Name of Journal: World Journal of Clinical Cases
ESPS Manuscript NO: 28459
Manuscript Type: Case Report

Fatality in Kikuchi-Fujimoto Disease: A Rare Phenomenon
Running title: Fatality in Kikuchi-Fujimoto Disease

Answering Reviewers

Reviewer- 2346872
Discussed the risk of mortality in a usually benign, self-limiting condition.

Reviewer- 740394
The patient was a previously healthy, 21-year-old female who presented with a two-day history of dyspnea, fever, and malaise. Initial set of vitals revealed a blood pressure of 109/57 mmHg, temperature of 38.2°C, heart rate of 118 bpm, respiratory rate of 24 breaths/min, and oxygen saturation of 78% on room air. On 4 liters of nasal cannula, her oxygen saturation improved to 97%. A chest x-ray demonstrated multifocal pneumonia. Treatment for community-acquired pneumonia was initiated with ceftriaxone and azithromycin. On physical examination, she was noted to have significant axillary, cervical and inguinal lymphadenopathy. Her respiratory status continued to decline despite supplemental oxygen therapy and antibiotics, requiring emergent endotracheal intubation with mechanical ventilation. A computerized tomography (CT) chest, abdomen, and pelvis was performed, which revealed significant cervical and axillary lymphadenopathy, bilateral lung consolidation, and a moderate pericardial effusion (Figure 1A&B).

As the patient's presentation was very severe, a comprehensive differential was considered. Among the entire laboratory data that was performed HIV, streptococcus pneumonia, legionella, histoplasma, brucella, aspergillus, tuberculosis, influenza**,** respiratory syncytial virus were negative. There was a mild elevation in mycoplasma IgM and chlamydia antibody titer. The patient's antibiotic therapy was tailored to include a broader spectrum of organisms. Bronchoscopy with bronchoalveolar lavage was performed given the above CT findings. There was no evidence of mucus plugs, active bleeding, endobronchial lesions or anatomical abnormalities. Pathology of the fluid revealed presence of acute inflammatory cells. A transthoracic echocardiogram revealed normal systolic function with a moderate pericardial effusion without tamponade physiology.

Due to the significant lymphadenopathy, pericardial effusion, and an elevated LDH of 2,319 unit/L, a concern for lymphoma was raised. Therefore, a cervical lymph node biopsy was performed. Histopathology demonstrated variable involvement of patchy small to large areas of necrosis within the paracortex. The necrotic areas

were composed of karyorrhectic debris with abundant histiocytes consistent with KFD **(Figure 2).**

Septic work up consisting of blood, sputum and urine cultures remained negative throughout her admission. Despite aggressive antibiotic therapy, high dose steroids, and supportive care, the patient's condition continued to decline. She required increasing pressure support to maintain oxygenation. Intravenous immune globulin was given without any improvement in the patient's symptoms. The hemoglobin level began to precipitately decrease without any active sites of bleeding. A hemolytic work up was initiated, which revealed a haptogobin < 10 mg/dL and schistocytes on peripheral smear. She then developed significant thrombocytopenia with platelet level recorded as low as 26 K/mcL. Partial thromboplastin time, prothrombin time levels and D-dimer levels started to rise. Fresh frozen plasma was transfused for impending DIC. The patient's clinical condition and laboratory parameters continued to deteriorate despite resuscitative efforts in the intensive care unit. Unfortunately, she expired secondary to development of DIC.

Reviewer- 214317

A definite diagnosis of KFD is made by biopsy, typically excisional, but fine needle aspiration has also been used. There are some characteristic histologic features of KFD including patchy necrotizing areas primarily in the paracortical regions that contain fibrinous material with karyorrhexis. A distinctive mottled appearance may be noted as immunoblasts tend to border necrotic zones. [15]Early diagnosis is important as the clinical and laboratory presentations can imitate situations needing time-consuming and expensive interventions.[9] KFD can be easily misdiagnosed; literature estimates as high as 40% of the time with lymphoma being the most commonly mistaken diagnosis.[10]

Once the diagnosis is made, symptomatic and supportive treatment is usually adequate. When symptomatology requires treatment, a short course of corticosteroids is preferred. Currently, there are no recommendations on exact dosage or route of administration.[16] In severe cases, high dose intravenous steroids have been shown to be effective and aid in symptom reduction.[6] Intravenous immunoglobulin (IVIG) has been shown to be successful in several, critical cases. Once again, no formal recommendations on dosing and duration exist. IVIG has been routinely implemented as empiric therapy in autoimmune and inflammatory processes secondary to its immunomodulatory properties.[17] In individuals with a benign hospital course, it is important to have adequate follow up as patients have an increased risk of relapse. One study showed that hydroxycholorquine could be used in the treatment of relapsed KFD.[7] On rare instances, despite these treatment modalities, KFD may progress to mortality such as the patient we presented.