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KIKUCHI – FUJIMOTO DISEASE. CASE REPORT AND A BRIEF REVIEW OF THE LITERATURE

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Abstract
Kikuchi Fujimoto disease (KFD) was first described in Japan in 1972 almost simultaneously by Kikuchi and Fujimoto. It is a rare, self-limiting, benign form of histiocytic necrotizing lymphadenitis, which can be mistaken for tuberculosis, lymphoma or systemic lupus erythematosus. Although the pathogenesis of KFD is not fully understood, infectious and autoimmune etiologies have been proposed. It generally presents as cervical lymphadenopathy with associated systemic signs and symptoms. Definitive diagnosis requires histopathological examination of the affected lymph nodes. There are only few cases described in the literature, as far as we are aware we report the first case of KFD in the Dominican Republic.

Key words: Kikuchi Fujimoto disease; Histiocytic necrotizing lymphadenitis; lupus erythematosus, tuberculosis

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Introduction

Kikuchi – Fujimoto disease (KFD), also called histiocytic necrotizing lymphadenitis, was first reported in 1972 simultaneously by two Japanese authors, Kikuchi and Fujimoto as a "Lymphadenitis characterized by a focal proliferation of reticular cells accompanied by nuclear debris and phagocytosis" and a "cervical subacute necrotizing lymphadenitis" respectively [1,2]. After its initial publication in Japan this entity was described outside the Asian continent for the first time by Pileri and coworkers that reported a series of cases from West Germany, Iran, Italy, South Korea, and Spain [3]. Many similar cases have subsequently been reported and it is now an entity recognized worldwide.

KFD is a benign disorder, predominantly affecting young women. It generally presents as cervical lymphadenopathy but other involved locations have been reported [4]. It is diagnosed by lymph node biopsy with distinctive features that include histiocytic necrotizing lymphadenitis without granulomas or caseous necrosis. Tuberculosis (TB), sarcoidosis, lymphoma and autoimmune diseases should be excluded [5]. Certain authors have reported association of the disease with autoimmune diseases such as systemic lupus erythematosus (SLE) [6-9].

Case Report

A 40 year-old female visited our institution complaining of cervical and axillar nodules for the past 3 months. On examination tender mobile nodules were found on palpation of right axillar region. Past medical history was positive for axillar nodular adenopathies 6 years before with a biopsy performed reporting granulomatous infiltrate with giant cells and caseous necrosis (Fig. 1). Anti-tuberculosis drug regimen was given for 9 months with resolution of the symptoms. 25 years before patient also presented to our institution with a malar rash and a biopsy consistent with chronic discoid lupus showing spontaneous remission thereafter.

An excisional biopsy of the node was performed by the dermatologic surgery department of our institution which showed a lymph node with an architecture partially effaced by a paracortical expansion with wide areas of apoptotic necrosis and diffuse atypical changes (Figs. 2 - 4). Immunohistochemestry analysis were done with positive markers for CD45, CD20, CD3, CD5 and CD10. Serologic analysis reported positive for the presence of antinuclear antibodies (ANA), other tests that included complete blood count, urianalysis, erythrosedimentation rate were reported within normal limits.

Three months later the patient reported the presence of new nodes in her right breast. An ultrasound of soft tissue was performed reporting three ovoid hypoechogenic images with an echogenic hilus suggestive of necrotized lymphadenopathies.

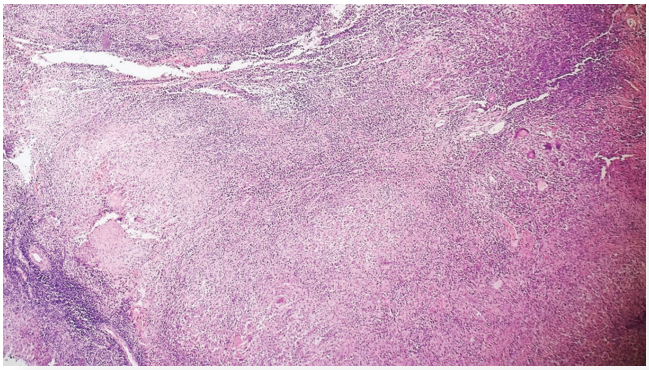

Figure 1. Lymph node with a dense granulomatous infiltrate with foci of caseous necrosis. HE 4X

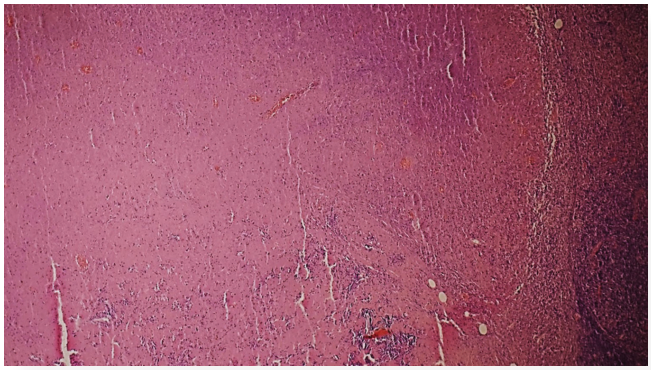

Figure 2. Lymph node with architecture partially effaced by paracortical expansion. HE 4X

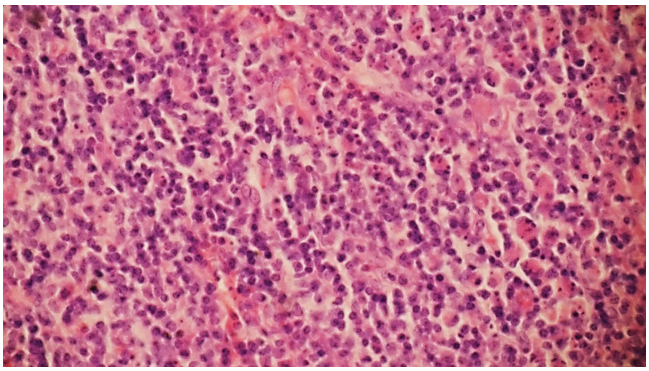

Figure 3. Dense infiltrate constituited by histiocytes, some lymphocytes with augmented nuclei and karyorrhexis. HE 40X

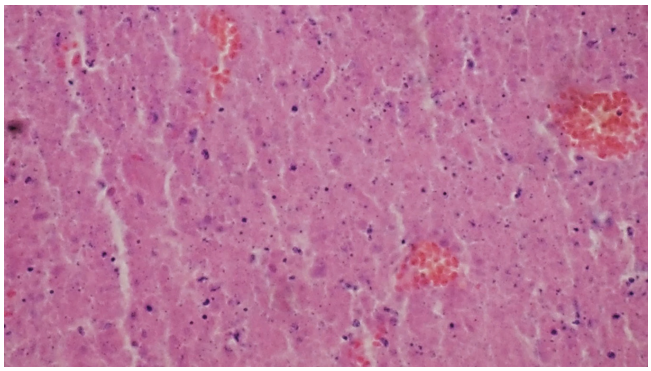

Figure 4. Marked apoptotic necrosis with kariorrhectic debris and dilated and congestive vessels. HE 20X

Discussion

KFD remains an enigmatic condition of unclear etiology with a low prevalence in our geographic area with no reported cases in our country. It is suggested that viral agents, hyperimmune reactions triggered by different antigens and cellular apoptosis are involved in its etiology [10]. Toxoplasma and other bacteria like Yersinia, Bartonella and Brucella have also been implicated as possible triggering agents [11].

The viral hypothesis has been subject of intense research, in fact, it has been emphasized the role of Epstein Barr virus, cytomegalovirus and human herpes virus 6 in eliciting a hyperimmune reaction lead by cytotoxic lymphocytes T towards infected lymphocytes [10,12]. Among the viral antigens listed above, Epstein-Barr virus has been studied most extensively in KFD, but no causal relationship has been demonstrated [13].

Other investigators emphasize the role of immunological mechanisms involved in the pathogenesis of KFD, related with SLE [6-9]. Electron microscopic studies have revealed tubular reticular structures in the cytoplasm of activated lymphocytes and histiocytes in KFD similar of those found in endothelial cells and lymphocytes in patients with SLE [14]. Associations with other autoimmune diseases have been also reported such as Hashimoto's thyroiditis, polymiosytis, mixed connective tissue disease, Still's disease and autoimmune hepatitis [10]. It has been suggested that ANA test should be performed in patients with suspected Kikuchi's syndrome in order to exclude SLE [11].

Clinically the presentation of KFD and TB and SLE may overlap and it may be difficult to segregate them. They may present with fever, upper respiratory sign symptoms, skin rashes, hepatosplenomegaly, weight loss, night sweats, anorexia, diarrhea, vomiting and chest and abdominal pain [15].

Histology and immunohystochemestry studies help to exclude lymphoma. Involved lymph nodes in KFD characteristically demonstrate architecture partially effaced by paracortical expansion composed of circumscribed foci of apoptotic necrosis with abundant karyorrhectic debris and numerous hystiocytes of different types at the edge of necrotic foci [4]. The karyorrhectic foci are formed by different cellular types, predominantly histiocytes and plasmacytoid monocytes but also immunoblasts and small and large lymphocytes. Neutrophils are characteristically absent and plasma cells are either absent or scarce.

Atypia seen in the reactive imunoblastic component is not uncommon and can be mistaken for lymphoma in approximately 30% of patients [4,16].

KFD in the intramammary lymph node is very rare, there has been only one report of involvement in this area [4]. Although not confirmed by biopsy we have ultrasound evidence of necrotic intramammary lymph nodes in our patient. Ultrasonographic features of cervical lymph nodes in KFD have been previously reported. Ying and coworkers described them as hypoechoic, round or oval and tended to have an echogenic hilum and an unsharp border [17]. In our case the breast mass agreed with the findings mentioned above.

In conclusion, we report an unusual case of axillar, intramammary and cervical lymphadenopathy caused by KFD in a patient previously diagnosed with lupus erythematosus and tuberculosis. It is important to differentiate KFD from lymphoma and tuberculosis in an endemic country as ours. Histopathologic findings and immunohystochemical analysis had paramount significance in our case to conclude in a diagnosis.

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