# Kimura's Disease with Prolonged History and Prominent Vascular Involvement

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*Sir,*

Kimura's disease (KD) is a well-established entity, which usually occurs as post-auricular nodules with massive eosinophilic infiltration, lymphoid follicle formation and vascular hyperplasia (1–3). Its histopathological findings resemble those of angiolymphoid hyperplasia with eosinophilia (ALHE), which was once considered synonymous with KD, but is now known as a different entity (2, 3). ALHE has vascular involvement including endothelial hyperplasia with atypical endothelial cells, and some cases have been reported with vasculitis. KD rarely shows vasculitis (2, 3). We report here a case of prolonged history of eosinophilia with subcutaneous infiltration on the lower back showing massive vascular involvement, and lymphoid follicle formation with prominent eosinophilic infiltration, which suggested the diagnosis of KD.

## CASE REPORT

A 56-year-old man was referred to our hospital complaining of an itchy subcutaneous lesion on his lower back for 6 months. He had a history of developing a subcutaneous nodule in his upper arm when he was 10 years old, which was diagnosed as an eosinophilic lymphoid granuloma. He also had a post-auricular nodule when he was 22 years old, which was diagnosed as an eosinophilic lymphoid granuloma as well. The nodule in his arm had been resected, and the post-auricular nodule had been treated successfully with 20 mg/day of oral prednisolone. There was no history of involvement of any other organs.

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The lesion on his lower back was greyish-brown and presented as a slightly lichenified plaque with deep and massive induration. There were several prurigo-like papules in the lesion (Fig. 1). Peripheral lymph nodes were not palpable except in the groin (3 cm in size, soft).

A skin biopsy, taken from his lower back lesion, revealed massive infiltration of mature eosinophils throughout the dermis, and subcutaneous fat with prominent vascular hyperplasia (Fig. 2). Occasional lymphoid follicle formation was observed. In the vessels of the dermis and subcutaneous fat, prominent eosinophilic infiltration with fibrinoid degeneration of the vessel walls was observed, which looked like eosinophilic vasculitis. However, atypical endothelial cells or endothelial protrusions to the vascular lumen, which are usually seen in angiolymphoid hyperplasia with eosinophilia, were not observed. Infiltrating lymphocytes were small with dark nuclei without atypia. Lymphocytes in the follicular centre were larger than those surrounding the follicle with pale nuclei, without atypia. Infiltrating eosinophils showed no atypia.

The majority of the infiltrating mononuclear cells were positive for CD3 and CD45RO. CD56 and CD30 were negative. Immunoglobulin kappa and lambda chain showed positive staining almost to the same extent, which revealed no monoclonality in the lesion.

Direct immunofluorescence revealed no deposition of IgG, IgA, IgM or complement to the vessel walls. IgE was stained in the vascular walls of small vessels. Positive eosinophil major basic protein and eosinophil cationic protein staining were seen among the infiltration of lymphocytes, eosinophils, and on the vessel walls. Epstein–Barr virus (EBV) DNA was detected from the lesion with PCR technique, while EBV-encoded RNA (EBER) was negative with in situ hybridization technique.

Laboratory findings were within normal range except elevated white blood cell count (10,400 $mm^{-3}$) with increased eosinophils (35.0%). Serum IgE level was high (1900 IU $ml^{-1}$). Serum c-ANCA, p-ANCA and anti-nuclear antibodies were negative, and complement levels were normal. He had no signs of larval infestation. Chest X-rays, respiratory functions, ECG and cardiac echograms were normal. An abdominal CT scan showed a subcutaneous muscle density-lesion from the Th12 to the sacral level. Ga and Tc scintigrams showed no abnormal uptake other than the skin lesion.

He was diagnosed with KD and was treated with oral prednisolone 20 mg daily, which resulted in reduction of the subcutaneous lesion and the size of the left inguinal lymph node. The dose of steroids was gradually tapered to 10 mg/day over 12 months, according to the reduction of the indurated lesion.

The second biopsy was taken from the indurated lesion of the back (recurrence of induration after tapering of prednisolone to 5 mg/day), which revealed similar findings to the first biopsy.

Eosinophil count was decreased to 1% during the treatment, then increased to 8% again when the prednisolone was tapered to 5 mg/day.

The patient has been followed up for the last 6 years, the skin lesion on the back gradually disappeared and the left inguinal lymph node became non-palpable, which was also confirmed by the CT scan. He has had no recurrence or exacerbation with 5 mg/day of prednisolone for the past 6 years. Eosinophil count continues to be around 5%.

Serum thymus and activation-regulated chemokine (TARC) level was measured by an ELISA technique before treatment and in recently drawn serum, which revealed 4986.2 pg/ml and 428.1 pg/ml, respectively (normal: $215 \pm 26.79$).

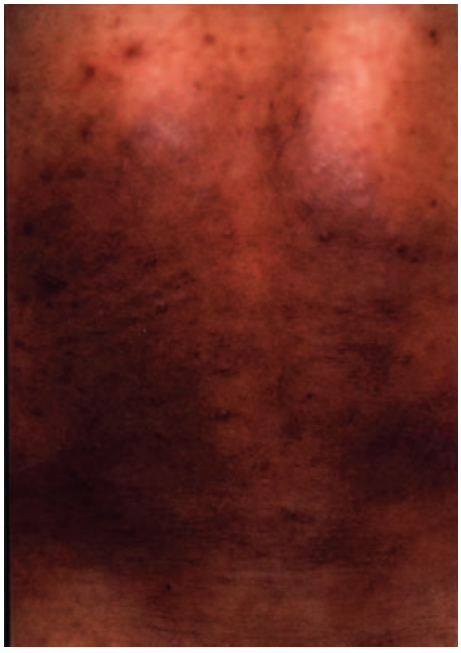

*Fig. 1.* Greyish indurated plaque on the lower back.

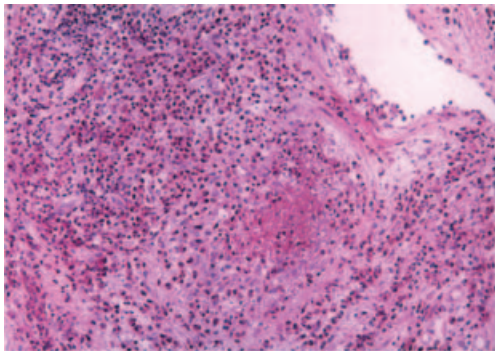

*Fig. 2.* H&E staining of a biopsy specimen from the lesion showing massive infiltration of eosinophils throughout the dermis and subcutaneous fat, as well as vascular involvement.

## DISCUSSION

Notwithstanding an unusually long disease duration, multiple lesions instead of recurrence of the same lesion and a prominent vascular involvement, the histological findings with massive eosinophilic and lymphoid cell infiltration with lymphoid follicle formation along with the benign course and history of post-auricular nodular lesions strongly suggested the diagnosis of KD.

KD, also called eosinophilic lymphoid granuloma, usually occurs in middle-aged people, responds to oral steroids, but tends to recur during tapering. Surgical resections are often carried out to treat this disease (4, 5).

Eosinophilic vasculitis is usually seen in Churg-Strauss syndrome and Wegener's granulomatosis (6), but was recently reported in KD too (7). The formation of lymphoid follicles in the dense eosinophilic infiltration, and the history of post-auricular nodule formation favoured the diagnosis (2, 3, 8). The lack of respiratory

involvement and negative ANCAs did not support a diagnosis of Churg-Strauss syndrome or Wegener's granulomatosis. Vessel involvement is often seen in angiolymphoid hyperplasia with eosinophilia. However, typical vessel lesions in angiolymphoid hyperplasia have hyperplastic and atypical endothelial cells (2, 3, 8), which were not seen in this case.

In line with its occasional findings in Well's syndrome (9), it may not be surprising that KD can occur with vascular involvement. The massive eosinophil infiltration could mean that the vessels in the lesion were incidentally involved. Our data suggest that immunochemical events through IgE and eosinophil degranulation occurred at the vascular walls, which may have led to vascular damage.

So far, there has been no case of KD reported which transformed into malignant lymphoma. Chim et al. (10) reported a case with indolent and recurring course, but no TCR or IgH re-arrangements. On the other hand, there are plenty of cases of cutaneous lymphoma with prominent eosinophilic infiltration (11–13). These cases show atypical lymphocytes with positive TCR or immunoglobulin re-arrangement, which would be essential for a diagnosis of malignant lymphoma. However, the lymphocytes in our case were mostly small and showed no atypia, monoclonality or architectural abnormality. In addition, our case did not have TCR or immunoglobulin re-arrangements, and had not shown any signs of recurrence over the last 6 years.

EBV involvement in KD has not been established except in one case with positive EBV DNA from the lesion (14). EBV DNA was detected in our case, but in situ hybridization could not detect EBER in the lesion. The contribution of EBV to the present disease is thus not clear.

Serum TARC level was highly elevated to 4986.2 pg/ml compared with normal controls (15), but decreased after systemic glucocorticoid treatment to 428.1 pg/ml.

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