Kikuchi-Fujimoto Disease in a Crohn’s Patient

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Abstract
Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare, benign, focal, self-limiting disease. We report a unique case of KFD in a patient with coexisting Crohn’s disease. Our patient is a 23-year-old African American female with a past medical history significant for Crohn’s disease who presented to the clinic because of a painless lump over the right side of the neck for the past 3 weeks. On physical examination, the patient was found to have enlarged nontender right cervical lymph nodes from levels 2 to 4. An excisional biopsy of the right neck lymph node was done which revealed necrotizing histiocytic lymphadenitis, favoring a diagnosis of KFD. Over the course of the next 2 months, her lymphadenopathy got resolved. This is the first case of KFD in a patient with Crohn’s Disease. Lymphoma remains a feared adverse outcome for immunomodulatory drugs, thus necessitating their cessation upon signs of lymphadenopathy. Our case highlights the importance of a detailed workup in order to access the underlying cause of the lymphadenopathy so that the immunomodulatory drugs can be resumed in these patients.

Introduction
Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a relatively rare condition characterized by subacute necrotizing regional lymphadenopathy [1]. A higher prevalence is seen among Japanese individuals and east Asians [2]. A study
analyzing 244 cases of KFD found that the mean age of the patients was 25 years, and more than 70% of the patients were younger than 30 years of age [2]. Out of the 244 cases, only 6.6% had been reported from the USA. KFD has been found to be more prevalent in females as compared to males [3].

This benign and self-limited disease is frequently presenting with mild fever and cervical lymphadenopathy. Patients can have occasionally systemic symptoms like fatigue, rash, arthralgia, night sweats, and weight loss. Diagnosis of KFD requires an excisional biopsy of the affected lymph nodes. In this case report, we report a patient with coexisting Crohn’s disease (CD) and KFD.

**Case Presentation**

We present a case of a 23-year-old African American female with a past medical history significant for CD who presented to the clinic because of a painless lump over the right side of the neck for the past 3 weeks. The lump had gradually grown in size over the course of 3 weeks. She denied any nights’ sweats, fever, fatigue, abdominal pain, or diarrhea. Her past medical history was significant for CD, which was diagnosed 1 year ago. She denied any past surgical history. Her family history was unremarkable. She had no known drug allergies. She denied smoking, drinking alcohol, or using any recreational drugs. Her medications included azathioprine 50 mg once daily, adalimumab 40 mg every 2 weeks, folic acid 1 mg once daily, cyanocobalamin 100 μg once daily, and ferrous sulfate 325 mg once daily. She has no known drug allergies.

Her vitals included a temperature of 98.8°F, a blood pressure of 99/68 mm Hg, a pulse rate of 77 beats per minute, and a respiratory rate of 18 per minute. On physical examination, the patient was found to have enlarged nontender right cervical lymph nodes from levels 2 to 4. She had normal heart sounds and bilateral vesicular breathing. Abdominal examination was unremarkable. The patient was instructed to stop azathioprine and adalimumab. She underwent a CT scan of the neck, which showed enlarged right and left lymph nodes. CT chest was unremarkable. An excisional biopsy of the right neck lymph node was done which revealed necrotizing histiocytic lymphadenitis, favoring a diagnosis of KFD. This has been presented in Figure 1.

Her infectious workup was negative. This is presented in Table 1.

Over the course of the next 2 months, her lymphadenopathy resolved spontaneously without the need for any medication. She was started on oral budesonide with plans to restart biological therapy after repeating a colonoscopy.

**Discussion**

Histologically, KFD is characterized by paracortical lymph node expansion with patchy, well-circumscribed areas of necrosis showing abundant karyorrhectic nuclear debris and an absence of neutrophils and eosinophils. Although KFD has also been described in association with a number of systemic diseases, most commonly autoimmune conditions such as systemic lupus erythematosus, Wegener granulomatosis, Sjogren syndrome, Graves’ disease, and Still disease; there has been no prior reported association of KFD with CD [4]. Epstein-Barr virus, human immunodeficiency virus, human herpes virus, varicella-zoster virus, parvovirus, paramyxovirus, parainfluenza virus, rubella, and human T-lymphotropic virus have been proposed as possible infectious causes for KFD [5–7]. Despite many studies in the literature, the etiology and pathogenesis of KFD remain unknown.
CD is characterized by transmural inflammation and may involve any portion of the gastrointestinal tract, from the oral cavity to the perianal area. Pathogenesis of inflammatory bowel disease involves dysregulated immune responses to luminal bacteria and their products. Histologically, CD is characterized by areas of chronic inflammation, comprising increased lamina propria plasma cells and lymphocytes, in association with chronic architectural distortion with patchy, neutrophilic inflammation, including neutrophilic cryptitis, crypt abscesses, or erosions. Another feature of CD is transmural inflammation and non-necrotizing granulomas. Granulomas in CD are defined as an accumulation of epithelioid histiocytes characterized as noncaseating without central necrosis [1].

CD has been shown to have widespread extraintestinal manifestation. According to a review study, it was concluded that CD can present with a myriad of presentations involving the mouth, nose, and larynx. According to the CESAME study done in France, it was shown that duration of inflammatory bowel disease is an independent risk factor for lymphoproliferative disorders [8]. Various mechanisms have been suggested for the underlying pathology of KFD. Viral and autoimmune are the two most common suspected etiologies behind KFD [8]. One of the mechanisms suggested is that individuals with KFD may have an exuberant T-cell mediated response to various nonspecific stimuli [9]. CD has a similar underlying pathological mechanism. Various studies have shown that patients with CD have an underlying defect in the regulatory T cells [10]. According to a study done on 240 patients, it was shown that 25.4% of the CD patients had enlarged regional lymph nodes [11]. In the same study, it was shown that 50% of patients who were less than 30 years of age had regional lymph nodes (p < 0.0001). As per our literature review, we did not find any association between CD and KFD syndrome.
Lymphoma remains a feared adverse outcome for immunomodulatory drugs, thus necessitating their cessation upon signs of lymphadenopathy. Our case highlights the importance of a detailed workup in order to access the underlying cause of lymphadenopathy so that the immunomodulatory drugs can be resumed in these patients. Our patient was found to have a benign and self-limiting KFD, and the patient was slowly restarted on the immunomodulatory drugs.

**Statement of Ethics**

The patient has given written informed consent to publish this case including publications of images. Research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. This study protocol was reviewed, and the need for approval was waived by the Bronxcare Health System Ethics Committee.

**Conflict of Interest Statement**

The author(s) of this manuscript do(es) not have any conflict of interest to declare.

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**Author Contributions**

The first author (Danial H. Shaikh) and the coauthors (Haider Ghazanfar, Tegveer Sandhu, Ali Naqqi Ul Hussain, and Harish Patel) were all involved in summarizing this case report, writing the manuscript, and proofreading the final version of the manuscript.

**Data Availability Statement**

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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