Kimura's disease masquerading as parotid malignancy

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This case report highlights the fact that Kimura's disease, although rare, can masquerade as cancer, especially when it involves the parotid gland.

Introduction

Kimura's disease is a rare chronic inflammatory disease of unknown etiology, which was initially described in 1937[1] but popularized in 1947 by Kimura.[2] Only about 200 cases have been reported in the literature hence mis-diagnosis and non-recognition are common. It generally affects the skin, soft tissues and lymphatics of the head and neck region and, rarely, it may involve other regions like retro peritoneum, groin, and trunks and limbs.[3–6] The lymph node groups, especially the axillary, epitrochlear, popliteal and inguinal, may be more commonly involved. Presentation in the form of subcutaneous swellings, lymphadenopathy and recurrences after treatment being common make confusion with malignancy likely as in the presented case. All forms of treatment have been tried – including surgery, radiotherapy, immunosuppressive therapy, etc. However, there is no consensus on the correct modality in view of the limited number of reported cases and the treatment remains individualized. There is a very high incidence of recurrence following surgery or other treatment modalities.[6–8]

The disease more commonly affects Asian men in their second and third decades. The usual clinical features include multiple, painless, subcutaneous swellings and generalized lymphadenopathy accompanied by peripheral eosinophilia and raised serum immunoglobulins, especially IgE. Unlike most allergic disorders, the overlying skin is usually healthy. The only known systemic manifestation is renal involvement in the form of glomerulonephritis and, rarely, nephrotic syndrome. It is thought to be more common in Asia – especially in Japan and China – however, sporadic cases from the West have also been reported.[3]

In the presented case, on account of history of recurrence and the hard consistency of the gland associated with regional lymphadenopathy there was reason to suspect malignancy. Fine needle aspiration cytology (FNAC) was inconclusive on two occasions and the patient was treated as a suspected case of parotid malignancy. Kimura's disease was thus a histo-pathological surprise.

Case history

A 32-year-old Indian man, a cobbler by trade, presented in May 2003 with a recurrent right parotid swelling which was gradual in onset but had started growing rapidly in the previous six months. There were no symptoms suggestive of facial nerve involvement. He had undergone superficial parotidectomy for pleomorphic adenoma of the right parotid four years previously. He also had a history of chronic generalized itching for the past 10 years for which he was on irregular medication in the form of antihistamines and steroids. Examination revealed a hard, fixed and non-tender, 6 × 6 cm, right parotid swelling with a well-healed scar of previous surgery (Figure 1). There were no features of inflammation or facial nerve involvement.

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There were two discrete, mobile, non-tender and firm level-II lymph nodes on the right side (Figure 1). He also had multiple, non-tender subcutaneous swellings all over the body including the chest, arms and neck (Figure 2).

Investigations revealed anaemia (Hb = 10.5 gm %), and marked eosinophillia (Eosinophils 20%). Other biochemical investigations, including liver and kidney function tests, urine examination were within normal limits. As the FNAC from the parotid swelling, as well as the lymph nodes and biopsy from the subcutaneous swellings, were inconclusive on two occasions, malignancy was suspected in view of the history of recurrence and presence of regional lymph nodes, which did not disappear on antibiotic therapy. The patient was treated by total conservative parotidectomy and selective neck dissection on the right side (Figure 3). Postoperative recovery was good with minimal neuropraxia of the facial nerve, which recovered within a week. The histopathological examination of the resected specimen showed near-complete replacement of the gland by lymphoid follicles, which showed high percentage of eosinophils and epitheloid cells. The blood vessels were hyalinised, sclerosed and showed perivascular eosinophilic infiltration (Figure 4). Histopathological examination of the subcutaneous nodules showed numerous giant cells and eosinophilic granulomas with infiltration of the entire background with lymphatic tissue – predominantly eosinophils. A diagnosis of Kimura's disease was thus made.

Figure 1
The right parotid swelling with level-II, level-V lymph node enlargement

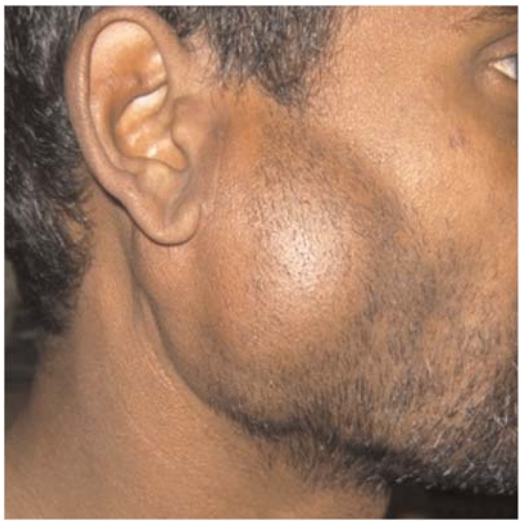
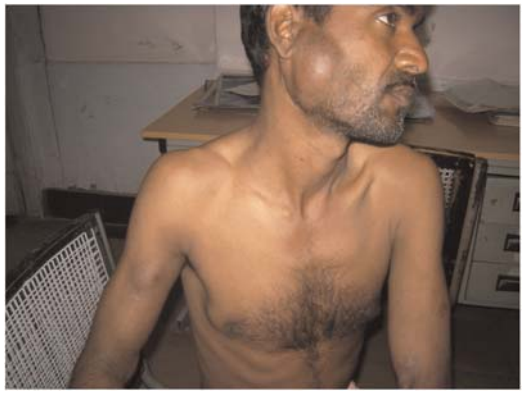


Figure 2
The subcutaneous swelling on the arm



Investigations were carried out in view of the histopathological diagnosis to conclusively rule out other possibilities. These included differential immunoglobulin levels, which showed increased levels of IgE and normal levels of other immunoglobulins. ELISA for HIV was negative. Stain for acid fast bacillus in the specimen was negative.

The patient was put on steroids and received radiotherapy in fractionated doses of 25–30 Gy

Figure 3
Total conservative parotidectomy in progress. The facial nerve is clearly visible and the affected gland is about to be removed

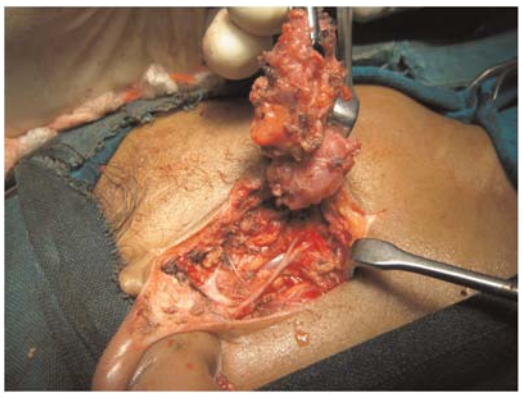
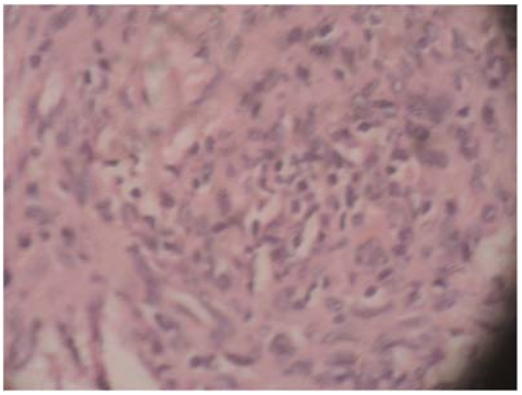


Figure 4
Photomicrograph showing the gland parenchyma replaced by lymphoid follicles showing high percentage of eosinophils and epitheloid cells. The blood vessels hyalinised, sclerosed and showed peri-vascular eosinophilic infiltration



over six weeks. Since he was already taking occasional antihistamines for atopic dermatitis, he was also put on a regular third-generation antihistamine, which is known to prevent relapses. A follow-up of eight months has been satisfactory.

Discussion

Kimura's disease is a rare chronic inflammatory lymphoproliferative disorder and usually presents as multiple soft tissue swellings along with lymphadenopathy in the head and neck region with a predilection for parotid and submaxillary glands. The aetiology is not known and many theories with varying degrees of evidence have been hypothesized. It is believed to be a form of chronic allergic disorder due to atopic reaction to a stimulus which is most commonly *Candida albicans.*[4] Human herpes virus-8 and Epstein-Barr virus have also been suggested as the causative agents without any conclusive evidence.[5,6] An increased incidence of the disease occurring in patients undergoing haemodialysis and patients of nephrotic syndrome has also been considered very significant and immunosuppression may be a contributory factor.[7] An association of Kimura's disease with juvenile temporal arteritis has also been suggested.[8]

It is believed that an unknown stimulus persistently activates the immune system and leads to clonal proliferation of Helper T cells, which may also lead to high expression of IL-4, IL-5, IL-13, which are potent stimulators of eosinophilic proliferation. This may finally lead to peripheral eosinophilia and increased levels of IgE in the serum.[8]

The histopathological picture is characterized by destruction of the normal architecture and replacement with a heavy lymphoid infiltrate along with numerous lymphoid follicles with prominent germinal centres. The interfollicular infiltrates are rich in eosinophils and plasma cells that form micro-abscesses. Numerous thin-walled vessels showing sclerosed walls and perivascular eosinophilic infiltrates are also found.

Kimura's disease closely resembles angiolymphoid hyperplasia and they were earlier thought to be the same disease. The latter, however occurs mostly in middle-aged women in contrast to young men suffering from Kimura's disease. Angiolymphoid hyperplasia causes erythematous plaques or nodules in the skin and shows vacuolated endothelial cells with destruction of blood vessel architecture but preservation of the germinal follicular and glandular structure, unlike Kimura's disease. Also, germinal centres in Kimura's disease stain positively for IgE unlike angiolymphoid hyperplasia.

Other differential diagnoses of Kimura's disease include Mikulicz disease, acute lymphocytic leukemia, Hodgkin's disease, angioimmunoblastic lymphadenopathy and eosinophilic granuloma.[6–9]

The treatment of this disease is not yet standardized as there are only few reported case series.[3,4] However, various modalities are in use including surgery, radiotherapy, steroids and immunosuppressive therapy with cyclosporine. In general, surgery is recommended for large lesions causing discomfort or cosmetic deformity or those not responding to conservative treatment. Steroids and radiotherapy in doses of 25–30 Gy prevent relapses and may even cause regression, but side-effects such as xerostomia have to be considered. Cyclosporine is useful for multiple relapses.

In this case, a recurrence of parotid swelling and involvement of regional lymph nodes led us to consider the possibility of parotid neoplasm. However, the non-involvement of facial nerve despite recurrence and finally the histopathological and biochemical investigations conclusively excluded the possibility of a neoplasm and proved this to be a case of Kimura's disease.

Conclusions

This case provides an interesting and instructive insight as to how recurrent parotid swellings with architectural destruction may also prove to be benign and how certain rare diseases can pose as major diagnostic dilemmas.

References

1 Kim HT, Szeto C. Eosinophilic hyperplastic lymphogranulomas, comparision with Mikulicz's disease. *Proc Chin Med Soc* 1973;**23**:699–700

2 Kimura T, Yoshimura S, Ishikawa E. On the unusual granulation combined with hyperplastic changes of lymphatic tissue. *Trans Soc Pathol Japan* 1948;**37**: 179–80

3 Atar S, Oberman AS, Ben-Izak O, Flatau E. Recurrent nephrotic syndrome associated with Kimura's disease in a young non-Oriental male. *Nephron* 1994;**68**:259–61

4 Armstrong WB, Allison G, Pena F, Kim JK. Kimura's disease: two case reports and a literature review. *Ann Otol Rhinol Laryngol* 1998;**107**:1066–71

5 Jang KA, Ahn SJ, Choi JH, *et al*. Polymerase chain reaction (PCR) for human herpes virus 8 and heteroduplex PCR for clonality assessment in angiolymphoid hyperplasia with eosinophilia and Kimura's disease. *J Cutan Pathol* 2001;**28**:363–7

6 Nagore E, Llorca J, Sanchez-Motilla JM, Ledesma E, Fortea JM, Aliaga A. Detection of Ebstein-Barr virus DNA in a patient with Kimura's disease. *Int J Dermatol* 2000;**39**: 618–20

7 Hung CC, Liao PL, Chang CT, Wu MS, Huang CC. Steroid-sensitve anemia in a boy on dialysis – an association with Kimura's disease. *Paediatr Nephrol* 2000;**15**:183–5

8 Watanabe C, Koga M, Honda Y, Oh-I T. Juvenile temporal arteritis is a manifestation of Kimura's disease. *Am J Dermatopathol* 2002;**24**:43–9

9 Hareyama M, Oouchi A, Nagakura H, *et al*. Radiotherapy for Kimura's disease: the optimum dosage. *Int J Radiat Oncol Biol Phys* 1998;**40**:647–51