Case Report

Extranodal Marginal Zone Lymphoma of Mucosa Associated Lymphoid Tissue Arising in The Pleura

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Keywords: *Lymphoma, B-Cell, Marginal Zone, MALT Lymphoma*

ABSTRACT

A 77-year-old Haitian woman complained of two months history of cough and left upper quadrant abdominal pain. She had a remote history of tuberculosis that was treated back in Haiti many years ago. Imaging studies showed a left pleural effusion with posterior pleural thickening as well as lymphadenopathy in the left hilum and left supraclavicular area. The Pleural biopsy was consistent with extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (EMZL/MALT). The supraclavicular lymph node also showed partial involvement by EMZL/MALT but was largely effaced by non-necrotizing granulomatous inflammation. Culture from this lymph node grew Mycobacterium tuberculosis complex. Primary pleural lymphoma is a rare entity and to the best of our knowledge only ten cases of pleural EMZL/MALT have been reported. We report a new case and a review of literature.

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Introduction

Malignant lymphoma arising in pleura comprises only 2.4% of primary chest wall tumors [1]. Body cavity-based lymphomas can happen in forms of: primary effusion lymphoma (PEL), a high grade B-cell lymphoma associated with HHV-8 and EBV in immunodeficient patients[2]; pyothorax associated lymphoma (PAL), a high grade B-cell lymphoma associated with a long standing iatrogenic pyothorax and EBV[3]; or extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (EMZL/MALT) which is a low grade B-cell lymphoma that in other sites are often associated with chronic infection or autoimmune disease.

Case Report

The patient was a 77-year old Haitian woman with hypertension, diabetes mellitus, gastroesophageal reflux disease, as well as a remote history of tuberculosis (that was treated with antibiotics in Haiti) who presented with a two month history of cough and left upper quadrant abdominal pain. Her chest CT scan showed a left-sided pleural effusion as well as diffuse nodular thickening in the left posterior pleura. In addition there were prominent lymph nodes in the left hilum, aortic pulmonary window, and left supraclavicular area with the largest measuring 2.2 cm which had a SUV max of 4.4 by PET scan. Video assisted thoracic surgery (VATS) was recommended but the patient refused this procedure. Thoracocentesis was performed and cytopathology of the pleural fluid showed small mature lymphocytes with admixed mesothelial cells and was interpreted as being benign. Cultures were negative for microorganisms.

Ten months after, the patient continued being symptomatic with no improvement and also had a 15 lbs weight loss. Eventually she agreed to have VATS and a pleural biopsy and supraclavicular lymph node excision was performed. An intraoperative frozen section was performed on the pleural biopsy, which prompted separate submission of the pleural biopsy and left supraclavicular lymph node for flow cytometry. Both the pleural biopsy and supraclavicular lymph node were also submitted for culture by the surgeon. A bronchial washing was also submitted in addition to sputum for culture.

Pathologic findings: The pleural biopsy showed a dense lymphoid infiltrate with a hyperplastic mesothelial lining. The dense sheets of lymphocytes showed infiltration into adipose tissue and skeletal muscle. There were a few scattered germinal centers with an expanded interfollicular component or marginal zone that was composed of monomorphic monocytoid lymphocytes. These monocytoid lymphocytes had round to oval nuclei, irregular nuclear contours, granular chromatin, and abundant clear cytoplasm with ill-defined borders [figure 1a]. The scattered germinal centers had a moth-eaten appearance and lacked a mantle zone [figure 1b].

Immunohistochemical studies revealed that the lymphocytes were predominantly B-cells as highlighted by Pax-5 [figure 2a]. The B-cells showed aberrant CD43 expression (figure 2b) and were also weakly MUM1 positive. Immunohistochemistry showed that the germinal centers were partially colonized with a subset of lymphocytes being Bcl-6 positive and Bcl-2 negative. CD23 highlighted disrupted follicular dendritic cell meshworks associated with these colonized germinal centers [figure 2c]. CD3 and CD5 highlighted a minor component of T-cells. The B-cells showed no aberrant CD5 expression [figure 2d]. Cyclin D1 and CD138 were negative. Ki-67 showed a 10% proliferation index within the interfollicular component.

Flow cytometry of the pleural biopsy showed a predominant monotypic B-cell population that was positive for CD19 and surface kappa light chain accounting for 83% of all nucleated cells [figure 3], they were negative for CD5, CD10, , and CD23. Culture submitted from the pleural biopsy was negative.

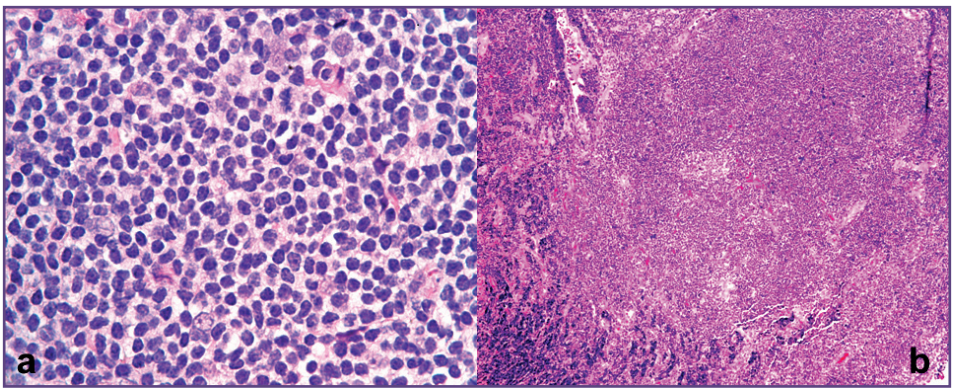

Fig. 1: a) 400X view of expanded interfollicular or marginal zone composed of monomorphic monocytoid lymphocytes; b) 40X view of Moth eaten germinal center lacking a mantle zone with expanded interfollicular or marginal zone (H&E, 400X & 40X)

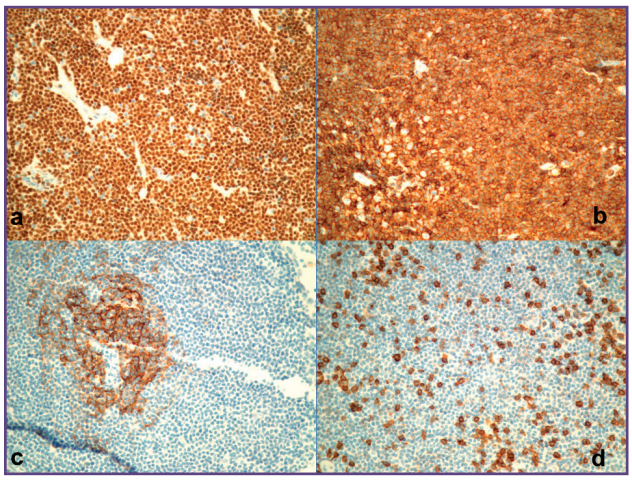

Fig. 2: Immunohistochemistry; a) PAX-5; b) aberrant expression of CD43; c) disrupted follicular dendritic cells highlighted by CD23; d) CD5 negative B-cells

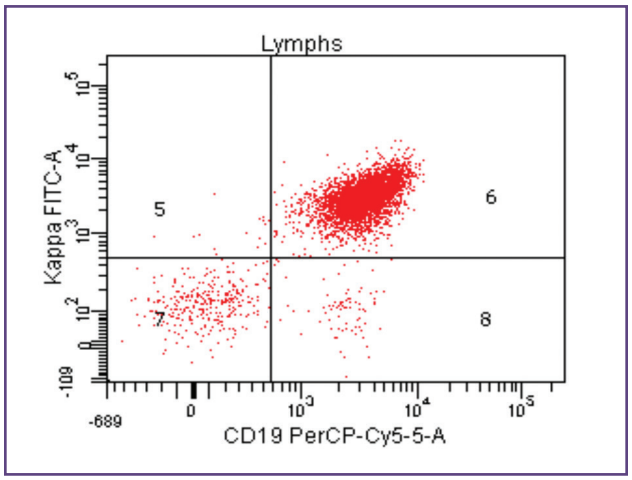

Fig. 3: Flow cytometry on pleura shows majority of cells are B-Cells (positive for CD19), monoclonal Kappa restricted

On the other hand, the supraclavicular lymph node showed partial effacement by exuberant non-necrotizing granulomas with an associated dense sclerosis. Immunohistochemistry with Pax-5 highlighted follicles as well as small clusters of interfollicular B-cells. CD3 highlighted the paracortex. Flow cytometry performed separately on the supraclavicular lymph node showed a monotypic B-cell population that was kappa-restricted accounting for 28% of all nucleated cells. In addition, special histochemistry with AFB showed no acid fast bacilli. Despite such, the lymph node culture grew out mycobacterium tuberculosis complex after 4 weeks. Bronchial washing and sputum cultures showed no pathologic microorganisms, including mycobacterium tuberculosis.

The findings were consistent with a primary pleural extranodal marginal zone lymphoma of mucosa associated lymphoid tissue (EMZL/MALT). In addition there was evidence of regional involvement as seen in the left supraclavicular lymph node. Interestingly the supraclavicular lymph node showed an exuberant non-necrotizing granulomatous response with cultures that grew out mycobacterium tuberculosis complex.

Discussion

Extranodal marginal zone lymphoma is one of the three types of marginal zone lymphoma in addition to nodal and splenic forms. Extranodal marginal zone lymphoma of mucosa associated lymphoid tissue comprises 7-8% of all B-cell lymphomas. Median age of involvement is 61-years with a slightly higher rate in females (female:male is 1.2:1). Common sites of EMZL/MALT include the stomach (associated with Helicobacter pylori), small intestine (known as immunoproliferative small intestinal disease [IPSID] and is associated with Campylobacter jejuni), skin (associated with Borrelia burgdorferi), eye (associated with Chlamydia psittacii), submandibular gland (associated with Sjogren or lymphoepithelial sialadenitis), and thyroid (associated with Hashimoto thyroiditis) [4]. Although pleural involvement by systemic non-Hodgkin lymphoma has been observed in 16% of the patients [5], primary MALT lymphoma in the pleura is very rare.

There have been only 10 cases of primary pleural marginal zone lymphoma with the first case reported in 1999. Half of these cases were reported in Japan [table1]. In fact the first case reported in 1999 by Kodama et al. was a case of pleural dissemination of an EMZL/MALT from the lung [6]. The second and third primary pleural EMZL/MALT cases were reported by Ahmad et al. in 2003 with one of the patients having a remote history of tuberculosis and the other having history of asbestos exposure [7]. Seven more cases were reported, all of which were localized to the pleura and none had regional lymph node involvement. The only case with systemic involvement was reported by Gomyo et al. who described bone marrow involvement with the presence of t (14; 18) involving the IGH and MALT1 genes [8].

The mean age of these ten cases was 66 years with male:female ratio being 4:1. The most common presentation at the time of diagnosis was dyspnea and chest pain. The majority of the patients were non-smokers at the time of diagnosis and no common risk factor was proposed. However, there was one case in which the patient was a lathe operator for 40 years [9]. 50% of the cases had followed up after diagnosis and initial therapy, and the majority of these patients had complete remission after resection, pleurodesis and or chemotherapy without any complication. [6-14]

Table 1: summary of previous reported cases with pleural EMZL/MALT

Source	Age	Sex	Symptoms	Potential Risk Factors or Exposures	Smoking Status	Other Accompanying Findings	Staging	Treatment	Survival
Kodama et al. 1999 [6]	79	M	Asymptomatic	Unknown	Unknown	Lung MALT lymphoma	No metastasis beyond pleura	Surgical resection	Unknown
Ahmad et al. 2003 [7]	59	M	Dyspnea, chest pain	Asbestos	No	No	Pleural disease only	Pleurodesis + chemotherapy	No recurrence (18 months)
Ahmad et al. 2003 [7]	49	M	Dyspnea, couph, weight loss	Remote history of TB	No	No	Pleural disease only	Anti TB + chemotherapy	No recurrence (14 mon)
Hirai et al. 2004 [10]	72	M	Exertional dyspnea	Unknown	Unknown	No	Unknown	Surgical resection+RXT	Unknown
Mitchell et al. 2006 [11]	47	M	Fever, chest pain	Pyothorax	stopped 4 yrs prior	IgM-γ monoclonality	Pleural disease only	No treatment	Stable disease after 8 months
Gomyo et al. 2007 [8]	67	F	Dyspnea	No	No	Waldenstrom's macroglobulinemia	Bone marrow involve, t(14;18)	chemotherapy	Complete lymphoma remission, stable IgM (19 mon)
Kawahara et al. 2008 [12]	79	M	Back pain	No	Smoker	No	Unknown	surgical resection (IT-Knife)	Unknown
Motta et al. 2010 [13]	74	F	Couph, weakness	No	No	No	Pleural disease only	Pleurodesis + Rituximab	Relapse after 2 yrs
Barahona et al. 2011 [14]	52	M	Obstructive sleep apnea	No	No	No pleural effusion	Unknown	Unknown	Unknown
Nakatsuka et al. 2012 [9]	86	M	Asymptomatic	40 years Lathe operator	Smoker	Pneumoconiosis	Pleural disease only	Surgical resection	Unknown

Conclusion

Primary pleural lymphomas are quite rare with both primary effusion lymphoma (PEL) and pyothorax associated lymphoma (PAL) being more common than extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue. Both PEL and PAL show high-grade morphologic and clinical features. Primary pleural marginal zone lymphomas in contrast to PEL and PAL, show low-grade morphology. EMZL/MALT is often associated with an infectious or autoimmune etiology, however no common etiologic agent or risk factor has been proposed for pleural EMZL/MALT. Our patient had a remote history of tuberculosis with a positive supraclavicular lymph node culture that grew out mycobacterium tuberculosis complex. However culture from pleural biopsy was negative. We propose that the evidence of mycobacterium tuberculosis infection seen within the supraclavicular lymph node is a concurrent unrelated process in addition to primary pleura marginal zone lymphoma involving regional lymph nodes.

Acknowledgements

Department of Pathology and Laboratory Medicine at Boston Medical Center, Department of Cardiothoracic Surgery at Boston Medical Center

Funding

None

Competing Interests

None

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