TECHNICAL REPORT
19-73
業 績 報 告 書

EOSINOPHILIC LYMPHADENITIS (KIMURA'S DISEASE)

好 酸 球 性 リ ン パ 節 炎 (木 村 氏 病)

CASE REPORT
症 例 報 告

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ABCC JNIH

ATOMIC BOMB CASUALTY COMMISSION

国立予防衛生研究所－原爆傷害調査委員会

JAPANESE NATIONAL INSTITUTE OF HEALTH OF THE MINISTRY OF HEALTH AND WELFARE

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HIROSHIMA AND NAGASAKI, JAPAN

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好酸球性リンパ節炎(木村氏病)

CASE REPORT

症例報告

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SUMMARY

A case of eosinophilic lymphadenitis noted in a 40-year-old male who repeatedly experienced swelling of the lymph nodes in the antecubital regions, neck and axilla without evidence of malignancy but with intense and persistent eosinophilia in the peripheral blood (35%-38%) and with histological finding of eosinophilic lymphadenitis is reported. References in the literature are discussed.

EOSINOPHILIC LYMPHADENITIS

The disease observed in this case showing specific histological findings of marked eosinophilia in peripheral blood and superficial lymphadenopathy is relatively rare and is called by various names. Though the pathogenesis is entirely unknown, it has recently been considered as a specific disease. Moreover, this disease is peculiar to Japan and China; no identical disease has reportedly been found in the western literature. As we recently experienced a case which was deemed to be this disease, the clinical course and pathological findings are reported together with a summary of the available literature.

CASE REPORT

The patient was a 40-year-old Japanese man who worked in a cement factory. Review of the past medical history indicated that he never had anemia, asthma, urticaria, or parasitic disease.

要 約

40歳の男性に認めた好酸球性リンパ節炎の1症例について報告する．本例においては，肘前部，頚部および腋窩にリンパ節腫脹を頻発したが，悪性腫瘍の形跡はなかった．しかし，末梢血液で高度の持続性好酸球増多(30－38%)が認められ，組織学的には好酸球性リンパ節炎の所見が認められた．文献考察を行った．

好酸球性リンパ節炎

本症例に認められた末梢血の著しい好酸球増多と表在性のリンパ節症の特殊組織学的所見を示す疾患は，概してまれな疾患であり，種々の名称で呼ばれている．この疾患の病因は全く不明であるが，近年独立した疾患と考えられている．さらに，この疾患は，日本や中国に特有の病気であり，欧米の文献にはこれと同一の疾患は報告されていないといわれている．著者らは最近本症例と思われる1例を経験したので，その臨床経過ならびに病理学的所見を若干の文献的考察を加えて報告する．

症例報告

患者はセメント工場に勤務する40歳の日本人男子である．既往歴には，貧血症，喘息，蕁麻疹および寄生虫疾患は全くなかった．

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He was diagnosed as having duodenal ulcer and stomach ptosis 4 or 5 years ago but reveived no medical care. No abnormalities had been found at the annual physical examinations held at the company.

Family History. His parents are alive, in good health, and had eight children. The first died of unknown cause at the age of 24. The second died in battle at the age of 21. The remaining children are alive in good health, the patient being the sixth child. The patient has two children who are both healthy. As far as he remembered, none of his relatives had suffered from such diseases accompanied by lymphadenopathy.

Present History. About 1964, small masses were noted in the flexor region of both elbows. But they were left untreated because there were no subjective symptoms. No other masses were noted. The mass in the left elbow remained unchanged but the one on the right elbow gradually increased in size though it caused no trouble. In February 1967, four nodules in the right cubital area were removed. They were all firm and enclosed within a thin capsule. The cut surface was greyish white. The largest nodule measured 3.0 × 2.0 × 2.0 cm. The pathological diagnosis was chronic lymphadenitis with follicular hyperplasia.

When examined about 10 February 1971 the left cervical and submandibular regions were enlarged and a subcutaneous mass about the size of a pigeon's egg, elastic firm and immobile was palpated. Around it, 3-4 other nodules were palpated. It varied in size and consistency without relation to meals. Both tonsils were enlarged and reddened. Sialolithiasis was ruled out by otorhynological examination. No spontaneous pain nor pressure pain was noted. Two or three nodules were palpated in both axillary regions. In the left cubital region, three or four masses about the size of the tip of a little finger were palpated.

Examination Results (15 February 1971). Laboratory tests on 15 February 1971 revealed the ESR to be 15.8/hr, RBC 4.51 × 10^6, Hb 86%, Ht 47%, WBC 10,000 with a differential of stabs 1%, segmented forms 36%, eosinophils 35%, and lymphocytes 28%. The right axillary lymph nodes were not adherent to the surrounding tissues and were surgically removed. They were oval measuring 2.5 cm in long diameter and enclosed within a thin connective tissue capsule. They were elastic, firm, and with a greyish white cut surface. No hemorrhage nor necrosis was noted.

4－5年前十二指腸潰瘍と胃下垂の診断を受けたことはあるが，治療を受けていない．会社での年1回の健康診断では毎年著変なしといわれてきた．

家族歴．両親は健在で同胞は8人であったが第1子は24歳の時病名不明で死亡した．第2子は21歳の時戦死した．第3子から第8子までは健康で，本人は第6子である．本人には2人の子供があり，いずれも健康である．患者の知る限りでは，近親者にリンパ節の腫大を来たすような病気にかかった者はないという．

現症歴．昭和39年ごろから両肘部内側に小腫瘤があるのに気づいたが，自覚症状がなかったので放置していた．他の部位にはこのような腫瘤はなかった．左肘の腫瘤はほとんど不変であったが右肘のものは漸次大きくなってきた．けれどもそれによる苦痛はなかった．昭和42年2月，右肘の腫瘤4個を摘出した．いずれも硬く，薄い被膜に覆われていた．割面は灰白色であった．最大の腫瘤は3.0×2.0×2.0cmであった．病理学的診断は慢性リンパ節炎およびリンパ濾胞増生であった．

昭和46年2月10日ごろの診察時には，左頚部から下顎部にかけて腫大があり，鳩卵大の皮下腫瘤を触れたが，弾性硬で，移動性はない．この付近にも3－4個の腫瘤を触れた．腫瘤の大きさや硬度は種々変化したが，食事とは無関係であった．両側の扁桃は大きく腫大し発赤していた．耳鼻科の診察で唾石症は否定された．自発痛や圧痛はない．両側の腋窩部にも2－3個の腫瘤を触れた．また左肘部にも小指頭大ぐらいのもの3－4個が触れた．

昭和46年2月15日の検査成績は次のとおりである：赤血球沈降速度15.8mm／時，赤血球数4.51×10^6，Hb 86%，Ht 47%，白血球数10,000，また白血球分類は，単核1%，分葉核36%，好酸球35%，リンパ球28%であった．右腋窩リンパ節は周囲組織と癒着なく，外科的に摘出した．リンパ節は長径2.5cmの長円体形で，表面は薄い結合織性の被膜で包まれており，割面は灰白色で弾性硬であった．出血も壊死もなかった．

Histologically, the lymph follicles were markedly increased in size and number and were markedly infiltrated by eosinohpilic leukocytes varying in density by location. Reticular cells and lymphocytes were also increased in number. Lymph follicles consisted mostly of large round or polygonal reticular cells with vesicular nuclei. An outer layer was formed by small lymphocytes around the germinal center. The eosinophilic leukocytes around the lymph follicles had one or two nuclei of normal appearance and were all well differentiated. Infiltration to lymph follicles was hardly noted. The pathological diagnosis was eosinophilic lymphadenitis. The patient was thereafter transferred to the Department of Internal Medicine, Tagawa City Hospital, and underwent various examinations. Laboratory tests on 22 March 1971 showed total protein 7.7g/dl, Gross's test negative, Kunkel's test 8.3 units, total serum cholesterol 171mg/dl, icterus index 3, SGOT 12.5 units, SGTP 21.5 units, alkaline phosphatase 3.9 units. The peripheral blood had an RBC of 4.03×10^6, Hb 95%, platelet 250,000, WBC 10,800, differential blood count showed marked eosinophilia.

The patient returned to work, having no subjective symptom. At the beginning of July 1971 he had a pain in the left elbow region with paresthesia of the ulnar side. A mass of the size of the tip of a thumb was noted in the left antecubital region. In the cervical and axillary regions, masses were palpated as in the previous examination but they seemed to be somewhat decreased in size. The left cubital mass was removed. There were tight fibrous adhesions to the surrounding tissues. Macroscopically, the nodule was enclosed in a thin fibrous capsule and measured $3.0 \times 2.0 \times 1.5$ cm. It also was elastic and firm and greyish white on cut surface. The histological findings were the same as those of the previous examinations showing marked eosinophilia among lymph follicles.

Laboratory tests in July 1971 were negative for occult blood, parasites and ova in the stools. The RBC was 4.51×10^6, Hb 97%, Ht 50%, WBC 6,800 with 40% segments, 18% lymphocytes, 4% monocytes, and 36% eosinophiles. Chest X-ray showed no abnormalities. No further follow-up is available.

DISCUSSION

This disease appears in various parts of body and is classified into four major types by the site of occurrence: 1) soft tissue as observed in this case (Kimura's disease); 2) bone; 3) digestive, urinary, and respiratory tracts; and 4) skin. Eosinophilic granuloma of soft tissue has been given various names; abnormal granuloma with lymphatic hyper-

組織学的には，リンパ濾胞は著しく大きくなり，また数も増え，極めて強い好酸性白血球浸潤が認められた．細網細胞およびリンパ球も数が増加していた．リンパ濾胞は，大部分水胞核をもつ大きな円形または多角形の細網細胞より成っていた．胚を中心に小さなリンパ球がそれをとりまいていた．リンパ濾胞の周囲の好酸性白血球に，正常な様相を呈する１－２個の核があり，いずれもよく分化していた．リンパ濾胞への浸潤はほとんど認められなかった．病理学的診断は好酸球性リンパ節炎であった．その後，内科へ転科し，種々の検査を受けた．昭和46年３月22日の検査成績は，総蛋白量7.7ｇ／dl，Gross 試験(－)，Kunkel 試験8.3単位，血清総コレステロール171mg／dl，黄疸指数３，SGOT 12.5単位，SGTP 21.5単位，アルカリ性ホスファターゼ3.9単位であった．末梢血液検査では，赤血球数4.03×10^6，Hb 95%，血小板250,000，白血球数10,800で，白血球分類では著しい好酸球増多症が認められた．

その後，自覚症状なく就労していたが，昭和46年７月初めより左肘部の疼痛と尺骨側の知覚異常が発現した．左肘部屈側には拇指頭大の腫瘤を認め，また，頚部，腋窩部には前回検査時と同様な腫瘤を触れたが，前回より幾分か小さかったようであった．左肘部の腫瘤を摘出したが，周囲組織との線維性癒着が強かった．肉眼的所見では結節の大きさは$3.0 \times 2.0 \times 1.5$㎝で，表面は薄い線維性の被膜に覆われていて，弾性硬であり，割面は灰白色であった．組織学的所見では，前回の検査所見と同様リンパ濾胞に著しい好酸球増多が認められた．

昭和46年７月実施の検査成績は次のとおりであった：潜血反応(－)，寄生虫および虫卵(－)．血液検査では赤血球数4.51×10^6，Hb 97%，Ht 50%，白血球数6,800で，白血球分類では分葉核40%，リンパ球18%，単球４%，および好酸球36%であり，胸部Ｘ線検査では異常は認められなかった．これ以降の資料は入手されていない．

考　察

この疾患は身体の各部に発現し，発現部位によって次の四つの主要な型に分類されている．すなわち，1) 本症例(木村氏病)で認められるように軟部組織が浸される，2) 骨，3) 消化管，泌尿器管および呼吸器管，4) 皮膚．軟組織の好酸性肉芽腫には，種々の名称がつけられている；すなわち，リンパ性増殖を伴う異常な肉芽腫，[1] 好

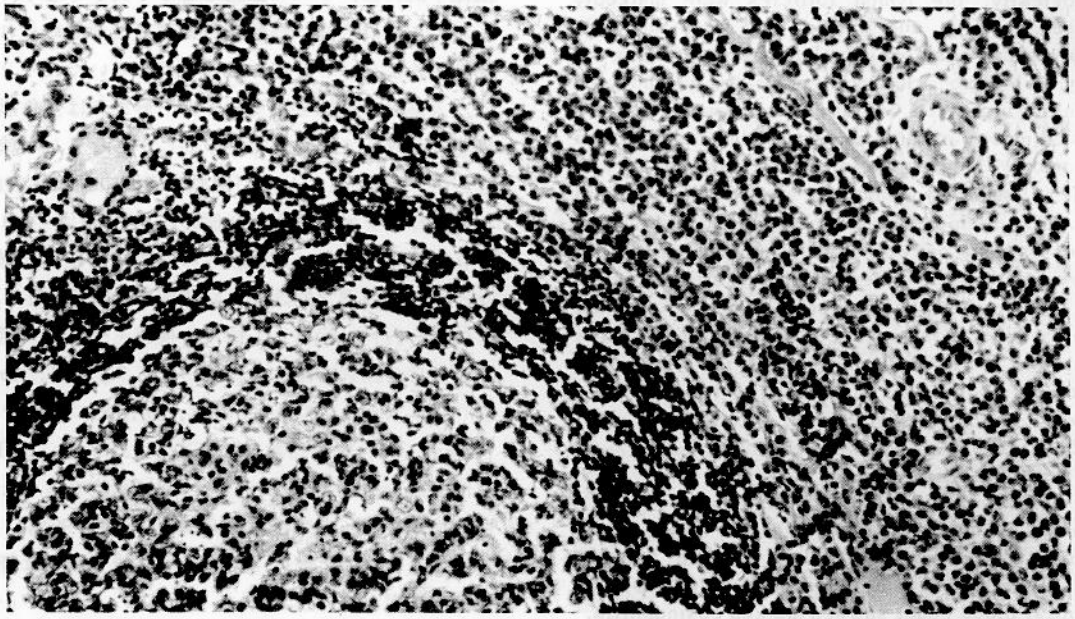

Figure 1 Right axillary lymph node. Lymph follicles are markedly increased in size and number. Marked infiltration by eosinophilic leukocytes are seen around the lymph follicles. HE stain ×100

図1　右腋窩部のリンパ節．リンパ濾胞の大きさと数は著しく増加している．リンパ濾胞の周囲に好酸性白血球による著しい浸潤が認められる．

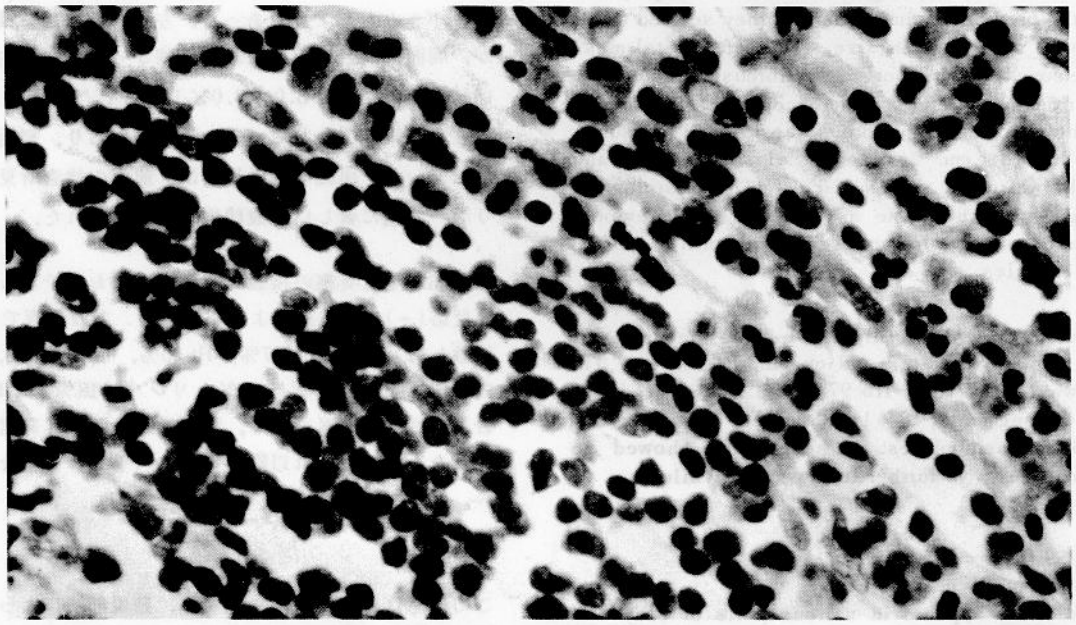

Figure 2 Higher magnification of Figure 1. Marked eosinophilic leukocytes are noted. HE stain ×400

図2　図1をさらに大きく拡大したもの．著しい好酸性白血球が認められる．

plasia,[1] eosinophilic follicular granuloma,[2] eosinophilic lymphoid granuloma or Kimura's disease,[3,4] eosinophilic panniculolymphfolliculopathy,[5] eosinophilic granuloma of lymph nodes and soft tissue,[6] eosinophilic granuloma of soft tissue,[7] eosinophilic granuloma of soft region,[8] eosinophilic folliculocentric syndrome,[9] and eosinophilic lymphfolliculosis.[10]

Beatty[11] reported a case of a 5-year-old Caucasian boy with the primary complaint of sponge-like swelling of both parotid glands. However, because the histological findings involved mostly histiocytes, Beatty's case seems to be different from the disease in question.

From its clinical course and pathologic findings this disease is considered to be a reactive proliferation of the lymphoreticular system. The pathogenesis is entirely unknown. There are some theories attributing the pathogenesis to inflammation, virus, parasite, or allergy but none have been verified. Histologically, the lymphadenopathy is due to intensive eosinophilia in the interfollicular tissue with lymphohistocytic medullary reticulosis. The tissue in this region is not degenerated. This disease is called eosinophilic lymphadenitis when observed in the lymph node and eosinophilic granulomatosis when noted in extranodal lymphoid tissues. Iizuka asserted that the clinical and histological findings are not identified with known diseases but proposed to handle this disease as a unit and to call it Kimura's disease after the first report[8] of this disease in Japan.

Fuse et al reported two similar cases. These were also male adults and were characterized by subcutaneous masses in the anterior auricular region and by the enlargement of lymph nodes particularly in the neck, elbow and inguinal region. The masses were smaller than an egg in size, oval or spheric with smooth surfaces, and were firm. They were not accompanied by spontaneous pain or pressure pain; adhesion to surrounding tissue was hardly noted and there were no inflammatory changes. The picture was similar to that of systemic enlargement of lymph nodes. The clinical course was long. There was no finding to suggest malignant lymphoma although the swelling varied in degree to some extent. Eosinophilia was remarkable in the peripheral blood, bone marrow and tissue specimens despite the absence of causative diseases such as allergic or parasitic diseases, swelling of the liver or spleen, and abnormality in liver function test. Whereas the enlarged lymph nodes were little changed by X-irradiation, they reacted well to adrenocortical hormone and were restored to the original state showing some change during the course.

酸性・濾胞性肉芽腫,[2] 好酸性リンパ肉芽腫または木村氏病,[3,4] 好酸性パニキュロリンパ濾胞病,[5] リンパ節および軟組織の好酸性肉芽腫,[6] 軟組織の好酸性肉芽腫,[7] 軟部好酸性肉芽腫,[8] 好酸性 folliculocentric 症候群[9] および好酸性リンパ濾胞症[10] である.

Beatty[11] は,両耳下腺の海綿状腫脹の主訴を有する5歳の白人少年の症例を報告した.しかし,組織学的所見では,大部分が組織球であるので,この症例は,本疾患とは異なったものであるようである.

本疾患は,その臨床経過および病理学的所見からみて,リンパ細網系の反応性増殖であると考えられる.その発病機序は全く不明である.病因は,炎症,ウイルス,寄生虫またはアレルギーなどにあるという説があるが,いずれも証明されていない.組織学的には,リンパ節症は濾胞間における強い好酸球増多とリンパ組織球性骨髄細網症のために発生するものである.この部における組織には変性はない.この疾患がリンパ節内に認められる場合は,好酸性リンパ節症といわれ,リンパ節外にリンパ様組織が認められる場合は,好酸球性肉芽腫症と呼ばれている.飯塚は,これらの臨床所見および組織学的所見は従来の既知の疾患とは一致せず,本疾患を1疾患単位として取り扱い,本邦で,この疾患を最初に報告した木村[2]の名をとって木村氏病と呼ぶことを提唱した.

布施らも同様な2症例を報告している.この2例は成人男子で,耳殻前部の皮下腫瘤並びにリンパ節,特に頚,肘および鼠蹊部などの腫脹を特徴とし,その大きさは鶏卵大以下で,楕円形ないしは球形で,表面は平滑で,弾性硬である.自発痛および圧痛はなく,周囲組織との癒着はほとんど認められず,炎症所見はなく,系統的リンパ節腫脹に類似した像を示している.臨床経過は長く,腫脹の程度には多少の消長はあっても悪性リンパ腫を思わせる所見は全くない.末梢血および骨髄組織標本中に好酸球の増加が著明であるが,アレルギー性疾患,または寄生虫性疾患といった原因となるような疾患は認められず,肝・脾の腫脹もなく,肝機能検査でも異常は認められない.X線照射に対してほとんど反応を示さないのに反し,副腎皮質ホルモンにはよく反応し,経過中にも多少の消長をみせながら旧に復した.

Our case strongly resembles the above two reported cases. Our patient was a 40-year-old male without past history of allergic or parasitic disease. The lymph nodes were markedly enlarged but not accompanied by dysfunction. The enlargement recurred twice at intervals of 3 years indicating some change during the course. Remarkable eosinophilia was noted in the peripheral blood (35%-38%) as well as histologically in the lymph nodes, indicating the picture of so-called eosinophilic lymphadenitis. Except for some minor differences, our case quite resembles the above mentioned cases in clinical course and histological picture and accordingly this case seems to belong to the same category of disease.

われわれの症例も上記2報告例に酷似している．患者は40歳の男性で，既往歴にはアレルギー性疾患を思わせるものはなく，寄生虫性疾患もない．リンパ節の腫大は著しいが，それに伴う機能障害はない．3年の間隔で2回腫大を生じており，経過中に消長の起こったことを示している．末梢血に著しい好酸球増多(35－38%)があり，組織学的にもリンパ節に極めて強い好酸球増多があり，いわゆる好酸球性リンパ節炎の像を示した．わずかな差異を除けば，本症例は上記症例とその臨床経過や組織像においてよく類似しているので，本症例は上述の症例と同じ疾患分類に属するものであると考えられる．

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