

Case report

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Lymph node infarction – a rare complication associated with disseminated intra vascular coagulation in a case of dengue fever

I Satish Rao*¹, Anand C Loya¹, KS Ratnakar¹ and VR Srinivasan²

Address: ¹Department of Pathology, Nizam's Institute of Medical Sciences, Hyderabad, India and ²Department of General Medicine, Nizam's Institute of Medical Sciences, Hyderabad, India

Email: I Satish Rao* - isatishrao@rediffmail.com; Anand C Loya - anandloya@rediffmail.com; KS Ratnakar - ratnakarkamaraju@yahoo.com; VR Srinivasan - medicinenims@eth.in

* Corresponding author

Published: 12 December 2005

Received: 06 May 2005

BMC Clinical Pathology 2005, 5:11 doi:10.1186/1472-6890-5-11

Accepted: 12 December 2005

This article is available from: <http://www.biomedcentral.com/1472-6890/5/11>

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Abstract

Background: Lymph node infarction is known to occur in association with many non-neoplastic and neoplastic conditions however its occurrence in association with DIC is not reported hitherto in the literature.

Case presentation: We describe an unusual case of lymph node infarction in a twenty seven year old male following disseminated intravascular coagulation (DIC) in a case of dengue fever. Multiple sections of the infarcted and the surrounding non-infarcted lymph nodes failed to reveal any predisposing condition. However the parahilar vessels showed thrombotic occlusion, which must have been responsible for the infarction.

Conclusion: Global infarction of the lymph node may mask the underlying pathology. Any malignancy especially lymphoma may coexist or follow lymph node infarction, therefore the patient needs constant surveillance.

Background

Lymph node infarction is a rare occurrence as it has abundant vascularity. Infarction can be due to various non-neoplastic and neoplastic conditions. It may frequently fore shadow neoplastic conditions especially lymphoma and a diligent search should be undertaken to identify the cause. We present a case of lymph node infarction detected in association with disseminated intravascular coagulation in a serologically proven case of Dengue fever.

Case presentation

This twenty-seven year old male presented with complaints of fever with rigor and chills and sore throat for ten days. It was associated with myalgia and recurrent vomit-

ing followed by diffuse maculopapular rash all over the body with sparing of mucous membranes and periorbital tissues. On examination, he had conjunctival congestion with toxic facies. He had a past history of gout for which he received allopurinol for twenty days and phenytoin for sudden loss of consciousness in another institution. There was no past history of tuberculosis, diabetes or hypertension.

Bilateral hard indurated cervical lymphadenopathy and bilateral inguinal lymphadenopathy was also observed along with bilateral parotid and submandibular gland enlargement. Hepatosplenomegaly was detected on ultrasonography. Hemogram on several occasions from admission revealed normal hemoglobin and red blood

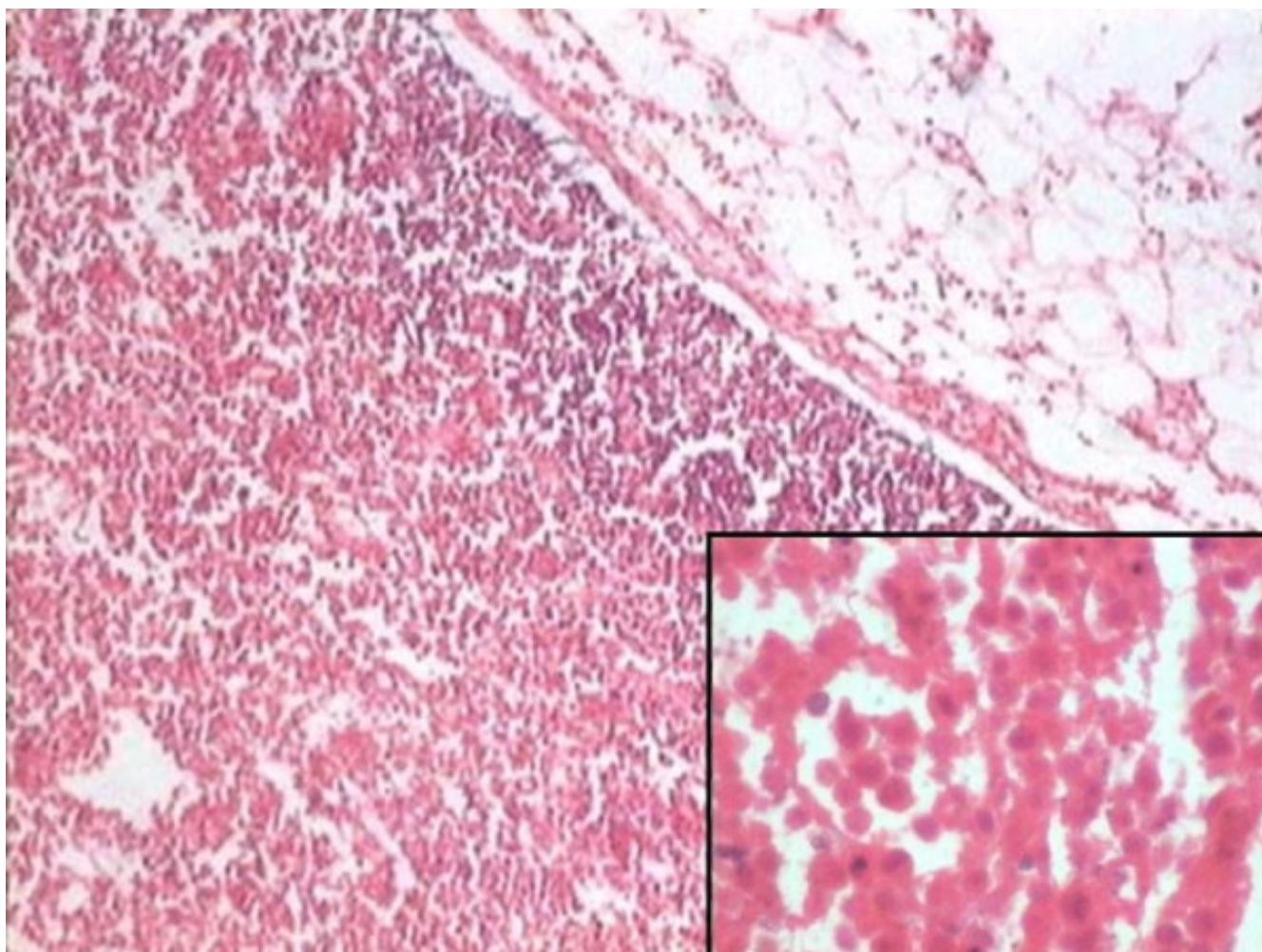


Figure 1

Lymph node infarction with viable rim of sub capsular lymphoid tissue. (40X, H & E) Inset: Note the cellular outlines of the individual lymphocytes, which have undergone coagulative necrosis. (400X, H&E).

cell morphology. There was transient neutrophilic leukocytosis, whereas platelet counts and erythrocyte sedimentation rate were normal throughout. During his treatment with ceftriaxone, he suddenly developed shock, cyanosis and acute renal failure for which he was given inotropic support, amoxicillin, ceftazidime and steroids. He gradually responded and recovered in due course of time. A clinical diagnosis of shock syndrome due to Dengue fever or Epstein Barr virus (EBV) or streptococcus or phenytoin induced hypersensitivity syndrome was made. The Dengue virus IgM antibody Elisa was positive and serum D-dimer levels were positive (>200 ng/ml). Anti EBV IgG antibody test was positive but EBV IgM antibody test was negative. The serology tests for anti- cytomegalovirus antibody, anti leptospira antibody, Widal test, brucella (abortus and melitensis), and HIV were negative. The blood, throat swab and urine cultures were sterile. Paul-Bunnell

and Weil-Felix tests were negative. Cervical lymph node biopsy was undertaken for histopathology.

Gross examination revealed four lymph nodes, the largest one measuring 1.5 cm and the rest below 1 cm. On microscopy, two of the lymph nodes (including the largest one) showed near total infarction of the parenchyma with preservation of cellular outlines of the lymphocytes (Fig 1). A thin rim of viable subcapsular normal mature lymphocytes along with neutrophils and plasma cells were identified. The medullary vessels showed vascular congestion however the blood vessels in the perinodal adipose tissue showed multiple fibrin thrombi with congestion in some of the vessels (Fig 2).

Multiple deeper sections revealed perinodal granulation tissue with viable subcapsular lymphoid tissue but no

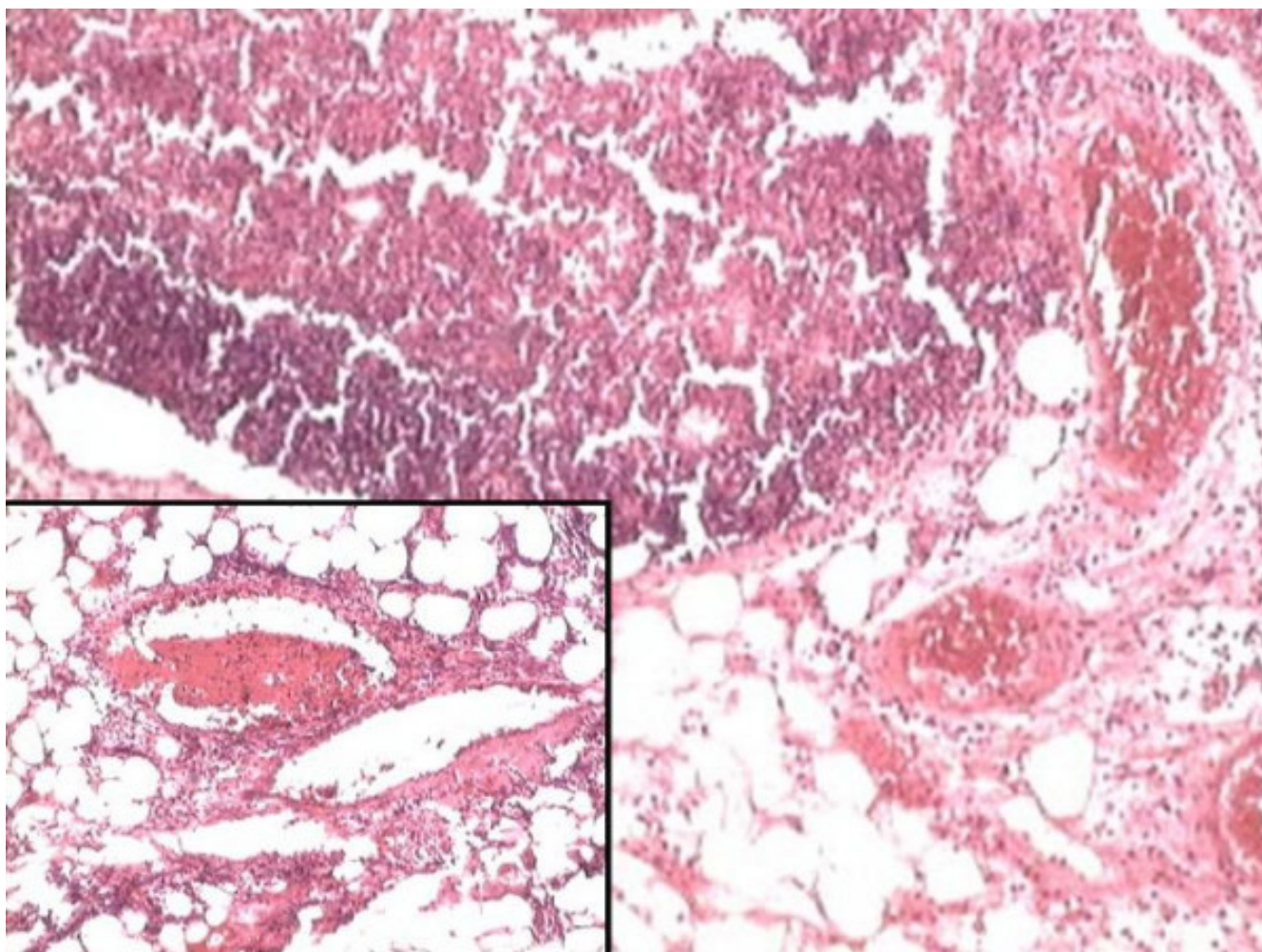


Figure 2
Perinodal blood vessels show marked congestion (H&E-40X), and fibrin thrombi (Inset-H&E-100X).

atypical cells, histiocytes or granulomas were seen. Stains for fungi and acid-fast bacilli were negative. The adjacent two uninvolved lymph nodes showed features of reactive change. Immunohistochemistry with B- cell (CD20) and T- cell (CD3) markers was performed. The viable lymphoid tissue showed an admixture of both B and T-cells. The infarcted tissue showed variable positivity and these markers highlighted few reactive follicles (Fig 3). The uninvolved lymph nodes also showed a normal positivity pattern.

The patient was asymptomatic thereafter and had complete regression of the lymph nodes. He was lost to follow up after two months of discharge from the hospital.

Lymph node infarction is a rare phenomenon reported in literature in association with various neoplastic and non-neoplastic conditions. The non-neoplastic conditions

associated with infarction are namely polyarteritis nodosa, viral infections (Parvovirus B19, Infectious mononucleosis), cholesterol atheromatous embolism, thrombosis, gold injections, intestinal volvulus, postmediastinoscopy, mononeuritis multiplex, fine needle aspiration cytology and finally may be idiopathic [1-11]. Hemorrhagic infarction of hilar lymph nodes has also been reported recently in association with heart lung transplantation. [1,2]

The neoplastic lesions most commonly associated with infarction are malignant lymphoma and metastatic melanoma [1,13-15]. The differential diagnosis pertaining to the present case would be the above mentioned two conditions along with necrotizing lymphadenitis (Kikuchi's lymphadenitis), mucocutaneous lymph node syndrome, and necrotizing granulomatous inflammation.

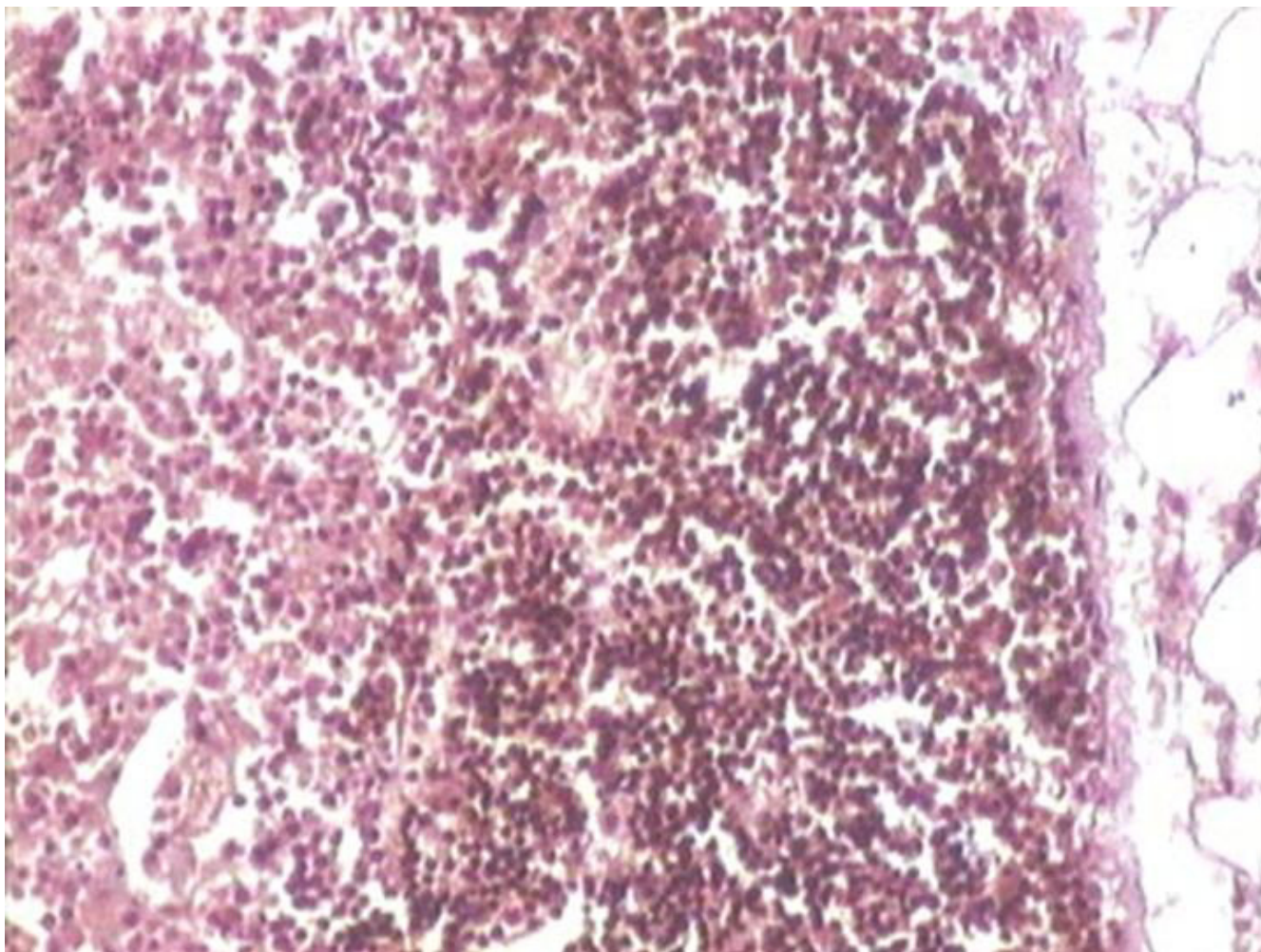


Figure 3

CD20 immunohistochemistry highlights the viable subcapsular lymphoid tissue, where as the adjacent infarcted area also shows focal positivity (H&E-200X).

Serial deeper sections failed to reveal any evidence of either lymphoma or melanoma, any granulomatous inflammation, and vasculitis or monocytoïd histiocytes, thus ruling out the above mentioned conditions. Drug induced hypersensitivity reactions in a lymph node especially due to phenytoin are known in the form of inter follicular expansion by a mixed infiltrate of immunoblasts, plasma cells and eosinophils with varying degrees of vascular proliferation. Focal necrosis has also been observed. Other drugs have been reported to show reactive change [16]. These changes were not seen in the present case in the non-infarcted lymph nodes. In the present case it appears that infarction of the lymph node occurred before the DIC became clinically evident.

A completely infarcted lymph node should alert the pathologist to the high possibility of malignant lym-

phoma, as it is the most common cause of spontaneous lymph node infarction [5]. Further investigation can be carried out by taking multiple deeper sections of the infarcted lymph node to visualize the viable subcapsular tissue for any clue of malignancy. Immunohistochemistry has been done on the infarcted lymph node sections to establish the underlying pathology. Although it is widely believed that necrotic tissue is not suitable for immunohistochemical study, this view may be inaccurate. [17-20]

The detection of spontaneous lymph node infarction should alert the pathologist and the clinician alike for an associated or underlying impending pathology. In a multicentre study of 51 cases of lymph-node infarction seen in the 30-year period, Maurer et al identified 14 cases of malignant lymphoma synchronously with the infarct. Of the remaining 37 patients, six showed manifestations of

malignant lymphoma in the follow-up period within 2 years of the lymph-node infarction.

On analyzing other cases in the literature these authors also confirmed that a minority (26 of 81) have developed malignant lymphoma, which appeared within 2 years of infarction. Therefore, a thorough examination of both the infarcted lymph nodes and others resected at the same time is mandatory in order to exclude concomitant or underlying malignant lymphoma. The risk of development of malignant lymphoma after infarction was found to be negligible after two years [15].

Conclusion

We report a very unusual case of lymph node infarction associated with disseminated intra-vascular coagulation in dengue fever not yet reported in the literature. The simple reason may be that usually lymph nodes are not sampled in DIC. However, any infarcted lymph node should be eyed with suspicion especially when it is enlarged in size. Multiple deeper sections and immunohistochemistry may be very useful to unearth the underlying cause and finally when the cause is not found out, these patients should be followed up for a minimum of 2 years.

List of abbreviations

- 1) DIC – Disseminated intravascular coagulation
- 2) ESR – Erythrocyte sedimentation rate
- 3) EBV – Epstein Barr virus
- 4) IgM – Immunoglobulin M
- 5) IgG – Immunoglobulin G
- 6) HIV – Human immunodeficiency virus

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

ISR – Has made substantial contribution to conception, design, data analysis & interpretation. Has drafted the article and finally approved the article for publication.

ACL – Has made significant contribution in conception, design and co-ordination. Also helped in drafting and revising critically the content of the article.

KSR – Has made critical analysis of the article and approved the article for submission.

VRS – Has provided clinical details and analyzed the article.

References

1. Rosai J: **Lymph nodes, Chapter 21.** In *Ackerman's Surgical Pathology Volume 2.* 8th edition. Edited by: Juan Rosai. Mosby – yearbook, Inc; 1998:1739-1741.
2. Johnson LB, Pasumarthy A, Saravolatz LD: **Parvovirus B19 infection presenting with necrotizing lymphadenitis.** *Am J Med* 2003, **114(4)**:340-341.
3. Kojima M, Nakamura S, Sugihara S, Sakata N, Masawa N: **Lymph node infarction associated with infectious mononucleosis: report of a case resembling lymph node infarction associated with malignant lymphoma.** *Int J Surg Pathol* 2002, **10(3)**:223-226.
4. Shah KH, Kisilevsky R: **Infarction of the lymph nodes: a cause of a palisading macrophage reaction mimicking necrotizing granulomas.** *Hum Pathol* 1978, **9(5)**:597-599.
5. Roberts C, Batstone PJ, Goodlad JR: **Lymphadenopathy and lymph node infarction as a result of gold injections.** *J Clin Pathol* 2001, **54(7)**:562-564.
6. Mahy NJ, Davies JD: **Ischaemic changes in human mesenteric lymph nodes.** *J Pathol* 1984, **144(4)**:257-267.
7. Miller RR, Nelems B: **Mediastinal lymph node necrosis: a newly recognized complication of mediastinoscopy.** *Ann Thorac Surg* 1989, **48(2)**:247-250.
8. Tsuboi Y, Hayashi I, Hori T, Takahashi M, Yamada T: **Subacute necrotizing lymphadenitis associated with mononeuritis multiplex- a case report.** *Rinsho Shinkeigaku* 1999, **39(4)**:465-467.
9. Davies JD, Webb AJ: **Segmental lymph-node infarction after fine-needle aspiration.** *J Clin Pathol* 1982, **35(8)**:855-857.
10. Tsang WY, Chan JK: **Spectrum of morphologic changes in lymph nodes attributable to fine needle aspiration.** *Hum Pathol* 1992, **23(5)**:562-565.
11. Watts JC, Sebek BA, McHenry MC, Esselstyn CB Jr: **Idiopathic infarction of intra-abdominal lymph nodes. A cause of fever of unknown origin.** *Am J Clin Pathol* 1980, **74(5)**:687-690.
12. Ren H, Hruban RH, Baumgartner WA, Reitz BA, Baker RR, Hutchins GM: **Hemorrhagic infarction of hilar lymph nodes associated with combined heart-lung transplantation.** *J Thorac Cardiovasc Surg* 1990, **99(5)**:861-867.
13. Bhargava S, Tewari CP, Arun A: **Lymph node infarction and lymphoma.** *Indian J Cancer* 1989, **26(4)**:233-239.
14. Toriumi DM, Goldschmidt RA, Wolff AP: **Lymph node infarction and malignant lymphoma: a case report.** *J Otolaryngol* 1988, **17(2)**:128-130.
15. Maurer R, Schmid U, Davies JD, Mahy NJ, Stansfeld AG, Lukes RJ: **Lymph-node infarction and malignant lymphoma: a multi-centre survey of European, English and American cases.** *Histopathology* 1986, **10(6)**:571-588.
16. Cousar JB, Casey TT, Macon WR, McCurly TL, Swerdlow SH: *Diagnostic surgical pathology Volume 2.* 3rd edition. Edited by: Stephen S Sternberg. Philadelphia Lippincott Williams and Wilkins; 1999:727-728.
17. Norton AJ, Ramsay AD, Isaacson PG: **Antigen preservation in infarcted lymphoid tissue. A novel approach to the infarcted lymph node using monoclonal antibodies effective in routinely processed tissues.** *Am J Surg Pathol* 1988, **12(10)**:759-767.
18. Vega F, Lozano MD, Alcalde J, Pardo-Mindan FJ: **Utility of immunophenotypic and immunogenotypic analysis in the study of necrotic lymph nodes.** *Virchows Arch* 1999, **434(3)**:245-248.
19. Nasuti JF, Gupta PK, Baloch ZW: **Clinical implications and value of immunohistochemical staining in the evaluation of lymph node infarction after fine-needle aspiration.** *Diagn Cytopathol* 2001, **25(2)**:104-107.
20. Strauchen JA, Miller LK: **Lymph node infarction. An immunohistochemical study of 11 cases.** *Arch Pathol Lab Med* 2003, **127(1)**:60-63.

Pre-publication history

The pre-publication history for this paper can be accessed here:

<http://www.biomedcentral.com/1472-6890/5/11/prepub>