Original Research Article

A case of concurrent Kikuchi-Fujimoto Disease and neuropsychiatric lupus in a patient with rheumatoid arthritis and systemic lupus erythematosus overlap syndrome

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Abstract

Kikuchi-Fujimoto disease is a rare, self-limited, histiocytic necrotizing lymphadenitis characterized by cervical lymphadenopathy and fever. An association has been made between the presence of this disease and systemic lupus erythematosus. We describe a unique case of a 31 year old female with a previous diagnosis of rheumatoid arthritis and lupus overlap syndrome who presented with severe headache and subsequently developed altered level of consciousness and seizures. She underwent an extensive assessment which included investigations for an infectious cause, numerous imaging studies, a lymph node biopsy, a bone marrow biopsy, and a brain biopsy resulting in a final diagnosis of concurrent Kikuchi-Fujimoto disease and lupus-associated encephalitis. In these overlap patients, neurological involvement is usually mild. In contrast, our patient presented with severe neuropsychiatric involvement eventually requiring ICU admission. This case highlights the difficulty of diagnosing and managing neuropsychiatric lupus in these complex overlap patients. Early recognition is important to avoid unnecessary and potentially harmful interventions and treatments.

Keywords: Kikuchi-Fujimoto, Lupus, Rhupus

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Introduction

First described in 1972, Kikuchi-Fujimoto disease (KFD) is a rare, self-limiting condition of histiocytic necrotizing lymphadenitis characterized by fever, cervical lymphadenopathy and elevated inflammatory markers.[1,2] The etiology of KFD is still unknown, though environmental factors such as infectious exposure have been proposed.[2] KFD has also been reported to be associated with systemic lupus erythematosus (SLE).[1]

Like KFD, the occurrence of overlapping clinical and immunological features of both rheumatoid arthritis and SLE, first described as "rhupus" by Schur in 1971, is a rare clinical condition.[3,4] Overall, rhupus has a prevalence of 0.09% and constitutes 0.01-2% of all systemic rheumatic disease.[5,6] In these overlap patients, erosive features of rheumatoid arthritis are more pronounced, while systemic lupus features, including neurological involvement, are usually mild.[6,7]

In contrast, we describe a case of a rhupus patient with severe neuropsychiatric involvement requiring ICU admission. After an exhaustive work up, the patient was diagnosed with concurrent Kikuchi-Fujimoto disease and lupus-associated encephalitis. She demonstrated remarkable recovery after treatment with corticosteroids and mycophenolate mofetil.

Case report

Our patient is a 31-year old female with a history of SLE and rheumatoid arthritis overlap syndrome, interstitial lung disease, pulmonary hypertension, treated latent tuberculosis, shingles and migraines who presented with headaches and an evolving clinical course resulting in a prolonged and complicated hospital stay. The following services were involved in her care: Internal Medicine, Intensive Care, Respirology, Infectious Disease, Dermatology, Gastroenterology, Pathology, Hematology, Neurology, Plastic Surgery, and Rheumatology.

She first presented to a local Emergency Department with a three week history of severe headache and was treated empirically with ceftriaxone and vancomycin for possible aseptic meningitis. She re-presented approximately two weeks later with an altered level of consciousness and subsequently developed seizures. Numerous investigations were performed to determine the etiology of this change in clinical status. Additionally, the patient was started on ceftriaxone, vancomycin and acyclovir. A lumbar puncture revealed high protein and lymphocytic pleocytosis. An MRI brain indicated diffuse leptomeningeal and pachymeningeal enhancement. Additionally, a CT chest included as part of the ongoing infectious work up demonstrated diffuse axillary lymphadenopathy. An excisional lymph node biopsy was performed to rule out lymphoma. A bone marrow biopsy was also performed, demonstrating moderate normocytic anemia. Investigations for an infectious cause were negative (blood cultures, fungal cultures, human immunodeficiency virus, herpes simplex virus, mononucleosis, varicella zoster virus, cytomegalovirus, polyomavirus, enterovirus, parechovirus, West Nile virus, rickettsiae, methicillin-resistant staphylococcus aureus, clostridium difficile, vancomycin resistant enterococcus, cryptococcus, urine culture, Hepatitis A/B/C, parvovirus, human T-cell

lymphotropic virus I/II, bartonella, histoplasma, coccidioides, blastomyces, and toxoplasma). She was noted to have low levels of complement C3 and C4. Due to the presence of high numbers of lymphocytes in her cerebrospinal fluid and her immunocompromised state on a background of prior treated latent tuberculosis, she was started on empiric anti-tubercular treatment (isoniazid, rifampin, pyrazinamide, levofloxacin). Her vancomycin was continued.

She developed new onset expressive aphasia one month after admission. A CT cerebral angiogram indicated new hypoattenuation of her right occipital lobe. She received three doses of pulsed intravenous solumedrol and was then treated with high dose oral prednisone. Her level of consciousness significantly improved. Incidentally, she was also noted to have upper extremity cephalic/basilic vein thrombosis and was started on dalteparin. A prior anti-phospholipid antibody work up was negative.

As her steroid dose was tapered, the patient's status deteriorated and she required intubation and admission to the Intensive Care Unit (ICU). Her lymph node biopsy returned as necrotizing lymphadenitis suggestive of Kikuchi-Fujimoto disease with no evidence of lymphoproliferative disorder (Figure 1). However, as her diagnosis was still unclear, a brain biopsy of the dura and right frontal area was performed. This indicated necrotizing leptomeningitis with no evidence of vasculitis, microglial nodules, perivascular cuffing or microbial organisms. A new MRI brain showed regression of the leptomeningeal enhancement. Cerebrospinal fluid flow cytometry was negative for malignant cells. Additionally, an electroencephalogram indicated abnormal and slow movements with no epileptiform activity. However, new black discoloration of the left hand 2nd and 3rd distal digits was noted, and Plastic Surgery was consulted. Skin biopsy results indicated epidermal necrosis likely secondary to the pressor support therapy she received while in the ICU.

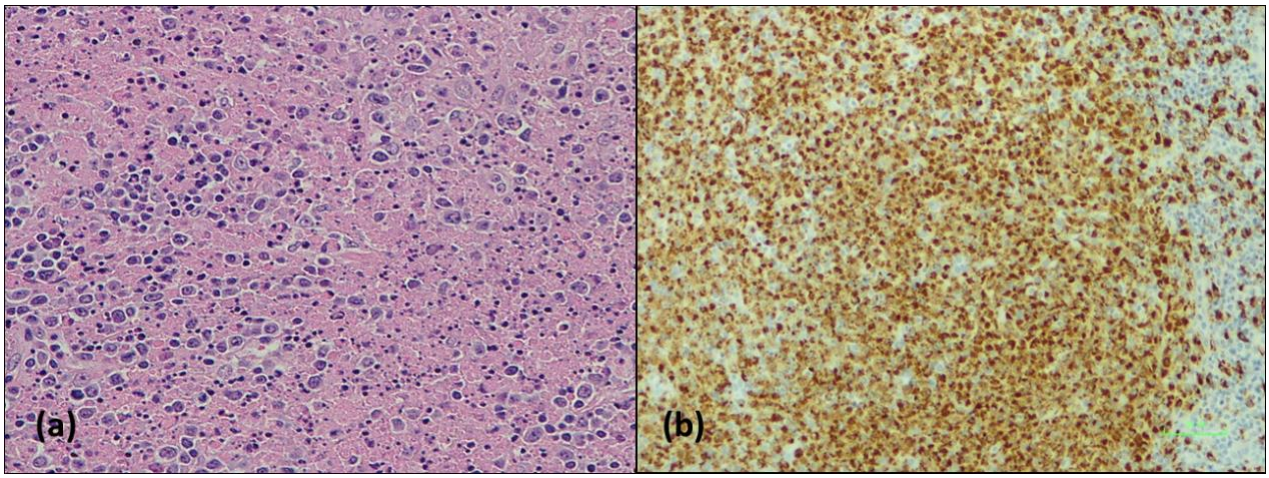

Figure 1. Right axilla lymph node biopsy highlighting (a) a necrotizing area featuring eosinophilic fibrinoid deposits with nuclear fragments, karyorrhexis, apoptotic cells, and paler staining histiocytes suggestive of Kikuchi-Fujimoto disease (Hematoxylin and eosin staining, 40X magnification) and (b) CD68/MPO positive histiocytes (immunohistochemical staining, 40X magnification).

Two weeks later, the patient began to experience cytopenias, fevers, and elevated liver enzymes attributed to the ongoing tuberculosis treatment. She also displayed diffuse erythema thought to be due to vancomycin sensitivity. Moreover, as part of an ongoing infectious work up, the patient was tested for possible additional sexually transmitted infections and was found to be positive for chlamydia. She was treated for chlamydia with azithromycin and started on meropenem for febrile neutropenia. Her tuberculosis medications and vancomycin were discontinued.

She was extubated one week later. Her cognitive status slowly improved. Following a comprehensive review of her clinical scenario at Rheumatology Rounds, a diagnosis of lupus-associated encephalitis was made and the patient was started on mycophenolate mofetil. Her clinical status continued to improve and repeat blood tests for complement levels were normal. Her anti-dsDNA antibodies, anti-neutrophil cytoplasmic antibodies, anti-phospholipid antibodies, and N-methyl-D-aspartate were negative. The lymph node biopsy results were revisited and the presence of Kikuchi-Fujimoto disease was confirmed. She was discharged from the hospital with follow up arranged with Respirology, Plastic Surgery, and Rheumatology.

Discussion

The diagnosis and management of central nervous system involvement in SLE remains challenging due to the wide range of symptoms and lack of diagnostic criteria.[8] This difficulty is magnified in complex patients with overlap syndromes such as rhupus. Our patient underwent an extensive work up for infectious, neoplastic, and autoimmune causes of her altered level of consciousness, seizures and aphasia. Ultimately, she was diagnosed with an exacerbation of her systemic lupus based upon the presence of hypocomplementemia and non-infectious encephalitis, with concurrent biopsy-proven Kikuchi-Fujimoto disease. She was successfully treated with corticosteroids and mycophenolate mofetil.

In rhupus patients, neurological involvement is usually mild. In contrast, our patient presented with severe neuropsychiatric involvement requiring a lengthy hospital stay with admission to the ICU. This case highlights the need for better guidelines for diagnosing and managing neuropsychiatric lupus in these complex overlap patients. Early recognition is important to minimize unnecessary and potentially harmful interventions and treatments. [2,7]

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Declarations

Consent for publication

Consent for case publication was obtained from the patient prior to submission.

Competing interests/source of funding

None to declare.

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