BACKGROUND
Kimura's disease is a rare chronic inflammatory condition of unknown aetiology which has been most commonly reported in Asian population, with young male preponderance. It is a benign disease which has an indolent course & gradually increases in size over months or years. It primarily involves the head and neck region, presents as subcutaneous masses and is often accompanied by regional lymphadenopathy, salivary gland involvement along with lymphadenopathy or presents with only lymphadenopathy. Peripheral blood eosinophilia and elevated serum immunoglobulin E (IgE) levels are characteristic features. Microscopy reveals lymphoid proliferation with eosinophilic infiltration. For years, Kimura’s disease was believed to be identical to or part of the same disease spectrum as angiolymphoid hyperplasia with eosinophilia (ALHE). Recent reports, however, have confirmed that the two are, in fact, separate entities.

MATERIALS AND METHODS
It was a retrospective study undertaken over a period of one year from November 2016 to November 2017 in the Department of Pathology, Government ENT Hospital, Hyderabad. We report a study of eight (8) cases of Kimura's disease with usual and unusual sites of presentation and rare histomorphological features / microscopic features in one of the cases. Initially FNAC was performed with 22 gauge needle; smears were fixed in ether- 95% alcohol solution and stained with Haematoxylin and Eosin stain, whereas air dried smears stained with toluidine blue stain. Subsequently excised specimens of those swellings and lymph nodes received were subjected to routine processing, cutting, staining and histopathological features were analysed. Haemogram, serum IgE levels and renal parameters of all these patients were studied.

RESULTS
Both cytomorphic and histomorphological features were in favour of Kimura’s disease.

CONCLUSION
We report characteristic cytomorphic and histomorphological findings associated with peripheral eosinophilia and elevated serum IgE levels in eight patients with Kimura's disease.

KEYWORDS


BACKGROUND
Kimura Disease (KD) is a rare chronic inflammatory disorder, which was first described in 1937 by Kim and Szeto in the Chinese literature as “eosinophilic hyperplastic lymphogranuloma” and has been known most often as Kimura’s disease since its description by Kimura et al. in the Japanese literature in 1948. The most common clinical feature of this disease is a soft-tissue mass in the head and neck area, with major salivary glands and lymph nodes frequently involved. The disease is endemic in Asians (especially in China and Japan), but rare in India, with about 200 reported cases worldwide since its histopathological diagnosis. Non-Asian cases also have some histopathological features. There is marked male predominance with M: F ratio 3.5-7:1. It is found almost exclusively in Asian individuals in their 2nd to 4th decade of life mostly in males (70–80%).

KD is rare in India, with about 200 reported cases worldwide since its histopathological diagnosis. The disease is characterized by the triad of painless subcutaneous masses in head and neck, blood and tissue eosinophilia, and increased serum IgE levels. The diagnosis may be suggested by a fine needle aspirate, but a definite diagnosis of Kimura’s disease is established by histopathology. In differential diagnosis particular attention has to be paid to angiolymphoid hyperplasia with eosinophilia and neoplasms. Therefore to diagnose a case as Kimura’s
disease a thorough histomorphological features along with laboratory parameters such as peripheral eosinophilia and raised serum IgE levels are essential, other parameters such as raised ESR, renal function tests also helpful as some of the patients may present with renal impairment i.e. nephritic, nephrotic syndrome in association with Kimura's disease.

MATERIALS AND METHODS
It was a retrospective study undertaken over a period of one years from November 2016 to November 2017 in the Department of Pathology, Government ENT Hospital, Hyderabad. We report case series of eight (8) cases of Kimura’s disease with usual and unusual sites of presentation and rare histomorphological features / microscopic features in one of the case. Initially FNAC was performed with 22 gauge needle; smears were fixed in ether-95% alcohol solution and stained with Haematoxylin and Eosin stain, whereas air dried smears stained with toluidine blue stain. Subsequently/further excised specimens of those swellings and lymph nodes received were subjected to routine processing, cutting, staining and histopathological features were analysed. Haemogram and serum IgE levels of all these patients were studied.

RESULTS

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Age Years</th>
<th>Sex</th>
<th>Site</th>
<th>Duration</th>
<th>Cytology Findings</th>
<th>Histology Findings</th>
<th>HB</th>
<th>TLC/WBC</th>
<th>Peripheral Eosinophils</th>
<th>Absolute Eosinophil Count (cells/μl)</th>
<th>Serum IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-1</td>
<td>9</td>
<td>M</td>
<td>Bilateral (B/L) posterior auricular lymph nodes</td>
<td>8 months</td>
<td>KD</td>
<td>KD</td>
<td>12.5</td>
<td>7600</td>
<td>16</td>
<td>1216</td>
<td>764</td>
</tr>
<tr>
<td>Case-2</td>
<td>17</td>
<td>M</td>
<td>Bilateral (B/L) posterior auricular lymph nodes</td>
<td>10 months</td>
<td>KD</td>
<td>KD</td>
<td>12.1</td>
<td>8000</td>
<td>18</td>
<td>1440</td>
<td>1016</td>
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<tr>
<td>Case-3</td>
<td>17</td>
<td>M</td>
<td>Right submandibular salivary gland and cervical lymphadenopathy</td>
<td>1 year</td>
<td>KD</td>
<td>KD</td>
<td>13</td>
<td>11100</td>
<td>29</td>
<td>3219</td>
<td>1586.1</td>
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<tr>
<td>Case-4</td>
<td>18</td>
<td>M</td>
<td>posterior auricular lymph nodes</td>
<td>1 year</td>
<td>KD</td>
<td>KD</td>
<td>11</td>
<td>10,200</td>
<td>22</td>
<td>2244</td>
<td>1293</td>
</tr>
<tr>
<td>Case-5</td>
<td>20</td>
<td>M</td>
<td>Bilateral (B/L) posterior auricular lymph nodes</td>
<td>1.5 year</td>
<td>KD</td>
<td>KD</td>
<td>14</td>
<td>9700</td>
<td>19</td>
<td>1843</td>
<td>1201.5</td>
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<tr>
<td>Case-6</td>
<td>20</td>
<td>M</td>
<td>Bilateral anterior cervical lymph nodes</td>
<td>2 years</td>
<td>KD</td>
<td>KD</td>
<td>10</td>
<td>7900</td>
<td>17</td>
<td>1343</td>
<td>1166</td>
</tr>
<tr>
<td>Case-7</td>
<td>21</td>
<td>M</td>
<td>Right posterior triangle neck lymph node</td>
<td>2.5 years</td>
<td>KD</td>
<td>KD</td>
<td>13.5</td>
<td>7200</td>
<td>23</td>
<td>1656</td>
<td>1248</td>
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<tr>
<td>Case-8</td>
<td>35</td>
<td>F</td>
<td>Right - suboccipital subcutaneous mass, lymph nodes: Right suboccipital, posterior triangle of neck &amp; jugulodigastric.</td>
<td>1 year</td>
<td>KD</td>
<td>KD</td>
<td>11.3</td>
<td>12,200</td>
<td>25</td>
<td>3125</td>
<td>1687.2</td>
</tr>
</tbody>
</table>

Table 1. Age, Sex, Site & Duration of the Swellings and Other Clinical & Laboratory Parameters of the Individual Patients
Initially all these patients underwent fine needle aspiration cytology (FNAC) of the swellings. (Figure 1)

![Figure 1. Showing Post Auricular and Cervical Swellings in Various Cases](image1)

Cytology Features / Findings
Cytology smears showed lymphocytes in various stages of maturation admixed along with numerous eosinophils, histiocytes and endothelial cells against scant haemorrhagic background. (Figure 2, 3, 4)

![Figure 2, 3, 4](image2)

Figure 2, 3 and 4. Cytosmears Showing Polymorphous Population of Lymphoid Cells Accompanied by Epithelioid Endothelial Cells and Eosinophils.

Based on these features we reported these cases as Kimura’s disease and further suggested correlation with blood eosinophils and serum IgE levels.

After undergoing further investigations, they underwent surgery and those excised specimens subsequently processed for histopathological examination.

Histomorphological Features / Findings

![Figure 5. Gross Features Depicting External and Cut Surfaces of Swelling and Lymph Nodes](image5)

Figure 5. Gross Features Depicting External and Cut Surfaces of Swelling and Lymph Nodes

![Figure 6. Microphotograph showing Numerous Reactive Follicles with Expanded Germinal Centres](image6)

Figure 6. Microphotograph showing Numerous Reactive Follicles with Expanded Germinal Centres

![Figure 7. Photomicrograph showing Eosinophilic Abscess and Granulomatous Reaction to Charcot Leyden Crystals](image7)

Figure 7. Photomicrograph showing Eosinophilic Abscess and Granulomatous Reaction to Charcot Leyden Crystals

Microscopic features of excised specimens revealed lymphoid follicles of varying sizes with hyperplastic prominent germinal centres with areas of eosinophilic infiltration, numerous eosinophils in inter-follicular areas, forming occasional eosinophilic abscesses, eosinophilic granules encrusted on collagen. There are numerous
vascular channels which are lined by flat endothelial cells. All these histological features are consistent with Kimura’s disease. In addition to the above findings in one case who had right submandibular gland swelling along with cervical lymphadenopathy showed multiple epithelioid granulomas with central eosinophilic abscesses and necrosis, Langhans-type giant cells, apoptotic eosinophils, and Charcot–Leyden crystals at the edges of the granulomas. These histopathological features were consistent with Kimura’s disease. Thus correlating the clinical, laboratory and histopathological features, the conclusive diagnosis of Kimura’s disease has been done.

DISCUSSION

The term Kimura’s disease came into usage after a detailed description by Kimura et al in 1948. It is a rare disease of unknown aetiology. Though its aetiology remains unclear, thought to be an aberrant immune response to some unknown antigenic stimulus. Most commonly prevalent in young males of Asia, whereas its prevalence in other ethnicities is considered low.

In our study among 8 patients, 7 of them were males and only 1 patient was female and the youngest was of 9 years old boy and the oldest was of 35 years old female. The disease is characterized by the development of soft subcutaneous masses commonly over the head and neck region with or without lymphadenopathy, in this study most of them presented with posterior auricular lymph node (5) swellings, cervical lymphadenopathy (1), left submandibular swelling along with cervical lymphadenopathy (1) of same side, right suboccipital subcutaneous along with right suboccipital, posterior triangle and jugulodigastric lymphadenopathy (1) and subcutaneous arm/forearm (1) swelling. In all these patients peripheral smear showed peripheral blood eosinophilia similar to that of studies done by Suguna et al, Kian et al as well as elevated total serum IgE levels similar to that of David et al, Nanzaan et al, Roslan Abdul Rahman et al and Arun saiin et al and marked increase in serum levels of immunoglobulin E (IgE). It can often have a relapsing course and recurrences are seen to occur despite treatment.

Kimura’s disease should be suspected when a patient—particularly an Asian male—exhibits the clinical trial of a painless head or neck mass, eosinophilia, and an elevated serum IgE level. There can also be salivary gland swellings and renal involvement presenting as nephrotic syndrome. The soft tissue masses in Kimura’s disease often mimic an inflammatory or neoplastic process clinically.

Our patients presented with asymptomatic painless swellings which on FNAC showed proliferating endothelial cells, lymphocytes in various stages of maturation, histiocytes along with eosinophils on H&E that are characteristic of Kimura’s disease. Raised peripheral blood eosinophils and serum IgE levels detected in all these patients. There was no renal functional impairment in these patients. Excision specimens are essential to make a definitive diagnosis, all those resected specimens showed almost similar histomorphological features. They are lymphoid follicles of varying sizes with hyperplastic germinal centers, infiltration of eosinophils, eosinophilic abscesses, and diffuse infiltrate of eosinophils in the interfollicular areas as well as in perivascular areas, vascular proliferation and varying degrees of fibrosis. Some lymphoid follicles show interstitial homogenous eosinophilic material between the germinal centre cells. There is also a tendency for eosinophils to infiltrate the germinal centers resulting in necrosis of the centre structure. Admixed along with them histiocytes, plasma cells and mast cells.

Unusual findings in one of the cases who had presented with right submandibular gland swelling and cervical lymphadenopathy of the same side was the presence of numerous apoptotic cells in the infiltrating eosinophils and epithelioid granulomas with central eosinophilic abscesses and necrosis and Charcot laden crystals, Phagocytosis of apoptotic eosinophils was also observed at the edges of the granulomas similar to that of HOSAKA et al. As well as destruction of the salivary gland tissue, areas of fibrosis and dense eosinophilic infiltrate seen.

Kimura’s disease has to be distinguished histologically from other entities such as angiolymphoid hyperplasia with eosinophilia (ALHE), Hodgkin lymphoma, angioimmunoblastic T-cell lymphoma, Langerhans cell histiocytosis, florid follicular hyperplasia, Castleman disease, dermatopathic lymphadenopathy, allergic granulomatosis, parasitic lymphadenitis and drug reaction. However, among these entities ALHE is the closest differential diagnosis of Kimura’s disease. ALHE presents superficially in the skin as dermal papulonodules, middle aged women and the characteristic feature of this entity is the peculiar epithelioid/histiocytoid endothelial cells whereas in Kimura’s disease vessels are lined by flattened endothelial cells.

Though Kimura’s disease is benign in nature, definitive treatment modalities are not available till date. Therapeutic options include surgery, radiotherapy, laser fulguration, photodynamic therapy and steroids. Steroid is effective in reducing size of the mass, but the lesions may recur while reducing the dose of steroid.

CONCLUSION

Presence of painless swellings in the head and neck region in young males should raise the suspicion of Kimura’s disease. A clinical triad of painless swelling, peripheral blood eosinophilia and raised serum IgE levels are one of the characteristic features. Though cytomorphology aids in diagnosing Kimura’s disease, histomorphological features are essential to establish a definitive diagnosis of Kimura’s disease.

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