Case Report

Cytological features of Kimura's disease: A case report with histological correlation

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ABSTRACT

Kimura's disease and angiolymphoid hyperplasia with eosinophilia (ALHE) together form a spectrum of chronic inflammatory disorders of unknown etiology with similar and overlapping histological features. We report a case of Kimura's disease in a young Indian girl with its cytohistological correlation. The cytological features of these inflammatory disorders are fairly specific and in an appropriate clinical setting, a cytological diagnosis of Kimura's/ALHE is possible. However, it may not be possible to differentiate between the two based on cytology alone.

Key words: Angiolymphoid hyperplasia with eosinophilia, cytology, Kimura's disease

INTRODUCTION

The earliest description of Kimura's disease dates back to 1937, when Kimm and Szeto reported 7 cases of eosinophilic hyperplastic lymphogranuloma from China.[1] The disorder is named after Kimura who in 1948 noted the vascular component and referred to it as an "unusual granulation combined with hyperplastic changes in lymphoid tissue."[2] Several publications have now conclusively separated this entity from angiolymphoid hyperplasia with eosinophilia (ALHE) with which it has several overlapping features.[3] It is believed that ALHE is an arteriovenous malformation with secondary inflammation. Kimura disease in contrast may represent a primary inflammatory process with secondary vascular proliferation.

Kimura's disease is endemic in Asia (Japan, China, Indonesia, etc.). It has been also been reported in Europe and America. It mainly affects young Asian men (male:female ratio 3.5 ~ 6.0:1). The lesions typically involve the subcutaneous tissues of the head and neck area, presenting as one or several deeper masses.[4] The masses are nontender, poorly circumscribed with diameters from 1 to 20 cm (mean 3 cm). The commonly involved sites were periauricular, groin, orbit, and eyelids. Other rare sites include the axilla, oral cavity, nasal sinuses, and median nerve.[5] Approximately 12-16% of the patients have nephropathy presenting as nephrotic syndrome with albuminuria and increased serum creatinine. Severe renal dysfunction has been found in rare cases.[6]

CASE REPORT

A 17-year-old girl from the Western Uttar Pradesh, India presented to the ENT outpatient department with complaints of bilateral postauricular swellings for the last 3 years. The right side swelling measured 3 cm × 2 cm × 1.2 cm [Figure 1] and the left side swelling measured 2.5 cm × 2 cm × 1.2 cm. The swellings did not increase in size and were painless. She experienced itching sensation every now and then in these soft tissue masses. There was no loss of weight or appetite or fever. She did not have associated cough, hemoptysis, or

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upper respiratory tract complaints. No urinary complaints or history of swelling all over the body could be elicited.

Her hemogram showed mild eosinophilia of 12%. She underwent fine needle aspiration cytology of both the swellings. The cytology report was descriptive and described reactive lymphoid tissue, Warthin–Finkeldey giant cells and eosinophils. No atypical cells were seen in Figure 2. The lesion was categorized as benign, and an excision biopsy was advised. The patient underwent excision biopsy of the left postauricular swelling. The excision specimen measured 2.5 cm × 1.2 cm × 1.0 cm in size and on cut section was gray white with areas of hemorrhage. The specimen was processed in entirety. The multiple sections examined showed several reactive lymphoid follicles with marked vascular proliferation. However, the endothelial lining of these vessels was not epithelioid – instead it was flattened [Figures 3 and 4]. Few Warthin–Finkeldey giant cells were also identified. Eosinophils were prominent, and eosinophilic folliculolysis was noted. The final histopathologic diagnosis of Kimura's disease was given. Immunocytochemistry for CD3 performed on destained cytology slide showed several Warthin–Finkeldey giant cells were immunopositive for CD3 [Figure 5].

A detailed history of urinary complaints was negative. The patient's blood urea nitrogen was 15 mg% and serum creatinine was 0.7mg%. The patient was advised excision of the other side swelling and educated about possible renal complications in future.

DISCUSSION

The cytological features of Kimura's disease are not very specific, however a good correlation with clinical findings and with blood eosinophilia can help one reach the right diagnosis in majority of cases. The main cytological differential diagnoses include parasitic infection and Hodgkin's lymphoma. The classical features of Kimura's disease on cytology include Warthin–Finkeldey giant cells, eosinophils, and reactive lymphoid background.

In 1931, Warthin and Finkeldey were the first to independently describe the appearance of the giant cells in tonsillar tissue during the prodromal stages of measles.[7] Warthin–Finkeldey giant cells have been described in measles infection, Human immunodeficiency virus (HIV) infection, and Kimura's disease and only rarely in lymphomas. Hence the presence

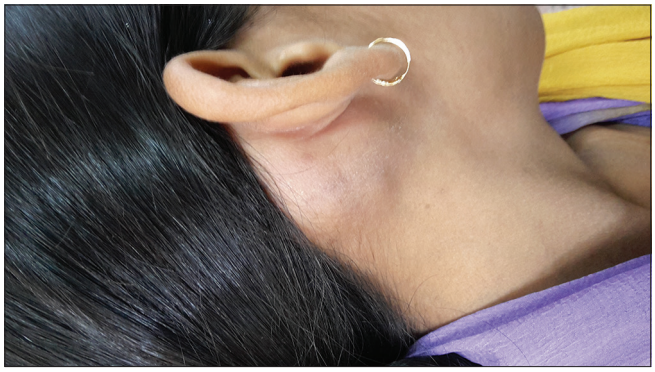

Figure 1: Clinical photograph of the right sided postauricular swelling. The overlying skin is mildly abraded due to scratching

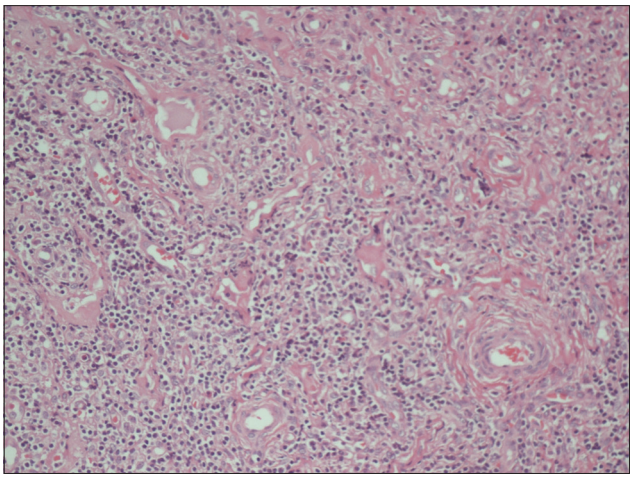

Figure 3: Hematoxylin and eosin (×20) thin-walled blood vessels with flattened endothelial lining and dense sclerosis in the surrounding areas. Many lymphocytes and few eosinophils are also noted

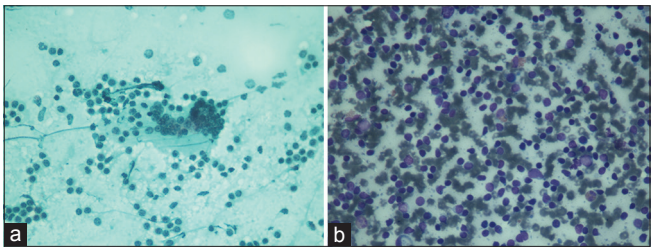

Figure 2: (a) Papanicolaou stained fine needle aspiration cytology smear showing Warthin–Finkeldey type giant cell (×40). (b) Giemsa stained cytology smear showing reactive lymphoid cells along with many eosinophils (×40)

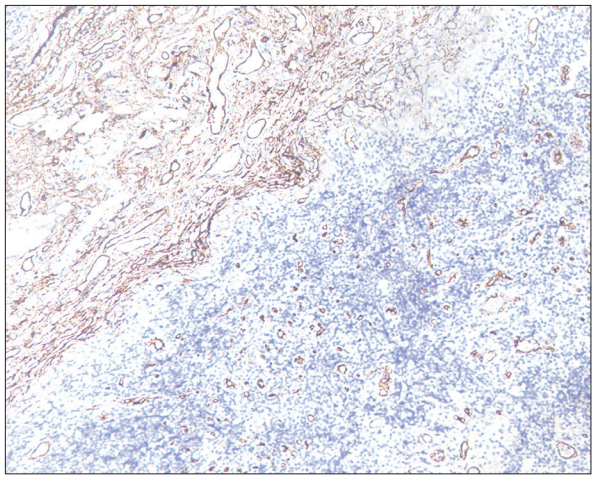

Figure 4: Immunohistochemistry for CD34 (×10) - Highly vascular lesion with thin-walled blood vessels and flattened endothelial lining

of these giant cells in any aspirate should prompt a careful search for atypical cells in the aspirate. Correlation with the clinical findings would also help since Kimura's disease usually presents with painless head and neck subcutaneous masses not associated with fever, weight loss, or constitutional symptoms. History of itching at the site, if elicited can help. The blood eosinophilia in Kimura's disease is usually mild (10-20%). History of nephrotic syndrome in the past or present may also be a pointer as 10-16% of patients with this disease have renal disease.

Warthin–Finkeldey giant cells have been reported in mucosa associated lymphoid tissue of stomach and appendix in cases of measles infection.[8] The origin of Warthin–Finkeldey giant cells have been studied in some detail. These cells express many T-cell markers including CD3.[9] In our case, too many Warthin–Finkeldey giant cells expressed CD3 [Figure 5]. In a study done on HIV patients, Warthin–Finkeldey-type giant cells and follicular dendritic cells shared characteristic morphologic (high N:C ratio; crowded, irregular nuclei; thin filaments with dense bodies; desmosomes; and cilia) and immunophenotypic (CD21+, CD35+, S-100+, p55+, and vimentin+) features.[10] Transmission electron microscopy revealed evidence of HIV expression by follicular dendritic cells but not Warthin–Finkeldey giant cells.[10]

Several authors have described the cytological features of Kimura's disease. All of them have stressed the need for the good clinical correlation for making the diagnosis.[11,12] Some authors use the terms ALHE and Kimura's disease interchangeably.[13] However, the clinical and histologic features of both the conditions are now well delineated [Table 1]. Coexistence of both the conditions in the same patient has also been reported.[14] Rare sites of involvement by Kimura's disease include orbit and epiglottis.[15,16] It is not possible to differentiate between the two based on cytological features alone.

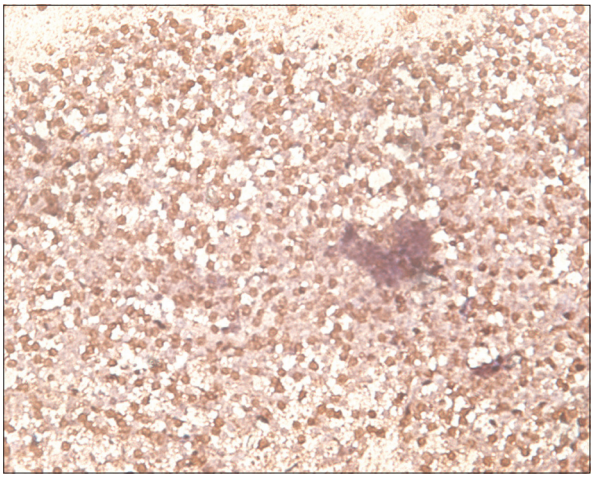

Figure 5: Immunocytochemistry for CD3 (×20) - Warthin–Finkeldey giant cell immunopositive for CD3 with several T lymphocytes in the background

Kimura's disease may affect kidneys in up to 16% of patients. In these cases, it may manifest as any of the glomerulonephritis or as a nephritic syndrome (12%).[6] In our case, there were no urinary complaints and the serum creatinine and blood urea levels were normal. However, the patient was informed about the possible renal implications of this disorder.

Histologically Kimura's disease shows reactive and prominent germinal centers with dense eosinophilic infiltration of the interfollicular zones, lysis of the follicles, and occasionally micro abscesses. Tissue fibrosis, sclerosis, and vascular proliferation are also present. Vessels are thin-walled. Rarely, the features include progressive destruction of germinal centers, and presence of polykaryocytes. Immunofluorescence tests show germinal centers containing heavy IgE deposits and variable amounts of IgG, IgM, and fibrinogen.[5]

There is no consensus on the management of Kimura's disease. Surgery is performed as a therapeutic and/or diagnostic procedure. Conservative treatment includes oral steroids which are reported to be responsible for decreasing size of the enlarged lymph nodes, but there is no evidence of reduction of the affected salivary gland size. Furthermore, the lesions usually get enlarged again when steroid treatment is terminated. Another positive effect of steroid treatment is that, it decreases renal symptoms as well.[17]

Remissions reach 25% in groups of patients treated surgically. Surgery and subsequent steroid treatment are proposed as an alternative regimen. Radiation therapy is useful to control lesions that are not responsive to steroids or with a relapse after surgery. Anti IgE therapy (omalizumab) has been recently tried in Kimura's disease with some success.[17]

Table 1: Comparison of clinical and histological features of Kimura's disease and angiolymphoid hyperplasia with eosinophilia

	Kimura's disease	Angiolymphoid hyperplasia with eosinophilia
Age	2nd–6th	3rd–4th
Sex	Male > female	Female > male
Ethnicity	Asians more common	Any
Peripheral eosinophilia	Usually present	Present in <10%
Histopathology	Marked follicular hyperplasia with eosinophil-rich infiltrate in the interfollicular area. Thin walled blood vessels with flattened endothelial lining are noted	Plump epithelioid appearance of endothelial cells is characteristic

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Conflicts of interest
There are no conflicts of interest.

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