Kikuchi-Fujimoto disease and prognostic implications

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Introduction: Kikuchi-Fujimoto disease (KFD) is a histiocytic necrotising lymphadenitis, identified by two Japanese pathologists Kikuchi and Fujimoto in 1972. KFD is a benign and self-limited disease, characterised by lymphadenopathy, fever, fatigue and leucopenia. KFD is more common in females in a ratio of approximately 3:2, and typically affects young adults, ages 20-30.

KFD is often misdiagnosed as a viral infection, but can often be mistaken for tuberculous lymphadenitis or malignant lymphoma. The aetiology of KFD is unknown, however the pathogenesis has been attributed to a virus or autoimmune component, most notably systemic lupus erythematosus (SLE). The diagnosis of KFD is made on histopathological examination of the affected lymph node.

Case report: 38 year old female was referred to our local ENT neck lump clinic via her GP, with a three-week history of painful swellings on the left side of her neck. She had no other associated symptoms, with a background of Graves 2006, thyroidectomy 2008.

Social history: Non-smoker, very active **Medication:** levothyroxine
Examination: 3 mobile lymph nodes in the posterior triangle of the neck. Nil else.

Investigations: ESR raised at 49mm/hr, other bloods unremarkable, including normal white cell count. Ultrasound scan: multiple left posterior triangle (level 5) nodes, with echogenic centre and central colour flow, suggesting reactive lymph nodes. Fine needle aspiration inconclusive. Node biopsy and culture: large area of necrosis, low ki67 proliferative activity, interpreted by our histopathologist as KFD locally, and was referred for a second opinion (Heartland's hospital in Birmingham), which re-confirmed a diagnosis of KFD. Culture negative. Chest X-ray revealed no suggestion of infection, sarcoidosis, TB or malignancy. **Treatment:** Nil. Following lymph node biopsy at nine weeks, her symptoms mostly resolved, and the patient has not have any further problems to date.

Figure 1: Low magnification image showing reactive lymphoid follicles and expanded paracortex with necrotic areas characterised by the absence of granulocytes. B. Paracortical expansion with a proliferation of lymphocytes, with a “starry-sky” pattern and crescentic nuclei.

Discussion:

Figure 2:

The most common examination findings in a 2006 case review of 266 KFD cases, by Kucukardali et al. Other findings include arthritis, weight loss, anorexia, hepatomegaly, splenomegaly and sweating. 18% of patients had leucopenia, with 16% having a raised ESR.

SLE association: KFD's association with SLE is illustrated in Kucukardali et al's case study, whereby 9% of European KFD patients and 28% of east-Asian patients had concomitant SLE. KFD can occur in patients with pre-existing SLE, coexist with SLE or evolve into SLE. The clinical and histopathologic features of KFD are closely simulated by SLE. Yilmaz et al reviewed two cases of KFD mimicking SLE, speculating that both SLE and KFD share a common hyperimmune reaction to antigenic stimuli, however then diverge into two distinct manifestations. It appears the association of KFD with SLE can predispose the patient to SLE at any time.

There is no clear evidence to determine the best way to follow up KFD in regards to long-term complications and associations. It appears it would be appropriate to perform an SLE screen following the initial diagnosis of KFD, followed by a yearly SLE screen. Likewise, ESR monitoring in primary care can be used to assess for any autoimmune, infectious or malignant developments. 3-4% of KFD cases recur, with the optimum management of patients with recurrent KFD yet to be reported. Regardless, KFD has an excellent prognosis with most cases resolving within six months.

Conclusion: Chronic lymph node enlargement and fever should be diagnosed carefully, with KFB a viable diagnosis. Gold standard is histological examination of involved lymph node. Although a self-limiting condition, KFD is associated with an increased risk of SLE, malignancy and other autoimmune diseases and therefore early diagnosis and long term follow up are recommended. Following initial investigations to rule out infectious and non-infectious aetiologies, we recommend long-term follow up in primary care with a yearly SLE screen and ESR blood test.

References: Kikuchi M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytes: a clinicopathological study. Nippon Ketsueki Gakkai Zasshi. 1972;35:379-80; Fujimoto Y. Cervical subacute necrotizing lymphadenitis. Naika. 1972;30:920-7; Kucukardali Y et al. Kikuchi–Fujimoto disease: analysis of 244 cases. Clinical rheumatology. 2007 Jan 1;26(1):50-4; Yilmaz M et al. Histiocytic necrotizing lymphadenitis mimicking SLE: a review of two cases. Lupus. 2006 Jun;15(6):384-7; Bezek S et al. State of the globe: Time to revisit KFD. Journal of global infectious diseases.2014Oct;6(4):139.