Kimura Disease

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• Kimura disease is a benign rare chronic inflammatory disorder of unknown etiology that involves the lymph nodes and subcutaneous tissue of the head and neck regions. Elevated serum immunoglobulin E levels and peripheral blood eosinophilia are also common. This disease is most common in middle-aged Asian men. Although the etiology is unknown, it most probably represents an aberrant chronic immune response. Treatment for Kimura disease includes surgical resection and regional or systemic steroid therapy. Cytotoxic therapy and radiation have also been utilized. The disease has an excellent prognosis, although it may recur locally.

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Kimura disease was first described in 1937 by Kim and Szeto in the Chinese literature as ''eosinophilic hyperplastic lymphograuloma''[1] and was later characterized by Kimura et al in 1948 in a manuscript titled ''On the unusual granulation combined with hyperplastic changes of lymphatic tissue.''[2]

CLINICAL FEATURES

Kimura disease is a rare benign chronic inflammatory disease that usually involves deep subcutaneous tissue and lymph nodes of the head and neck region with frequent regional lymphadenopathy or salivary gland enlargement. Other sites of involvement including the oral cavity, axilla, groin, limbs, and trunk have also been described. Systemic symptoms (fever, night sweats, and weight loss) are not common. This disease is most common in middle-aged Asian men. It is endemic in Asia (China and Japan) and sporadic in the non-Asian population. The peak age of onset is the third decade. Elevated serum immunoglobulin E (IgE) levels and peripheral blood eosinophilia are also common.

HISTOPATHOLOGY

The most common histologic features of Kimura disease include preserved nodal architecture (Figure 1); follicular hyperplasia with reactive germinal centers; well-formed mantle zones; eosinophilic infiltrates involving the interfollicular areas (Figure 2), sinusoidal areas, perinodal soft tissue (Figure 3), and subcutaneous tissue; and proliferation of postcapillary venules. The histologic features of Kimura disease were recently reviewed by Chen et al.[3] The following can also be observed: proteinaceous deposits in germinal centers, vascularization of germinal centers (Figure 1), necrosis of germinal centers, polykaryocytes (Warthin-Finkeldey–type giant cells), eosinophils in germinal centers, eosinophilic folliculolysis, eosinophilic microabscesses, postcapillary venule proliferation, stromal sclerosis, perivenular sclerosis, rare giant cells (Warthin-Finkeldey–type giant cells), or small eosinophilic granulomas. Sclerosis of variable degrees is often observed. Immunohistochemical staining with IgE shows a characteristic reticular staining pattern of germinal centers[3] (Figure 4).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes angiolymphoid hyperplasia with eosinophilia (ALHE), Hodgkin lymphoma, angioimmunoblastic T-cell lymphoma, Langerhans cell histiocytosis, florid follicular hyperplasia, Castleman disease, dermatopathic lymphadenopathy, allergic granulomatosis of Churg and Strauss, drug reaction, and parasitic lymphadenitis. Kimura disease and ALHE were often considered identical in the past literature. However, ALHE is a neoplasm of blood vessels, whereas Kimura disease is a chronic inflammatory disorder. Patients with ALHE present with a subcutaneous mass in the head and neck region. Microscopically, the vascular endothelium may form aggregates and lobules lined by plump cuboidal or hobnail endothelial cells, which frequently involve large muscular vessels. Regional lymphadenopathy, serum eosinophilia, and elevated IgE levels are uncommon in ALHE.[4]

PATHOGENESIS

The etiology and the pathogenesis of Kimura disease are unknown. The disease is classified as a benign reactive process. Allergic reactions, infections, and autoimmune reactions with an aberrant immune reaction have been suggested.[5] The findings of increased eosinophils, mast cells, and levels of interleukin 5 and IgE suggest an abnormal T-cell stimulation to a hypersensitivity-type reaction.[6] Molecular diagnostic studies for immunoglobulin heavy-chain and T-cell receptor gene rearrangement in 2 studies support a reactive nature.[7,8] Interestingly, a recent single case report by Chim et al[9] describes a clonal T-cell receptor gamma gene rearrangement by polymerase chain reaction in an elderly man with Kimura disease. The clonal T-cell rearrangement was also confirmed by complete sequencing of the VDJ rearrangement. Specimens from previous biopsies also showed the same rearrangement by polymerase chain reaction.

TREATMENT AND PROGNOSIS

The primary treatment for Kimura disease includes surgical resection. Additional medical therapy including regional or systemic steroid therapy, cytotoxic therapy, and radiation has also been utilized. Considered as an inflam-

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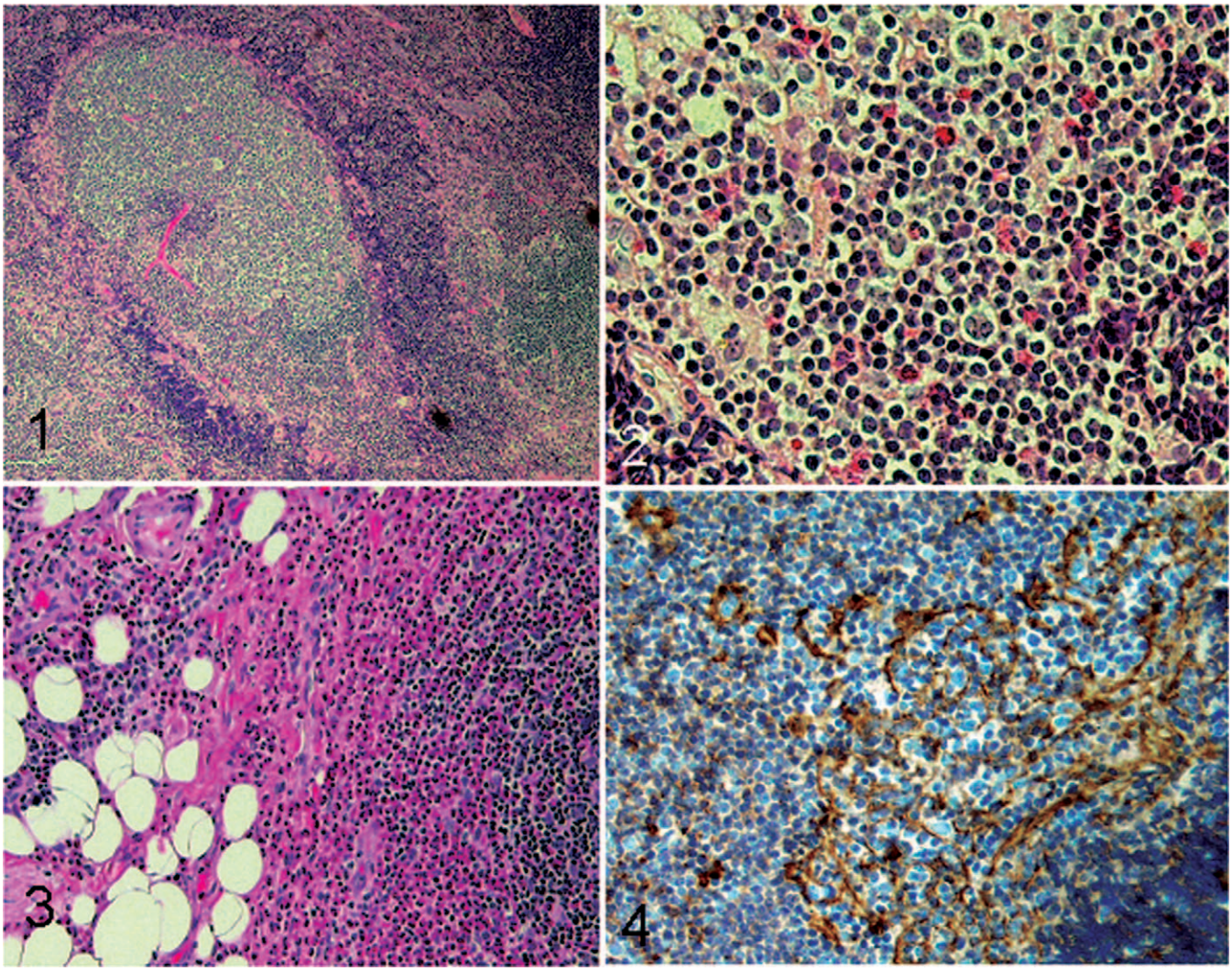

Figure 1. *Micrograph of preserved nodal architecture with hyperplastic follicles that were vascularized in a lymph node involved by Kimura disease (hematoxylin-eosin, original magnification ×100).*

Figure 2. *High-power photomicrograph demonstrating increased eosinophils in the paracortex (hematoxylin-eosin, original magnification ×1000).*

Figure 3. *Photomicrograph demonstrating increased eosinophils in the perinodal soft tissue (hematoxylin-eosin, original magnification ×200).*

Figure 4. *Immunohistochemical stain demonstrating the intact dendritic meshwork in a lymph node involved by Kimura disease (immunoglobulin E, original magnification ×1000).*

matory process, the disease has an excellent prognosis, although it may recur locally and wax and wane over time. Renal involvement in the form of nephrotic syndrome may affect up to 60% of patients.

CONCLUSION

In summary, Kimura disease is a rare chronic inflammatory disorder of unknown etiology that involves the subcutaneous tissue of the head and neck regions. It is usually associated with regional lymphadenopathy and/or salivary gland involvement. The most common histologic features are preserved nodal architecture; follicular hyperplasia with reactive germinal centers; well-formed mantle zones; eosinophilic infiltrates involving the interfollicular areas, sinusoidal areas, perinodal soft tissue, and subcutaneous tissue; and proliferation of postcapillary venules. This disease is most common in middle-aged Asian men. Kimura disease has a benign indolent course that may wax and wane over time.

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