



# Histiocytic Necrotizing Lymphadenitis Involving the Neck: Radiology-Pathology Correlation

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## Abstract

Histiocytic necrotizing lymphadenitis is an uncommon autoimmune condition characterized by fever, leukopenia, and neck swelling. Diagnostic imaging, including ultrasound and CT, typically demonstrates conglomerates of enlarged cervical lymph nodes with hypervascular cortices and areas of necrosis. Ultimately, the diagnosis is confirmed with the histopathologic findings of paracortical coagulative necrosis with karyorrhectic debris, abundant histiocytes, and absence of neutrophils. Other potential etiologies, such as other causes of infectious lymphadenitis, tuberculosis, lymphoma, and systemic lupus erythematosus, must be excluded. These features are exemplified in this sine qua non radiology–pathology correlation article.

**Keywords** Histiocytic necrotizing lymphadenitis · Neck · Lymph node · Radiology · Pathology

## History

The patient was a 14-year-old male who presented with fever, neck pain, and fatigue for several weeks. Physical exam demonstrated diffuse swelling and tenderness to palpation in right lateral neck without overlying skin changes. A complete blood count revealed leukopenia with a white blood cell count of  $3.0 \times 10^3$  per microliter and mild anemia with a hemoglobin of 11.8 g/dL at presentation. The differential was 38% neutrophils, 54% lymphocytes, and 7% monocytes. The ESR was elevated at 50 mm/h, as was the lactic dehydrogenase at 636 U/L. Serologic testing from peripheral blood for EBV and CMV was positive and consistent with past infections. Serologic testing for human immunodeficiency virus (HIV), *Histoplasma*, *Blastomyces*, *Bartonella* were negative. QuantiFERON<sup>®</sup>TB gold for *Mycobacterium tuberculosis* was also negative.

## Radiographic Features

Ultrasound performed in the right cervical region showed multiple enlarged, hypervascular lymph nodes (Fig. 1). CT of the neck with contrast was also performed, which revealed numerous enlarged right cervical lymph nodes involving levels 2B, 3, and 5A. The lymph nodes generally displayed cortical hyperenhancement and many of them contained central hypoattenuation, which was suggestive of necrosis (Fig. 2). In addition, there was diffuse stranding of the fat surrounding the lymph nodes, which was suggestive of inflammation. There was no significant lymphadenopathy in the left neck. The differential diagnosis based on the clinical and radiologic findings included autoimmune and infectious conditions.

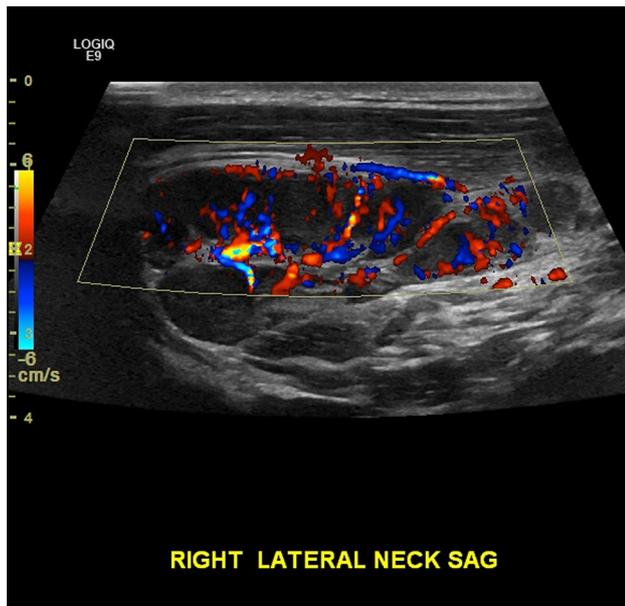
## Diagnosis

The patient underwent excisional biopsy of a right neck lymph node. Histologic examination showed lymph node fragments with large areas of necrosis in the paracortical region (Fig. 3a). These areas contained abundant necrotic debris and apoptotic cells with surrounding large, pale-staining histiocytes, many of which had crescent-shaped nuclei. Occasionally, cells consistent with plasmacytoid dendritic cells were also present in the H&E stained sections. These necrotic foci were devoid of neutrophils or eosinophils

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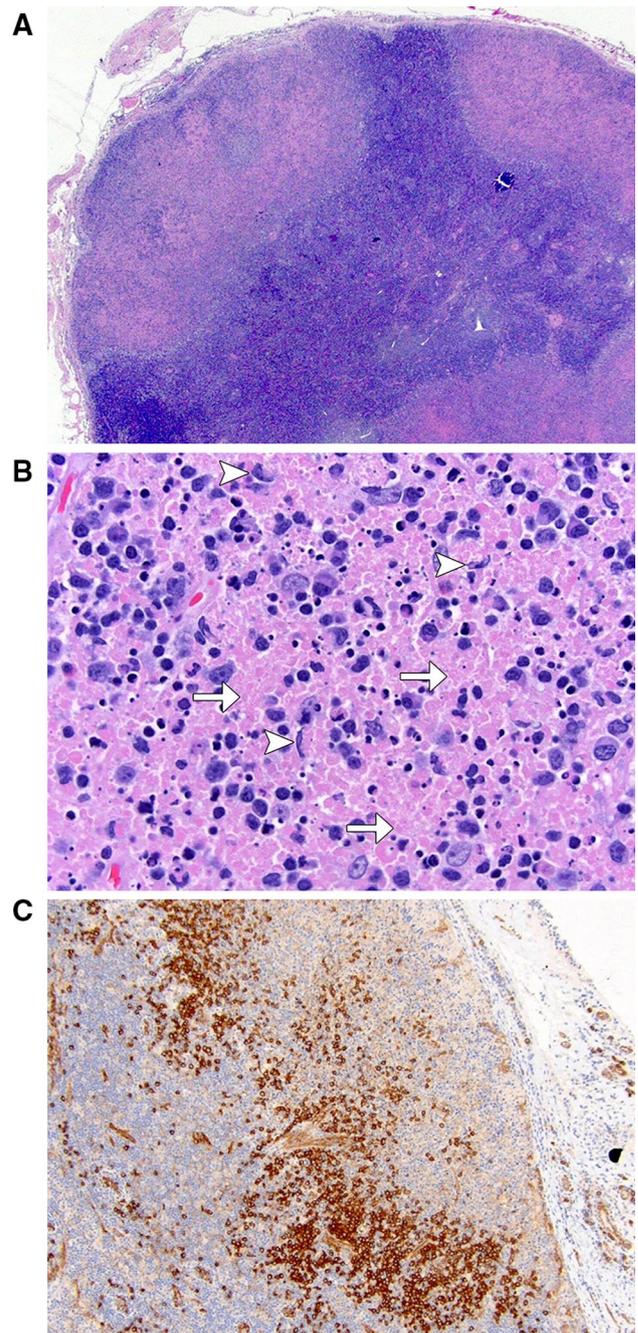
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**Fig. 1** Color Doppler ultrasound image shows a cluster of enlarged, hypervascular right neck lymph nodes



**Fig. 2** Axial (a) and coronal (b) CT images show extensive right cervical lymphadenopathy with peripheral hyperenhancement and central hypoattenuating areas compatible with necrosis, as well as diffuse stranding of the surrounding fat



**Fig. 3** Low power hematoxylin and eosin stained section of a lymph node shows multiple pale, well-circumscribed paracortical areas, which are demarcated from the medulla and show no extension into the perinodal adipose tissue (a). High power image of the pale areas shows abundant coagulative necrosis and karyorrhectic debris (arrows) and histiocytes, including crescentic histiocytes (arrowheads) but absent neutrophils (b). Immunohistochemical staining for CD123 highlights the plasmacytoid dendritic cells (c)

(Fig. 3b). Immunohistochemical stains were performed to confirm cell types. CD68 highlighted the abundant histiocytes, including crescentic forms. CD123 demonstrated

numerous plasmacytoid dendritic cells present in aggregates at the periphery of the necrotic foci, more than appreciated on the H&E stained sections (Fig. 3c). CD21 showed focal staining of the disrupted follicular dendritic cell meshwork remnants. Additionally, special stains were performed using Fite, PAS, and GMS, which were negative for acid fast bacilli and fungal organisms. In addition to the peripheral blood serologic testing mentioned previously, bacterial, fungal and AFB cultures obtained from the excision specimen were negative.

## Treatment

The patient was initially started on clindamycin and ceftriaxone to cover the possibility of an infectious etiology. Otherwise, over the course of several days the patient's symptoms and leukopenia improved spontaneously.

## Discussion

Histiocytic necrotizing lymphadenitis, or Kikuchi–Fujimoto disease, is an uncommon, self-limited, benign disorder that classically presents with tender cervical lymphadenopathy, fever, and leukopenia in young individuals, with a predilection for females [1–3]. Other clinical manifestations may include asthenia, weight loss, skin rash, arthromyalgia, hepatomegaly and splenomegaly, and positive ANA [3]. However, there is no clear etiology and no well-established diagnostic criteria for histiocytic necrotizing lymphadenitis. Furthermore, it has been reported that histiocytic necrotizing lymphadenitis may be associated with systemic lupus erythematosus, perhaps even representing a *forme fruste* of lupus, and there may be concomitant viral infection [1–3].

Diagnostic imaging can be useful for evaluating the extent and nature of the lymphadenopathy in a patient with histiocytic necrotizing lymphadenitis. The majority of cases have unilateral lymph node involvement, mostly in levels 2 and 5 [4–6]. Ultrasound typically demonstrates cervical lymphadenopathy in the form of lymph node clusters or conglomerates that may be accompanied by perinodal fat swelling [6]. On CT, the affected lymph nodes can display homogeneous contrast enhancement or with hypoattenuation areas that correspond to necrosis surrounding by cortical hyperenhancement, as demonstrated in this case [5, 7, 8].

The differential diagnosis for histiocytic necrotizing lymphadenitis on imaging includes autoimmune conditions, such as lupus, neoplastic conditions, such as lymphoma, and infections, such as tuberculosis. Certain imaging features favor histiocytic necrotizing lymphadenitis over some of the other conditions. For example, the presence of multiple necrotic foci, indistinct margins of necrotic foci, a relatively

high CT attenuation of nodal necrosis, and absence of nodal calcification can help differentiate histiocytic necrotizing lymphadenitis from tuberculous lymphadenitis [8].

Ultimately, excisional lymph node biopsy is the only reliable means of establishing a diagnosis [1]. As demonstrated in this article, the typical histologic findings of histiocytic necrotizing lymphadenitis include paracortical areas of coagulative necrosis with abundant karyorrhectic debris, which consists of various types of histiocytes (including the so-called crescentic histiocytes), plasmacytoid dendritic cells, immunoblasts, and small and large lymphocytes, in the absence of neutrophils [1, 9]. The plasmacytoid dendritic cells can be highlighted by CD123 staining. Immunohistochemistry may also reveal CD3+ and CD8+ T lymphocytes and histiocytes expressing CD68/PGM-1 and myeloperoxidase [2].

The disease course tends to be favorable with only supportive therapy, in which symptoms generally resolve spontaneously between 2 weeks and 4 months [2, 9]. However, complications involving the central nervous system, eyes, respiratory tract, kidney, and liver may occur [2]. Systemic corticosteroids or hydroxychloroquine may be administered in such cases [3]. Furthermore, it is important to perform a work up for systemic lupus erythematosus in these patients.

## Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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