An unusual association between splenectomy and Kikuchi's disease

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ABSTRACT

Kikuchi's disease is a clinico-pathologic entity of unknown etiology characterized by subacute inflammatory process of lymph nodes. It affects mostly women around the age of 30 years. It is usually a self limiting illness characterized by pyrexia, neutropenia, and cervical lymphadenopathy. We report a case of Kikuchi's disease in a patient with past history of splenectomy. A 35-year-old otherwise healthy female patient presented with 15 days history of fever, night sweats, and right cervical lymphadenopathy. She was on no medication and had no contact with animals or patients with tuberculosis. Her past history revealed splenectomy for thrombocytopenia 14 years before presentation. Lymphoma was suspected and she was referred for a cervical lymph node biopsy. The final histopathology diagnosis revealed subacute necrotizing lymphadenitis consistent with Kikuchi's disease. This is the first case of Kikuchi's disease presenting in a post splenectomy patient.

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Fujimoto Kikuchi's in 1972 described subacute cervical lymphadenitis in a young Japanese patient, which now bears his name.[1] The disease is usually associated with fever, sore throat, weight loss, chills, myalgias, arthralgias, splenomegaly, and skin rash. It is usually self limiting and resolves within 1-3 months.[2-3]

Pathologically Kikuchi's disease (KD) is characterized by atypical mononuclear cells, which are probably transformed monocytes in association with geographic areas of necrosis and karyorrhexis and hence, other names were suggested for this entity, such as histocytic necrotizing lymphadenitis and apoptotic lymphadenitis.[2-4] The diagnosis of KD is not easy and many cases are still being mistakenly diagnosed as malignant lymphomas.[4] However, demonstration of nuclear fragmentation, necrosis, and karyorrhexis on a lymph node biopsy, especially in young women presenting with cervical lymphadenopathy should suggest the diagnosis of KD rather than lymphoma.[4] Although the disease has been recognized worldwide, to our knowledge no cases have been reported in the literature in association with previous splenectomy.

Case Report. A 35-year-old woman presented with 15 days history of fever, night sweating and right cervical lymphadenopathy. She had been well until the onset of her current illness. She was on no medication and had no contact with animals or patients with tuberculosis. Her past history revealed splenectomy for idiopathic thrombocytopenia 14 years before presentation. On admission, she was found to have right deep cervical mass involving the upper and middle group of cervical lymph nodes. There were no significant lymph nodes enlargement elsewhere and her abdominal examination revealed the presence of previous splenectomy scar. During hospitalization, the patient had swinging intermittent pyrexia of up to 39°C. Marked elevation of liver enzymes was noted; gamma glytamyl transpeptidase 784 U/L (normal <64U/L), alkaline phosphatase 702 U/L (normal< 92 U/L),

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lactate dehydrogenase (LDH) 1193 U/L (normal 480 U/L), alanine aminotransferase 240 U/L (normal <42 U/L), aspartate aminotransferase 647 U/L (normal <42 U/L). Blood and urine cultures, Epstein-Barr virus serology, and hepatitis surface antigen titres were all negative. Investigations revealed a white cell count at 6.7 x 10^9/l with a neutrophil count of 4.75 x 10^9/l, erythrocyte sedimentation rate 92 (normal<20). Computed tomography of the neck revealed soft tissue mass lesion along the posterior belly of the digastric muscle with cystic necrosis measuring 2.5 x 1.5 x 1.0 cm in dimension (**Figure 1**). Chest and abdominal computed tomography (CT) scan was unremarkable and the spleen was not seen. Bone marrow aspiration and trephine biopsies revealed normal pathology. Fine needle aspiration biopsy of the cervical swellings attempted twice and the result was negative for malignant cells. Excisional biopsy of the dominant deep cervical lymph node was performed. Microscopic examination revealed a disturbed architecture with large foci of necrosis and karyorrhexis. The necrotic foci were surrounded by histiocytes with cresent-shaped nuclei engulfing apoptotic debris. In between, a mixed population of small lymphocytes, immunoblasts, and plasmacytoid monocytes was seen. Most of the cells were of T-cell origin as confirmed by the pan T-cell marker CD-3 with few B cells. The cells were mitotically active with high proliferative index. Scattered germinal centers at the edge of the lymph node were also identified. The findings were consistent with necrotizing lymphadenitis "Kikuchi's disease." **(Figure 2 & 3)** The clinical symptoms and signs improved gradually on no treatment. Her temperature settled after 2 weeks, and the size of her cervical lymphadenopathy started to decline gradually over the following 3-4 months from the beginning of the illness. When reviewed in outpatients one year after discharge from hospital she was well and all her lymph nodes had disappeared completely.

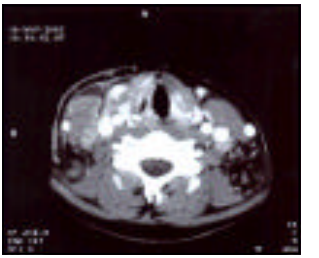

Figure 1 - Neck computed tomogram showing right cervical lymph adenopathy with cystic necrosis causing a mass affecting the right carotid artery and jugular vein.

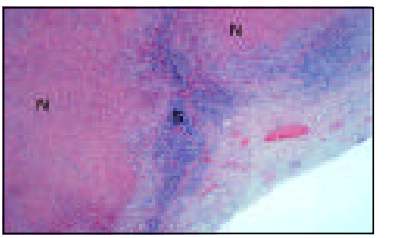

Figure 2 - Low power view of the lymph node showing areas of necrosis (N) separated by preserved sinuses (S). Hematoxylin and eosin x 40.

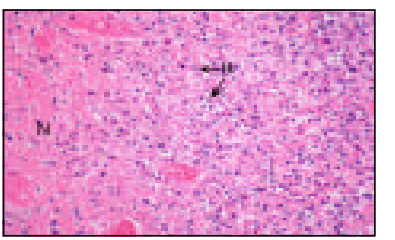

Figure 3 - Areas of necrosis and karyorrhexis (left), with histocytes (H) and activated lymphocytes at the edge. Hematoxylin and eosin A 200 X

Discussion. Kikuchi lymphadenitis is a benign disorder, affecting predominantly young women with a predilection for cervical lymphadenopathy.[1-4] Although the disease has been recognized worldwide, to our knowledge no cases have been reported previously in association with past history of splenectomy.

The exact etiology of KD has not been clearly identified. Familial cases have been identified, implying that there may be a genetic predisposition.[5] Viral infections have been suggested, with the suspected agents including Epstein-Barr virus, herpes virus type 6 and 8, parvovirus B19, and cytomegalovirus (CMV).[6-7] Autoimmune process has also been proposed due to the association with

systemic lupus erthymatosus and other autoimmune disorders (mixed connective tissue disease, Hashimoto's thyroiditis).[8,9] Several associated conditions were reported with Kikuchi-Fujimoto's disease; ruptured silicone breast implant, diffuse large B-cell lymphoma, psoriasis, Hashimoto's thyroiditis, systemic lupus erythematosus and hemophagocytic syndrome (HS).[3,5,8-10]

Several long term complications after splenectomy for hematologic disorders have been reported such as thyrombocytosis, thrombosis, and infection. The cause of these complications is thought to be related to the immunologic and hematologic function of the spleen and thus, its resistance to infections.[11] Extrapolating this data to our patient, the past history of splenectomy might explain the pathologic changes on cervical lymph node biopsy. Kikuchi's disease is a subacute necrotizing lymphadenitis characterized by the presence of patchy areas of necrosis and prominent mottling by histiocytes or transformed lymphoid cells with preserved sinuses in the uninvolved areas. The histiocytes have cresent-shaped nuclei that contain nuclear and cellular debris. The so called plasmacytoid T cells are usually identified at the periphery of or immediately outside the necrotic foci. Transformed medium to large size lymphocytes containing moderate numbers of mitotic figures may also be present.[4,12]

Our current case report indicates that Kikuchi's disease may be associated with past history of splenectomy. Similar to other reported cases, it was not possible to identify an underlying etiology that might explain the morphologic changes seen in our patient. However, it illustrates how important it is to be aware of this benign entity, which is readily diagnosed on lymph node biopsy especially in young patients suspected to have lymphoma.

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