ORIGINAL RESEARCH

Evaluation of Clinicopathological Spectrum of Necrotizing Lymphadenitis: An Institutional Based Study

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ABSTRACT

Background: Several diseases can present with necrotizing non-granulomatous lymphadenitis. The present study was conducted to assessclinicopathological spectrum of necrotizing lymphadenitis. **Materials & Methods:** This is a retrospective study to assess clinicopathological spectrum of necrotizing lymphadenitis. A total of 48 cases of necrotizing lymphadenitis diagnosed on lymph node biopsies over the 2 year period, were reviewed. Clinical details of all the cases were collected from electronic medical records and patients were followed up for a minimum period of 6 months. **Results**: A total of 48 cases of necrotizing lymphadenitis diagnosed pathologically were further categorized based on serological tests. 16.66% proved to be lupus lymphadenitis and 18.75% were EBV lymphadenitis. 64.58% with negative serological tests were classified as Kikuchi lymphadenitis. Lupus cases had a female preponderance (75%). Males (75%) were commonly affected by EBV lymphadenitis.Kikuchi lymphadenitis also was seen mostly in females (61.29%). **Conclusion:** The present study concluded that Kikuchis lymphadenitis is the most common cause of necrotizing lymphadenitis, followed by lupus and acute EBV lymphadenitis.

Keywords: Lupus, EBV Lymphadenitis, Kikuchi Lymphadenitis, Necrotizing Lymphadenitis.

INTRODUCTION

Necrotizing lymphadenitis represents a group of diseases characterized by nongranulomatous inflammation and necrosis of the lymph node.[1] This is caused by a variety of infective and inflammatory diseases, most common being Kikuchi-Fujimoto disease, acute Epstein-Barr viral (EBV) infection, and systemic lupus erythematosis (SLE/lupus lymphadenitis), and excludes Mycobacterial infections such as tuberculosis (TB). Clinically, patients present with features like fever and painful lymphadenitis which make them mimic the more common TB and lymphomas.[2] Kikuchi's disease (KD) is seen predominantly among women in their third and fourth decade of life.The disease primarily affects cervical lymph nodes and has a self-limiting clinical course, however, a low recurrence rate of 3.3% is reported. Extranodalinvolvement specially of the skin has been reported by several authors. The disease has unknown aetiology. Infection is often considered as an inciting agent. It is hypothesised that lymphokine production in an immunocompromised host may result in histiocytic proliferation. Association with Epstein-Barr virus, human herpes virus 6 and 8, Parvovirus B-19, Human T-cell lymphocytic virus, Human immunodeficiency virus, Toxoplasma gondii and Yersinia enterocolitica has been demonstrated.[3]The present study was conducted to assessclinicopathological spectrum of necrotizing lymphadenitis.

MATERIALS & METHODS

This is a retrospective study conducted in Department of Pathology, Rama Medical College Hospital & Research Centre, Kanpur, Uttar Pradesh (India) to assess clinicopathologicalspectrum of necrotizing lymphadenitis. Institutional ethical committee clearance was obtained.A total of 48 cases of necrotizing lymphadenitis (pathologic diagnosis, irrespective of etiology) diagnosed on lymph node biopsies over the 2 year period, were reviewed and the morphologic findings were recorded.All cases of

granulomatous/suppurative lymphadenitis and neoplasms were excluded. Based on the ancillary tests done, the cases were then categorized into different etiological subtypes like acute EBV lymphadenitis (EBV immunoglobulin M positive) and lupus lymphadenitis (antinuclear antibody (ANA) and ds DNA positive). Rest of the cases with negative results for both of these serological tests were classified as Kikuchi lymphadenitis (as specific test is not available, by excluding other 2 aetiologies and other infections).We studied the lymph node biopsy tissues which were formalin-fixed, paraffin-embedded, cut into 4-µm thick sections and stained with haematoxylin and eosin. Representative sections were also stained with histo chemical stains like Periodic acid Schiff's and reticulin stain. Clinical details of all the cases were collected from electronic medical records and patients were followed up for a minimum period of 6 months.

RESULTS

A total of 48 cases of necrotizing lymphadenitis diagnosed pathologically were further categorized based on serological tests. 16.66% provedto be lupus lymphadenitis and 18.75% were EBV lymphadenitis. 64.58% with negative serological tests were classified as Kikuchi lymphadenitis.

Lupus cases had a female preponderance (75%). Males (75%) were commonly affected by EBV lymphadenitis.Kikuchi lymphadenitis also was seen mostly in females (61.29%).

Table 1: Diagnosis of necrotizing lymphadenitis

Diagnosis of necrotizing lymphadenitis	N(%)
lupus lymphadenitis	8(16.66%)
EBV lymphadenitis	9(18.75%)
Kikuchi lymphadenitis	31(64.58%)
Total	48(100%)

Table 2: Prevalence of necrotizing lymphadenitis

Prevalence of necrotizing lymphadenitis	N(%)
lupus lymphadenitis	
Male	2(25%)
Female	6(75%)
EBV lymphadenitis	
Male	7(77.77%)
Female	2(22.22%)
Kikuchi lymphadenitis	
Male	12(38.70%)
Female	19(61.29%)

DISCUSSION

Necrosis in lymph nodes can be seen in a variety of neoplastic and non-neoplastic conditions. The most common non-neoplastic cause is TB, where granulomas with caseation type necrosis is seen. Neoplastic nodes can also undergo necrosis, for example, Hodgkin's lymphoma, nodular sclerosis subtype. Necrotizing lymphadenitis is characterized by nongranulomatous, noncaseating necrosis along with mixed inflammatory infiltrate composed of variable number of plasma cells, histiocytes, and neutrophils.[1]

A total of 48 cases of necrotizing lymphadenitis diagnosed pathologically were further categorized based on serological tests. 16.66% proved to be lupus lymphadenitis and 18.75% were EBV lymphadenitis. 64.58% with negative serological tests were classified as Kikuchi lymphadenitis. Lupus cases had a female preponderance (75%). Males (75%) were commonly affected by EBV lymphadenitis.Kikuchi lymphadenitis also was seen mostly in females (61.29%).

The histological findings of KD are distinctive. Patchy areas of necrosis without a polymorphonuclear leukocyte infiltration is characteristic finding. The necrotic areas show prominent karyorrhetic debris, immunoblasts, histiocytes and plasmacytoid T-cells/ monocytes. The histiocytes have a C-shaped nuclei and some contain cellular debris.[4]

Since the morphological features encountered in a lymph node are distinctive, it enables the pathologists to diagnose KD with confidence. Nonetheless, difficulty is encountered at times in differentiating it from certain malignant and benign disorders. It is not infrequently diagnosed as non-Hodgkin’s lymphoma (NHL) or Hodgkin’s disease (HD). High grade NHL with necrosis and karyorrhesis may be differentiated from KD by the lack of the larger cells with twisted nuclei seen in Kikuchi and additional evidence of lymphoma in the other parts of the lymph node. In case of the KD with focal lesions consisting of immunoblasts and histiocytes with no evidence of necrosis, it is very difficult to distinguish from lymphoma.[5]

Nair IR et al studied the morphological features in lymph nodes in cases of necrotizing lymphadenitis, to correlate them with specific etiological conditions. 62.2% of cases were Kikuchis lymphadenitis. Both

lupus and Kikuchis had a female preponderance (78% and 62% respectively). Among the morphological parameters, plasma cell infiltration and vascular proliferation showed significant association with lupus lymphadenitis. Kikuchis and EBV lymphadenitis showed self-limiting course, with only 2 cases of Kikuchis developing recurrence .4 cases developed complications. All cases of lupus lymphadenitis needed long term therapy.[2]

Lelii M et al described two case reports of Kikuchi Fujimoto disease presenting in Milan within the space of a few months. The first involved the recurrence of KFD in a young boy from Sri Lanka; the second was a rare case of severe KFD complicated by HLH. The study concluded that Pediatricians must consider KFD in the differential diagnosis of fever of unknown origin in children, even in western countries. Although rare, recurrence and severe complications are possible. Where symptoms suggest KFD, a systematic diagnostic approach is key. Since no guidelines on the management of KFD are available, further studies should be conducted to investigate the therapeutic options and long-term outcome in children.[6]

In KFD, the most common histologic finding is lymph node showing geographic necrosis with foci of apoptotic cells with abundant karyorrhectic fragments surrounded by histiocytes.[7] Characteristically, neutrophils and eosinophils are absent.[7]

The diagnosis of Kikuchi-Fujimoto disease is based on the histological findings of affected lymph nodes. Due to partial lymph node involvement an excisional biopsy is mostly preferred, although fine needle aspiration biopsy sometimes may prove helpful.[8,9]

Supportive measures were only offered to the patients with acute EBV lymphadenitis, and a spontaneous resolution was seen in all except 1 who developed HLH, in 2–4 weeks' time, as seen in other studies.[10]

CONCLUSION

The present study concluded that Kikuchis lymphadenitis is the most common cause of necrotizing lymphadenitis, followed by lupus and acute EBV lymphadenitis.

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