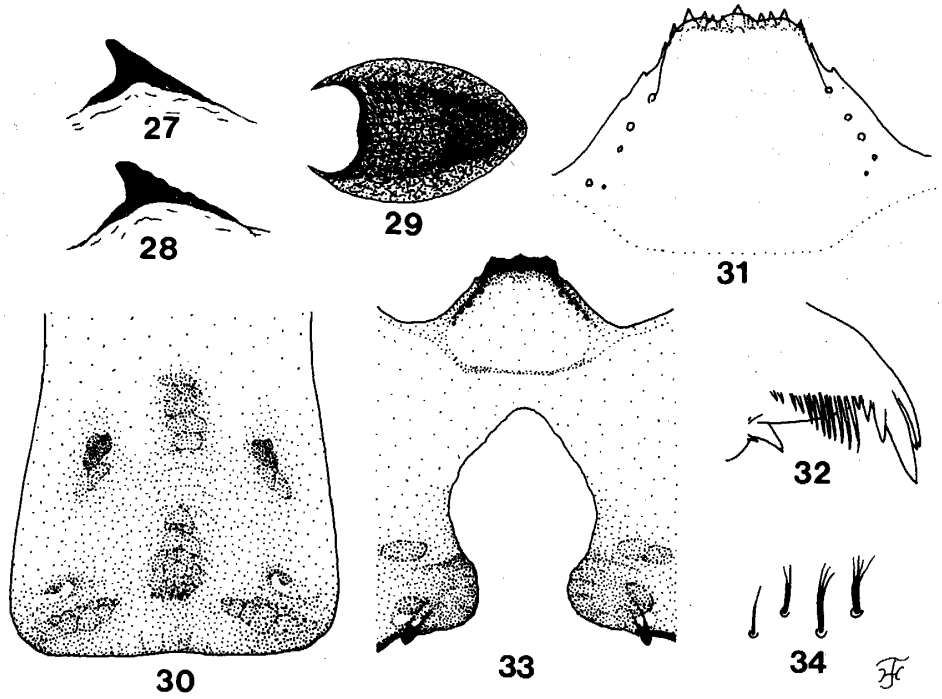
Figs. 10-18 Female and male genitalia of *S.* (*G.*) *yaeyamaense* sp. nov.: 10, ventral view of 8th sternite (a), anterior gonapophyses (b) and genital fork (c); 11 and 12, ventral and side views of paraproct (d) and cercus (e); 13, spermatheca; 14, ventral view of coxite (f), style (g) and ventral plate (h); 15, dorsal view of coxite and style; 16, end view of ventral plate; 17, paramere; 18, median sclerite.

Clypeus black, whitish grey pruinose, and densely covered with whitish yellow pubescence interspersed with several dark hairs. Antenna composed of 2+9 segments, black except scape, pedicel and basal 1/2 of 1st flagellar segment yellow. Maxillary palp black, composed of 5 segments with proportional length of 3rd, 4th and 5th segments being 1.0:1.2:2.2; 3rd segment not enlarged, and sensory vesicle of moderate size, 1.8× as long as its width and 0.36× length of 3rd segment, and with small round opening distally, its diameter 0.4× as long as width of sensory vesicle. Maxilla with 12 teeth on each side. Mandible with about 22 small inner teeth and 10 outer ones. Cibarium with heavily sclerotized arms but without any denticles medially. *Thorax.* Scutum black in ground colour, thinly whitish grey pruinose, with three dark longitudinal lines which are distinct when viewed anterodorsally; pruinose areas brightly iridescent when illuminated; scutum densely covered with whitish yellow and brassy recumbent pubescence as well as several dark long hairs on prescutellar area. Scutellum black with dark pubescence as well as long upstanding dark hairs along posterior margin. Postscutellum black, whitish grey pruinose and bare. Pleural membrane bare. Katepisternum black, whitish grey pruinose, with pale and dark hairs, and longer than deep; sulcus distinct. *Legs.* All legs almost black except hind trochanter, base of mid tibia and basitarsus, base of hind tibia, basal 3/5 of hind basitarsus, and basal 1/2 of hind 2nd tarsal segment whitish yellow; whitish yellow hairs largely on outer surface of fore tibia, basal 1/2 of mid tibia and basitarsus and basal 2/3 of hind tibia and basitarsus— these are brightly iridescent when viewed in certain angles of light. Fore basitarsus not delated, ca. 5.9× as long as its greatest width. Hind tibia swollen on distal 1/4 and to lesser extent on basal 1/3, and about 0.8× as wide as hind femur (Fig. 1b). Hind basitarsus slender, parallel-sided (Fig. 1c). Calcipala moderately developed, 1.2× as long as wide, and ca. 0.76× width of basitarsal



Figs. 19-26 Pupal gill filaments of *S.* (*G.*) *yaeyamaense* sp. nov.: 19, whole gill filaments; 20-26, basal parts of gill filaments showing various branching methods (20, normal form; 21-26, other forms less frequently seen) (a, b and c indicating upper and middle triplets and lower pair groups, respectively).

tip (Fig. 1c). Pedisulcus also distinct at basal 1/3 of 2nd tarsal segment. Claws each with large basal tooth which is 1/2× as long as claw (Fig. 2). *Wing.* Length 1.6 mm. Costa with spinules as well as hairs. Subcosta haired. Tuft hairs at base of stem vein dark brown. Basal portion of radius fully haired. *Abdomen.* Basal scale black, with a fringe of pale hairs. All segments almost black dorsally, laterally and even ventrally, and with dark hairs; 2nd segment with whitish grey pruinose band on basal 1/2 of dorsal surface; tergites of 6th, 7th and 8th segments shiny. *Genitalia.* Sternite 8 (Fig. 10a) bare medially, and with 18-22 dark macrosetae on each side. Anterior gonapophyses (Fig. 10b) thin, membraneous, rounded posteriorly, covered densely with microsetae except posterior margins narrowly bare, and with a few short setae near anterior border; inner margins well sclerotized. Genital fork (Fig. 10c) of usual inverted-Y form, with somewhat flattened tip; arms each produced inwards to some extent but lacking any projection directed forwards. Paraproct (Figs. 11 and 12d) of usual form, short, 1/2× as long as wide when viewed laterally, and with about 20 macrosetae ventrally and laterally. Cercus (Fig. 12e) short, 1/2× as long as wide, rounded posteriorly, when viewed laterally, and covered with about 20 macrosetae on outside surface. Spermath-



Figs. 27-34 *S.* (*G.*) *yaeyamaense* sp. nov.: 27 and 28, terminal hooks of pupal abdomen; 29, cocoon; 30, cephalic apotome of larval head; 31, larval hypostomium; 32, tip of larval mandible; 33, ventral view of larval head capsule showing deep postgenal cleft; 34, simple and branched black spines on larval abdominal cuticle.

eca (Fig. 13) oblong, well sclerotized except small area near tubal juncture unscle-rotized.

Male. Body length 2.0 mm. *Head* slightly wider than width of thorax. Upper eye consisting of about 14 vertical colums and 14 horizontal rows of large facets. Clypeus black, whitish grey pruinose, and covered with dark hairs interspersed with pale yellow hairs. Antenna composed of 2+9 segments, dark brown except scape, pedicel and base of 1st flagellar segment pale yellow; 1st flagellar segment somewhat elongated, 1.5× as long as wide. Maxillary palp with 5 segments; proportional length of 3rd, 4th and 5th segment 1.0:1.2:3.0; 3rd segment of normal size, with sensory vesicle small, almost globose in shape. *Thorax.* Scutum black, with semishiny, whitish grey pruinosity laterally and posteriorly and in 2 submedian longitudinal bands extending from anterlateral corners so as to enclose a black, non-pruinose spot on each side and to leave middle of scutum black widely, as shown in Figs. 4 and 5; middle black band narrowed towards anterior margin, appearing as a flat-bottomed flask; pruinose areas brightly iridescent in certain angles of light; scutum densely covered with bright brassy recumbent pubescence, although these are replaced by bright yellow pubescence on shoulders and also intermixed with yellow pubescence and upstanding long dark hairs on prescutellar region. Scutellum black, covered densely with dark pubescence as well as several marginal long hairs. Postscutellum black, grey pruinose and bare. Pleural membrane bare. Katepisternum shaped as in female, and with many dark hairs. *Legs.* Coloration and covering of bright yellowish hairs as in female. Fore basitarsus slender, not delated, about

7.7× as long as its greatest width. Hind tibia of similar shape to that of female except its greatest width subequal to that of hind femur. Hind basitarsus slender, parallel-sided. Calcipala as long as wide and ca. 0.66× as long as width of basitarsal tip. Pedisulcus well marked. *Wing.* Length 1.5 mm. Other features as in female except subcosta bare. *Abdomen.* Basal scale black with a fringe of dark hairs. All segments almost black, not shiny and sparsely covered with dark hairs; 2nd tergite with broad whitish greyish pruinose transverse band which is brightly iridescent when seen in light, and tergites 5-7 each with a pair of thinly greyish pruinose patches dorsolaterally which are shiny when viewed in certain angles of light. *Genitalia.* Coxite (Fig. 14f) nearly rectangular in ventral view, much longer than wide. Style (Fig. 14g) small, shorter than coxite, curved inwards and with a single apical spine. Ventral plate (Figs. 14h and 16) flat, rectangular in ventral view, about 0.6× as long as wide, slightly concave on posterior margin, slightly produced ventrally forming low posteromedial process, and densely covered with microsetae ventrally, posteriorly and dorsomedially; basal arms of moderate size, directed forwardly and slightly inwardly. Paramere (Fig. 17) of moderate size, with 3 long hooks and several shorter ones. Median sclerite (Fig. 18) broad, plate-like, somewhat broadened distally and ended roundly.

Pupa. Body length (excluding gill filaments) 2.0-2.3 mm. *Head* and *thorax.* Integument yellowish brown, covered moderately with tubercles. Head with 1 facial and 3 frontal pairs of simple long trichomes. Thorax with 5 pairs of simple long trichomes. Gill (Fig. 19) with 8 slender filaments arranged in 3 groups, i.e., upper and middle triplets and 1 lower pair; common stalk short, usually divided on the vertical plane into 3 subsequent stalks of which lower one is longest (Fig. 20), but occasionally stalk of upper triplet arising somewhat outwardly (Fig. 21), and also stalk of middle triplet rarely arising a little distally from lower stalk (Fig. 22) or a little upwardly from upper stalk (Fig. 23); stalk of lower pair stoutest of all and usually much longer than primary and secondary stalks of middle group put together, but it is rarely subequal to or even shorter than the latter (Figs. 22 and 24); lower paired filaments (3.0-3.5 mm long) much longer and stouter than 6 other filaments (1.5-1.8 mm long); stalks of upper and middle groups each usually branched into 1 individual filament and paired 2 filaments but sometimes divided into 3 filaments at the same level (Figs. 25 and 26); all filaments with numerous transverse ridges becoming less distinct towards apex, and covered with minute tubercles. *Abdomen.* Terga 1 and 2 darkened, without tubercles; tergum 1 with a long simple seta on each side, and tergum 2 on each side with 5 short simple setae and a long simple seta. Terga 3 and 4 each with 4 hooked spines directed forwards along posterior margin, and a short seta medially on each side. Tergum 5 with 5 very minute setae and with or without spine combs numbering 1 or 2, if present. Terga 6-9 each with spine combs in transverse row, and comb-like groups of very minute spines on each side of spine combs; terga 6-8 each also with a pair of minute setae on each side; tergum 9 with a pair of marked terminal hooks, of which outer ridges smooth (Fig. 27) or somewhat undulated (Fig. 28). Sterna 4-8 each with comb-like groups of minute spines scattered all over. Sternum 4 with 1 simple or bifid hook on each side. Sternum 5 with a pair of bifid hooks situated close together on each side. Sterna 6 and 7 each with a pair of inner bifid and outer simple or bifid hooks widely spaced on each side. Sternum 9 with 3 grapnel-shaped hooks on each side. Cocoon (Fig. 29) simple, slipper-shaped, moderately woven, extending ventrolaterally, and with thick anterior margin which has no anterior projection.

Mature larva. Body length 4.0-4.5 mm. Body colour yellowish with greyish brown transverse band on each abdominal segment. Head with pale or somewhat darkened cephalic apotome with positive head spots (Fig. 30). Antenna longer than cephalic fan stem, with 4 segments in proportion of 16:15:15:1. Cephalic fan with 34-38 main rays. Mandible with 2 mandibular serrations; comb teeth decreasing in length and thickness from 1st to 3rd tooth (Fig. 32). Hypostomium (Fig. 31) with a row of 9 apical teeth, of which corner and median teeth are moderately developed; lateral serration absent; 3 or 4 hypostomial setae lying parallel to lateral margin on each side. Postgenal cleft deep, about 6× as long as postgenal bridge, and much constricted at base (Fig. 33). Thoracic cuticle bare. Abdominal cuticle bare on segments 1 and 2, but dorsally covered with minute black spines very sparsely on segments 3 and 4 and moderately on the remaining posterior segments; most of these spines are split into 2 or 3 branches apically, although there are some simple and quadrifid spines (Fig. 34). Rectal gill lobes compound, each lobe with 6-8 finger-like lobules. Anal sclerite of usual X-form, posterior arms a little longer than anterior ones; basal portion of arms widely sclerotized. Ventral papillae well developed. Posterior circlet with about 78 rows of about 12 hooks each.

Type specimens: Holotype ♀, slide-mounted together with pupal skin and cocoon, taken as a pupa from a small stream at Inoda, Ishigaki Island, Yaeyama-island group, Ryukyu Islands, Japan, 12.V.1988, H. Takaoka. Allotype ♂, slide-mounted together with pupal skin and cocoon, same data as holotype. Paratypes, 9 ♀♀, 4 ♂♂, reared from pupae and pinned, 10 pupal skins and cocoons, 5 mature larvae in alcohol, same data as holotype. Holotype, allotype and some paratypes will be deposited in BMNH, and other paratypes in Bishop Museum, Hawaii.

Distribution: Ryukyus (Ishigaki Island and Iriomote Island).

Discussion

Simulium (*G.*) *yaeyamaense* sp. nov. is similar to *S.* (*G.*) *batoense* in having the dark coloration of legs of both adult sexes, the slender, parallel-sided male hind basitarsus and the pupal gill filaments of which lower paired filaments have a long stalk and are about twice as long as the other six filaments. The female of this species is readily distinguished from that of *S.* (*G.*) *batoense* by the large basal tooth on the claws (Fig. 2d), as already mentioned. The male of this species is also separable from that of the latter species by the difference in the pruinose pattern on the scutum which is, in *S.* (*G.*) *batoense,* of usual form having pruinose areas only on shoulders, along lateral margins and on prescutellar region. The pupal gill of this new species seemed very similar to that of *S.* (*G.*) *batoense* originally illustrated by Edwards (1934). However, a close examination indicates that the middle group of the gill filaments is, in *S.* (*G.*) *batoense,* composed of paired two filaments and two individual filaments arising inwardly from its stalk near the base (Fig. 8). The larva of *S.* (*G.*) *batoense* shows similarities to this new species in having the dark branched spines dorsally on posterior abdominal segments, but seems to differ by a much deeper postgenal cleft (Fig. 9).

This new species appears to be most closely related to *S.* (*G.*) *friederichsi* Edwards, 1934 from East Java in having the similar pruinose pattern on the male scutum, as well as parallel-

sided, male hind basitarsus, and dark legs. The pruinose scutal pattern of the holotype male of *S.* (*G.*) *friederichsi* preserved in BMNH shows that sublateral black spots are much larger and the medial vita is shaped like a round-bottomed bottle, as shown in Figs. 6 and 7. The female, pupa and larva of this species are not known yet.

The male of *S.* (*G.*) *siamense* Takaoka and Suzuki, 1984 from Thailand posesses a similar but different pruinose pattern on the scutum which exhibits the medial vita with the posterior half much narrowed (Takaoka and Suzuki, 1984, cf. Fig. 17). The female, pupa and larva of this species also resemble *S.* (*G.*) *yaeyamaense* sp. nov. in many features including the dark coloration of legs, the large basal tooth on the claws, the branching of the pupal gill filaments, the simple slipper-shaped cocoon, and the deep postgenal cleft. However, there are differences in the following features: in the female, frontal ratio 1.4:1.0:1.9, and macrosetae on the 8th sternite, the paraproct and the cercus fewer in number (about half the number of this new species); pupal gill filaments as long as pupal body; black spines on the dorsal surface of larval abdomen split into many more branches.

This new species shows some similarities with *S.* (*G.*) *torautense* Takaoka and Roberts, 1988 from North Sulawesi and *S.* (*G.*) *krombeini* Davies and Györkös, 1987 from Sri Lanka in the dark coloration of legs, and male hind basitarsus parallel sided. The characteristic pruinose pattern on the scutum separates the male of this new species from the latter two known species which do not bear such a scutal pattern. The female of the new species is barely distinguished from *S.* (*G.*) *torautense* by the wider frons (i.e., frontal ratio 1.5:1.0:1.65 vs. 1.3:1.0:2.5) and also from *S.* (*G.*) *krombeini* by the size of claw tooth (i.e., length of tooth/claw 1/2 vs. 2/3) as well as the frontal ratio (1.4:1.0:2.9 in the latter). The pupal gill with very short stalks and the cocoon with an anterodorsal projection in *S.* (*G.*) *torautense,* and the pupal gill filaments shorter than the pupal body in *S.* (*G.*) *krombeini* easily separate them from the present species, respectively. In the larval stage, *S.* (*G.*) *yaeyamaense* sp. nov. differs from *S.* (*G.*) *torautense* by the branched spines on the abdominal cuticle rather than simple spines as in the latter, and also from *S.* (*G.*) *krombeini* by the compound anal gill lobes and deep postgenal cleft (simple anal gill lobes and medium-sized cleft in the latter).

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琉球列島において *Simulium* (*Gomphostilbia*) *batoense* Edwards と同定されていたブユ種の分類学的再検討

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吸血性双翅目昆虫ブユ科のなかで，*Simulium* 属の *Gomphostilbia* 亜属に含まれる種は，一般に地理的分布が狭い。そこで，ジャワ島および琉球列島の石垣島と西表島から報告されている，ブユ種 *S.* (*G.*) *batoense* が両地域間で同一かどうかを明らかにする目的で，大英自然史博物館に保管されている本種の模式標本（ジャワ産雌雄成虫，蛹，幼虫）を観察し，琉球列島で採集された標本との比較を行った。その結果，琉球列島のブユ標本は，雌成虫の脚の爪の形態，雄成虫背胸部の斑紋，蛹の呼吸糸の分岐方法などで，ジャワ産の模式標本と明らかに異なることが分かった。この結果は，最近新たにジャワ島で採集された標本でも確認された。これらの結果をもとに，これまで *S.* (*G.*) *batoense* とされていた琉球列島のブユに，新種名 *S.* (*G.*) *yaeyamaense*（和名，ヤエヤマナンヨウブユ）を与え，記載を行った。さらに，ジャワ，タイ，スラウェシ，およびスリランカからそれぞれ報告されている，4類似種との形態的相違についても論じた。

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ACUTE RESPIRATORY INFECTIONS IN CHILDREN UNDER FIVE IN TWO RURAL COMMUNITIES IN SOUTHERN GHANA

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Abstract: A historical prospective study based on data collected on acute respiratory infections (ARI) from children aged 1-4 years at Gomoa Fetteh and Gomoa Onyadze/Otsew Jukwa, two rural communities in the central region of Ghana from January 1987 to December 1989 indicated that a child on average would have 5.3 to 7.0 episodes of ARI annually. Acute upper respiratory infections (AURI) constituted 99.4 and 99.7 per cent of all ARI in the two communities, and acute lower respiratory infections (ALRI) 0.3 and 0.6 per cent respectively. Incidence of ARI generally peaked in September/October in the two communities. The under five mortality rates due to ARI were 4.5/1,000 and 11.5/1,000 representing 23.3 and 33.3 per cent of all under five deaths respectively at the beginning of the programme in 1987 but these were reduced to nil in 1988 and 1989. Regular outreach services including EPI and curative services delivered to the two communities within the context of PHC in Ghana may have contributed to the decline in mortality rates due to ARI.

INTRODUCTION

The complex group of acute respiratory infections (ARI) constitutes one of the principal causes of morbidity and mortality in many developing countries. In many countries of Africa, about 50 per cent of all deaths are in children under five years old. ARI is generally estimated to be the cause in one fourth to one third of these deaths (Pio *et al.*, 1984). Accurate data on the incidence of ARI in the general population is scarce but the limited data available indicate that a child in an urban area has an average of five to eight attacks annually with a mean duration of 7-9 days (Pio *et al.*, 1984; WHO, 1986). The situation may not be much different in Ghana but there had not been any longitudinal studies as yet to provide data in the magnitude of childhood ARI although ARI for all age groups constitute 3.4-8.0 per cent

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of new outpatients attendances in some clinics in Ghana (Ashitey *et al.*, 1972; Ashitey and Nettey-Marbell, 1988). The objective of the present study was to determine morbidity and mortality associated with ARI in children under five years of age in two rural communities in Southern Ghana.

Population and Methods

This historical prospective study was based on data collected on ARI from children under five years of age in two rural communities —Gomoa Fetteh and Gomoa Onyadze/Otsew Jukwa— in the central region of Ghana, from January 1987 to December 1989. These two villages are approximately 82 km from Accra, the capital of Ghana. Gomoa Fetteh is a coastal village with a population of 2,316 of whom 19% (440) is under five years of age. Gomoa Onyadze/Otsew Jukwa, a twin village is few kilometers inland with a population of 1,300; 20% (260) are under five years. The people of these villages, are mainly farmers and petty traders. These two villages like the rest of Ghana, experience two major seasons in a year; a dry season from October/November to March, and a wet one from April to September.

The Noguchi Memorial Institute for Medical Research (NMIMR) of the University of Ghana maintains health research field stations in the villages mentioned above and provides PHC including maternal and child care services to them. Population censuses were conducted by the NMIMR in the two villages in 1986, and in 1988, and all children under five years old were registered for a weekly follow-up at community clinics in the villages. There were 350 children under five on the register at Gomoa Fetteh in January 1987; 358 and 300 at the same period in 1988 and 1989 respectively. During the same period the number of children under five years of age for Gomoa Onyadze/Otsew Jukwa were 220, 218 and 188 respectively.

A team of three doctors, two senior nursing officers and field technicians visited the villages and conducted clinics once every week on non-farming days. Services provided at the villages included growth monitoring, immunization, health education and health care including diagnosis and treatment. Morbidity data and health status of the children were recorded on a disease register. The data was then entered into a computer at the Institute.

Table 1 Incidence of acute respiratory infections in two rural communities in southern Ghana 1987-1989

Village	Year	Number of children	Acute respiratory infections		
			AURI	ALRI	Total
Gomoa Fetteh	1987	266	1,797 (6.8)	54 (0.2)	1,851 (7.0)
	1988	258	1,641 (6.4)	10 (0.04)	1,651 (6.4)
	1989	260	1,406 (5.4)	4 (0.02)	1,410 (5.4)
Gomoa Onya-	1987	199	1,046 (5.3)	1 (0.01)	1,047 (5.3)
dze/Otsew	1988	193	1,207 (6.3)	9 (0.05)	1,216 (6.3)
Jukwa	1989	174	931 (5.4)	3 (0.02)	934 (5.4)

AURI: Acute upper respiratory infections
ALRI: Acute lower respiratory infections
Episodes of acute respiratory infections/child/year in brackects.

Any child who failed to attend clinic was visited at home and the health status assessed. Nasal discharge, red throat (pharyngitis), red tonsils (tonsillitis), earache and ear discharge (otitis media) constituted acute upper respiratory infections (AURI), whilst wheeze, cough, chest indrawing and or fast breathing (respriatory rate over 50 per minute) were classified as acute lower respiratory infections (ALRI). These diagnoses were made clinically. Criteria for other diseases like malaria, diarrhoea diseases were also defined and children found to be ill were managed accordingly. All seriously ill children were referred to a district hospital for inpatient management. Two community health workers in each village were trained to record all deaths which were followed by verbal autopsy by the three doctors on the team. If a child had any of the above symptoms of ALRI immediately preceding death, then the death was associated with ALRI.

Data collected on children on the register for at least sixty per cent of the visit in each year from 1987 to 1989 in each village was included in the analysis of morbidity due to ARI. All deaths associated with ARI for the same period were also included in the data analysis.

RESULTS

In Gomoa Fetteh 266 (76.0%), 258 (72.1%) and 260 (86.7%) of registered children under five years of age were seen at least sixty per cent of clinic visits in 1987, 1988 and 1989 respectively. The figures for the same period for Gomoa Onyadze/Otsew Jukwa were 199 (90.5%), 193 (88.5%) and 174 (92.6%). The Table 1 presents incidence of ARI in the two villages for the period 1987 to 1989. AURI constituted about 99.4 and 99.7 per cent of all ARI and mean episodes of ARI per child per year in the two villages were 5.3 and 7.0 respectively. Incidence of ARI generally peaked in September/October (end of wet season) in the two

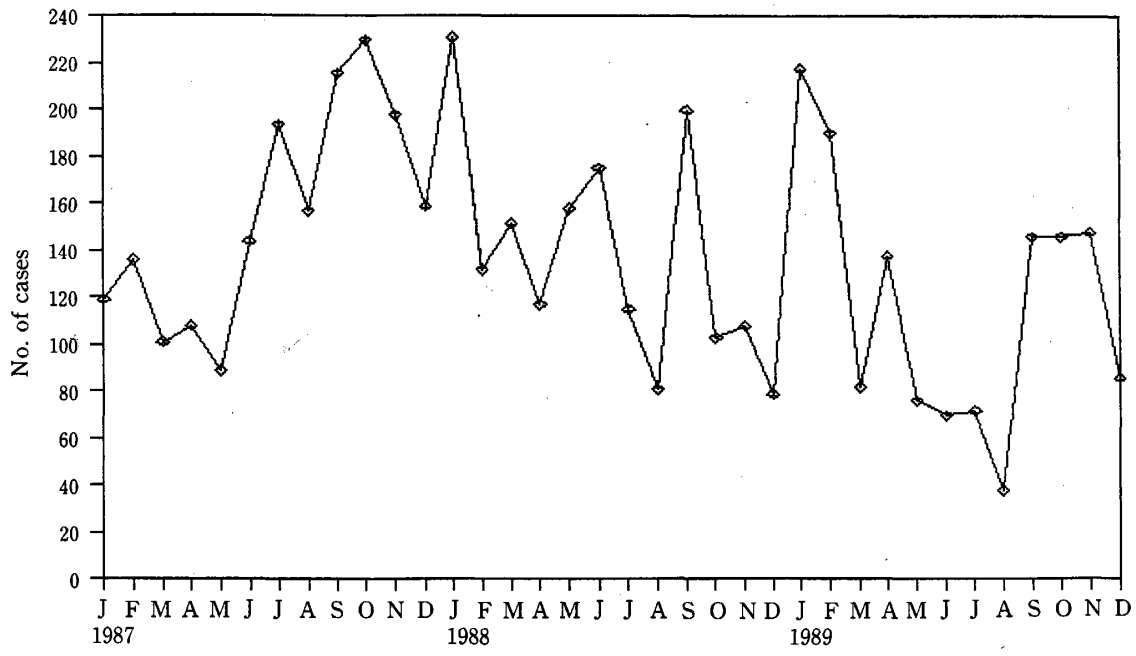

Figure 1 Acute respiratory infections in under five in Gomoa Fetteh 1987-1989.

communities (Figs. 1 and 2).

Gomoa Fetteh recorded six under five deaths in 1987, four in 1988 and two in 1989. Gomoa Onyadze/Otsew Jukwa also recorded eleven under five deaths in 1987, six on 1988 and four in 1989. Two of the deaths at Gomoa Fetteh (4.5/1,000 under five population) and three at Gomoa Onyadze (11.5/1,000 under five population) in 1987 were due to ARI and could be classified as post measles pneumonia. None of the under five deaths recorded in 1988 and in 1989 in the two communities were attributed to ARI. None of the children seen for at least sixty per cent of clinic visits in the villages by the staff of NMIMR during the period under review died from ARI.

Discussion

Acute respiratory infections rank among the most common diseases of children the world over. Available data on the incidence of ARI indicates that on the average a child in an urban area has from five to eight attacks annually. Most of these are the less serious AURI. In rural areas the incidence may be lower (Pio *et al.*, 1984; WHO, 1986).

The results of this rural community based study also show that children under five years of age had an average of 5.3 to 7.0 attacks of ARI annually for the three years study period, and most of these were due to AURI (99.4% to 99.7%). Indications are that the incidence of ARI in children in a rural area may not be different from that in an urban area.

The incidence of ARI generally peaked in September/October (end of wet season) in the two communities. The seasonal variation in ARI may help formulate hypotheses in relation to risk factors in the environment and changes in human behaviour which determine the changes in incidence in ARI during the year. These hypotheses may form the basis for further

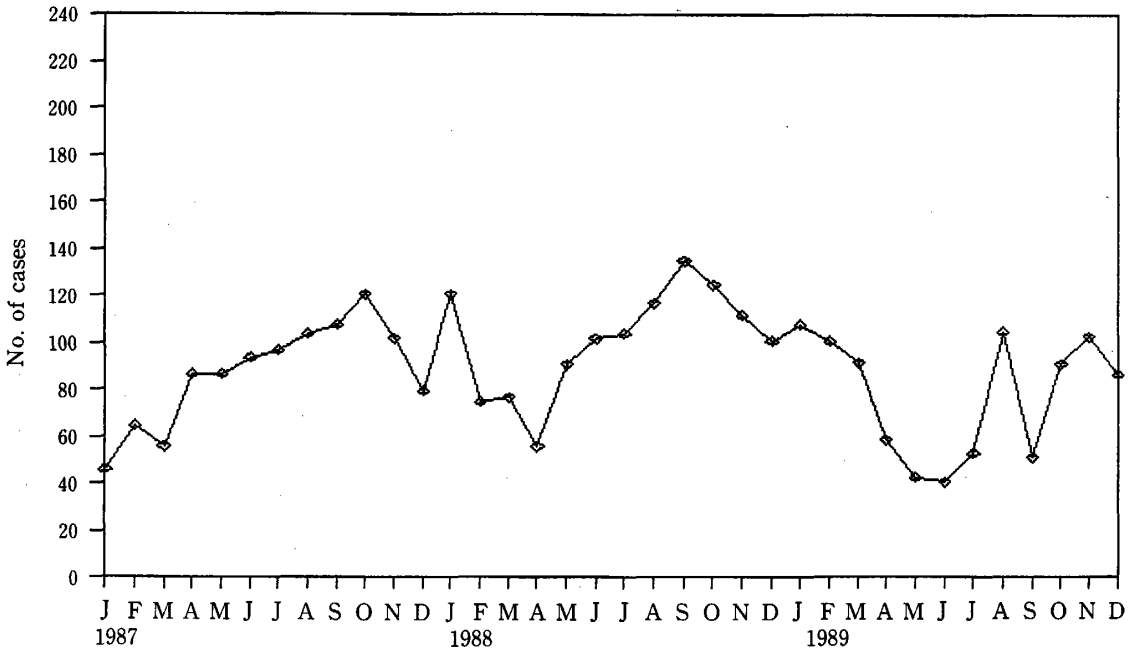

Figure 2 Acute respiratory infections in under five in Onyadze/Otsew Jukwa 1987-1989.

studies in ARI in the study area.

Data from 88 countries in five continents, with a total population of nearly 1,200 million, showed that deaths due to ARI in 1972 amounted to 660,000 and this represents 6.3 per cent of deaths from all causes (Bulla and Hitze, 1978).

Of the estimated 15 million deaths occurring each year in children under five years of age, 25-30 per cent are due to ARI, and the vast majority of these are caused by pneumonia (WHO, 1988). The under five mortality rates due to ARI recorded in this study (4.5/1,000 and 11.5/1,000 under five population) represent 23.3 and 33.3 per cent of all under five deaths in 1987 in the two communities studied respectively at the initial stages of the Institute's activities in the two villages. These deaths were mainly caused by post-measles pneumonia, and the children aged 1-4 years who died from pneumonia were those who for one reason or the other did not benefit fully from the Institute's outreach services especially the EPI. Proportion of deaths due to ARI recorded in the study does not differ much from what is reported world-wide (WHO, 1988). However, deaths due to ARI in the two communities were reduced to nil in 1988 and 1989. None of the children seen at least for sixty per cent of the visits to the villages by the staff of the NMIMR from 1987 to 1989 died from ARI. The results of this study indicate that an active health services out-reach programme within the context of the PHC can efficiently reduce high child mortality from ARI and other diseases.

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ガーナ南部の農村2地区における5歳未満児の急性呼吸器感染症

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1987年1月から1989年12月までの2年間，ガーナ共和国のセントラル地区の農村，フェテ村およびオンヤディ・オチュウジュクワ村の野口記念医学研究所のフィールドステーションを受診した，5歳未満の小児の急性呼吸器感染症について，追跡調査を実施した。それぞれの村では1人の小児に対して，年平均5.3回および7.0回の急性呼吸器感染が見られた。

急性呼吸器感染症のうち，急性上気道感染症の占める割合は，それぞれ99.4%および99.7%で，下気道感染症は0.4%，0.3%であった。

急性呼吸器感染症の罹患率は9月，10月にピークを示した。1987年調査開始時の，急性呼吸器感染症による1,000人あたりの5歳未満児の死亡率はそれぞれ4.5，11.5で，5歳未満小児の全死亡数の23.3%，33.3%を占めていたが，1988年および1989年には急性呼吸器感染による死亡は見られなかった。ガーナにおけるPrimary Health Care (PHC) に関連した拡大予防接種計画，および医療サービスを含む我々の診療活動により，急性呼吸器感染症による死亡率の減少に貢献したものと思われた。

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