

Nodular lymphoid hyperplasia of lung masquerading as tuberculosis

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Abstract

Nodular lymphoid hyperplasia (NLH) of the lung is a rare entity that is considered to be a benign reactive lymphoid hyperplasia. It shows localised reactive polyclonal lymphoid proliferations. Due to scant literature, very little is known about its clinical behaviour and outcome. It resembles the lymphoid neoplasm so closely that it becomes very difficult to distinguish between nodular lymphoid hyperplasia and low-grade B cell lymphoma of BALT (bronchus associated lymphoid tissue) on histology alone. Here we present a symptomatic case of 6 year old girl, which was misdiagnosed as tuberculosis initially. A mass lesion was detected on computed tomography and wide surgical resection done. On histopathology and immunohistochemistry, she was diagnosed as a case of nodular lymphoid hyperplasia of lung. The girl was kept on regular follow up for one year and was alright.

Keywords: Nodular; Lymphoid; Hyperplasia; Lymphoma; Lung; Tuberculosis.

Introduction

Pulmonary lymphoid lesions include a spectrum of inflammatory and reactive lesions that are often difficult to diagnose and differentiate from other reactive and neoplastic entities. They are intrapulmonary lymph nodes, follicular bronchitis/bronchiolitis, lymphocytic interstitial pneumonia, and nodular lymphoid hyperplasia. Pulmonary nodular lymphoid hyperplasia is term first given by Kradin and Mark in 1983. It is a rare benign lesion of unknown aetiology, which is thought to be localised form of reactive lymphoid proliferations.⁽¹⁻⁴⁾

Case Presentation

A 6 year old girl was presented with complaints of chest pain, expectoration and low grade fever since one year along with off and on haemoptysis for 6 months. She consulted a local physician and took ATT for 4 months. There was no response, and she was referred to our centre. She was anaemic (Hb -9.5 gm/dl) and rest of the biochemical parameters were within normal limits. CT scan revealed bilateral pulmonary mass. Right middle lobe of lung showed well defined hypo dense solid mass lesion with soft tissue attenuation measuring 70 x 60 mm and a similar small nodule also present in the left lobe of lung. No evidence of invasion seen in adjacent pleura or chest wall. No mediastinal lymphadenopathy was detected (Fig. 1a).

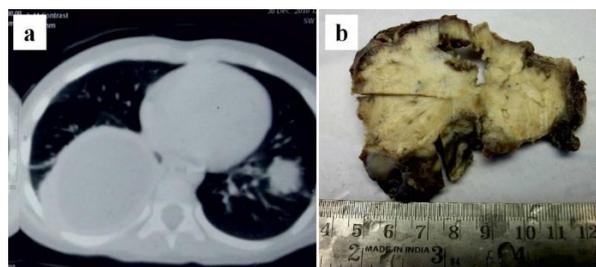


Fig. 1: (a) Computed Tomography (CT) showing bilateral solid mass lesion with soft tissue attenuation. (b) Gross showing solid grey-white area with peripheral brown lung parenchyma

CT guided biopsy showed collection of chronic inflammatory cells suggestive of chronic inflammatory pathology? Abscess. But there was no response with antibiotics treatment and finally, thoracotomy and wide surgical resection done. Grossly there was a solid grey white area measuring 6.5x 4.5x2.5 cm merging into peripheral brown lung parenchyma. There was no area of haemorrhage or necrosis found. (Fig. 1b). On histology lung parenchyma showed diffuse as well as nodular collection of small monomorphous lymphoid cells and reactive germinal centre formation with well preserved mantle zones. Lymphoid cells composed of mainly mature lymphocytes and plasma cells. Alveoli showed destruction and reactive pneumocytes proliferations. Intervening areas showed dense bundles of inter follicular hyalinised connective tissue, dilated congested blood vessels and mixed inflammatory cell infiltrate. Peribronchial inflammatory cell aggregates were present but underlying cartilage was spared (Fig. 2a- b). The main differential diagnosis was nodular lymphoid hyperplasia versus low grade lymphoma of BALT. Immunohistochemistry was done. Germinal centre showed positive staining for CD20 and negative

for BCL-2, whereas mantle zone expressed BCL-2 and Kappa and lambda light chain immunoglobulins (Fig. 3a-d). On the basis of above findings the diagnosis of nodular lymphoid hyperplasia of lung was made. On regular follow up for one year, the girl was alright.

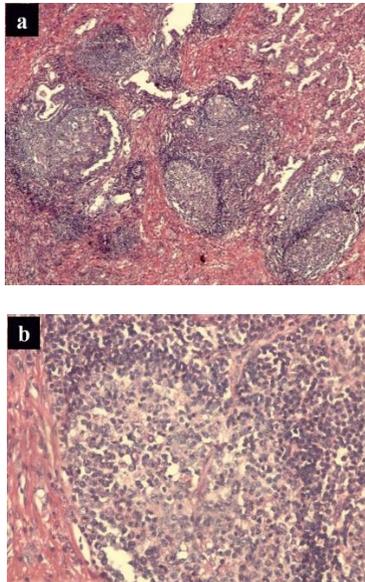


Fig. 2:(a) Photomicrograph shows nodular lymphoid hyperplasia. Lung parenchyma shows abundant reactive follicles and interfollicular area with infiltration of mature lymphocytes and plasma cells H &E x 40X. (b) Germinal centre H & E x 200X

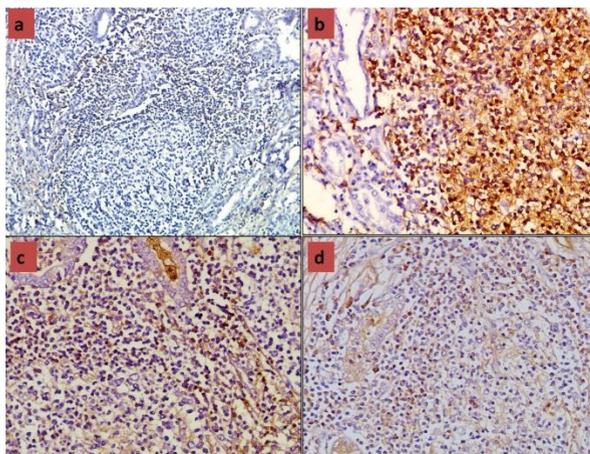


Fig. 3: Immunohistochemistry (a) Bcl2 expression absent in germinal centres, few cells in perifollicular area show positive reaction x 100X (b) CD-20 positive staining in germinal centres x 200X. (c-d) Polyclonal pattern of immuno-histochemical staining for kappa(c) and lambda(d) light chains x 200X

Discussion

Nodular lymphoid hyperplasia (NLH) of lung is a reactive polyclonal expression of BALT (bronchus associated lymphoid tissue). Very little is known about

its clinicopathological features because of its rarity.⁽¹⁻⁴⁾ Abbondanzo et al. reported largest series of 14 cases and concluded that NLH of the lung, although rare, does exist and deserves its place in the spectrum of reactive pulmonary lesions that ranges from follicular hyperplasia to diffuse hyperplasia of the bronchus-associated lymphoid tissue (BALT) including lymphoid interstitial pneumonia, follicular bronchiolitis.⁽²⁻⁶⁾

NLH is a localized but exaggerated form of hyperplasia and hence it is necessary to differentiate it from low grade B-cell lymphoma of BALT which is most common lymphoma of lung (encompassing 95% cases of pulmonary lymphoma).

Clinical features: Males and females are affected equally with mean age of 65 years (range 19-80 years). Usually patients are asymptomatic, but may experience cough, dyspnoea or pleuritic chest pain.⁽¹⁻²⁾ In our case the patient was 6 year old girl presented with chest pain, expectoration, haemoptysis and low grade fever mimicking as tuberculosis. NLH are solitary pulmonary nodules, mostly measuring 2 to 4 cm in diameter, and occasionally multiple lesions (30%).⁽⁴⁻⁵⁾ Approximately 90% of NLH lesions were located at the sub pleura without pleural indentation.^(2,7-8)

Histologically, NLH consists of abundant lymphoid tissue showing reactive lymphoid follicles with germinal centres, sheets of interfollicular mature plasma cells and reactive small lymphocytes, and diverse amounts of interfollicular fibrosis.^(2,6-7)

Immunohistochemical analysis of NLH favours reactive pattern. Germinal centres of follicles show positive staining for CD-20 (B cell marker) and negative for Bcl2. Inter-follicular area shows a polyclonal population of lymphocytes (admixture of B cells and T cells, express CD5, CD3 and CD43), and plasma cells that show both kappa and lambda light chain immunoglobulins.⁽⁶⁻⁸⁾ While BALT lymphoma is a diffuse infiltrating lesion that consists of polymorphic lymphocytes and plasma cells. In addition, most cases show a monoclonal population of plasma cells with light chain restriction.

Initially clinical diagnosis was lung abscess or tumour. Histological differential diagnoses of this case were nodular lymphoid hyperplasia versus low grade lymphoma of BALT, Follicular bronchiolitis, lymphoid interstitial pneumonia (LIP) and inflammatory pseudo tumour. In our case there was localise, discrete mass hence it was distinguished from of LIP and follicular bronchiolitis as they involve the lung in diffuse manner. There was no evidence of myofibroblastic or fibro-histiocytic spindle cell proliferation (inflammatory myofibroblastic tumour). BALT lymphomas also have reactive germinal centres with large mantle zones; hence it must be differentiated from NLH. The features that favour a BALT lymphoma include conspicuous infiltrative growth with prominent lymphangitic spread, plaque-like infiltration of the pleura, and invasion of bronchial cartilage.⁽²⁻³⁾

Lymphoepithelial lesions, monocytoid B cells are often seen in BALT lymphomas while these features are usually not common in nodular lymphoid hyperplasia. Immunohistochemical stains for lymphoid markers show coexpression of CD43 and CD20 and monoclonal pattern for immunoglobulin light chains. Molecular analysis shows immunoglobulin heavy chain gene rearrangements in the majority of BALT lymphomas, but not seen in nodular lymphoid hyperplasia.⁽²⁻³⁾

In our case germinal centre showed positive staining for CD20 and negative for BCL-2, whereas mantle zone expressed BCL-2 and Kappa and lambda light chain immunoglobulins (polyclonal pattern). On the basis of above findings the diagnosis of BALT lymphoma is excluded.

The diagnosis of NLH, by transbronchial biopsy or transthoracic needle biopsy, can often be difficult because findings of reactive lymphoid proliferation can also be detected in primary lung cancer, lymphoma, or inflammation. Surgical excision may be the diagnostic procedure of choice for NLH.^(3,7-9)

Our case was misdiagnosed as tuberculosis due to similar symptoms by local physician and also as an abscess on small endo-bronchial biopsy. Surgical resection is recommended for both diagnoses and therapeutic. No recurrences reported.^(2,7,9) Being a rare entity, the reporting of such cases of NLH with immunohistochemical and molecular studies will further required to elucidate its clinicopathological features.

Conclusions

Nodular lymphoid hyperplasia (NLH) although benign lesion must be differentiated from low grade lymphoma of BALT. Immunohistochemistry is main diagnostic aid which confirms the diagnosis. Transbronchial biopsy or transthoracic needle biopsy often be misleading. Wide surgical resection serves the purpose for both diagnoses as well as therapeutic.

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