CASE REPORT

Nodal mycobacterial spindle cell pseudotumor: A diagnostic pitfall

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ABSTRACT

Inflammatory pseudotumor (IPT) is a rare benign mass forming lesion that has been reported in virtually every organ, and can closely mimic spindle cell neoplasms. Mycobacterial spindle cell pseudotumor (MSP) represents a small proportion of IPT of the lymph node, which occur in immunocompromised patients, posing a diagnostic challenge. We report three cases of MSP involving two AIDS patients who presented with generalized lymphadenopathy, and one immunosuppressed patient with a mediastinal mass. Biopsy in these cases revealed effaced architecture replaced by proliferating fibrohistiocytic spindle cells, fibrosis and polymorphic inflammatory infiltrate. Inflammatory pseudotumors and other spindle cell neoplasms of the lymph node can show overlapping morphologic features, resulting in diagnostic confusion. A differential diagnosis of Mycobacterial spindle cell pseudotumor should be kept in mind when approaching localized or generalized lymphadenopathy in an immunocompromised patient.

Key Words: Inflammatory pseudotumor, Mycobacterial spindle cell pseudotumor, Mycobacterium avium, Immunocompromised, Diffuse lymphadenopathy, Spindle cell lesion

1. INTRODUCTION

The term "inflammatory pseudotumor" (IPT) was coined by Umiker and Iverson in 1954,[1] and represents a rare, benign, mass-forming lesion that has been reported in virtually every organ. The clinical, radiological and histological findings can closely mimic spindle cell neoplasms, including malignant tumors. Spindle cell pseudotumors of the lymph node are very uncommon. Histologically, IPT of the lymph nodes show proliferation of spindle cells in a polymorphous inflammatory background. The findings can closely mimic a neoplastic process and pose a diagnostic challenge. No clear etiological factors have been reported, although a small proportion are related to infection with mycobacteria in immunocompromised patients; this is known as Mycobacterial Spindle Cell Pseudotumor (MSP). MSP is the result of an unusual host response to mycobacterial infection in the setting of immunodeficiency. We report three cases of MSP involving two acquired immunodeficiency syndrome (AIDS) patients who presented with diffuse lymphadenopathy, and one immunosuppressed patient with a mediastinal mass. Biopsies in all cases demonstrated marked spindle cell and histiocytic proliferation in background of fibrosis. Modified Kinyoun stain for acid-fast bacilli (AFB) was positive in all three cases. These cases illustrate a potential diagnostic pitfall in diagnosis of spindle cell and fibroinflammatory lesions of the lymph node. Identification of the important

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histopathological findings and increased awareness of this entity can prevent diagnostic errors.

2. Case presentation

2.1 Case 1

A 44-year old man presented with complaints of fever and shortness of breath. The patient had a long history of AIDS originally diagnosed 12 years ago with multiple recurrent opportunistic infections due to noncompliance with highly active antiretroviral therapy (HAART). Laboratory testing on his latest admission revealed a CD4 count of 0 cells/mcL with a viral load over 300,000 copies/mL. An abdominal computed tomography scan (CT) revealed diffuse mesenteric and retroperitoneal lymphadenopathy, concerning for a lymphoproliferative disorder, and prompting a laparoscopic mesenteric lymph node excisional biopsy.

2.2 Case 2

A 53-year old man presented in January of 2015 with complaints of chest pain. Chest CT at that time revealed pulmonary nodules and prominent bilateral axillary lymph nodes. He was lost to follow-up until July 2015 when he presented once again with nonspecific abdominal pain, subjective fevers, and weight loss. His laboratory work up returned positive for human immunodeficiency virus (HIV) 1, with a viral load greater than 1 million, and CD4 count of 12 cells/mcL. An abdominal CT scan revealed hepatic lesions and abscesses, splenic lesions, and diffuse lymphadenopathy. A biopsy of the left inguinal lymph node was performed. Interestingly, a concomitant liver biopsy showed involvement by diffuse large B-cell lymphoma. AFB stain was negative in the liver biopsy.

2.3 Case 3

A 69-year old man with a history of renal transplant due to end stage renal disease on immunosuppression presented with cough, congestion, and fatigue. The patient additionally had a remote history of classical Hodgkin's lymphoma diagnosed over ten years ago, now in complete remission. Chest CT revealed a 4.1 $\times$ 4.6 cm right sided mediastinal soft-tissue mass, consistent with mediastinal lymphadenopathy. The clinical differential diagnosis included post-transplant lymphoproliferative disorder (PTLD) and a relapsed Hodgkin lymphoma. A surgical biopsy of the mediastinal mass was performed.

2.4 Histological findings

All three cases showed overtly similar morphological features. Microscopic examination of each specimen revealed effaced nodal architecture by fascicles of proliferating fibrohistiocytic spindle cells, collagen fibrosis, vascular proliferation, and polymorphic inflammatory infiltrate. The spindle cells showed a bland morphology. The background inflammatory infiltrate was comprised of small lymphocytes, macrophages and neutrophils. There was increased vascular proliferation. There were no well-formed granulomas, multinucleated giant cells or Reed-Sternberg cells/Hodgkin cells (see Figure 1). Immunohistochemistry (IHC) demonstrated that the spindle cells and macrophages were positive for CD45 and CD68. The spindle cells and histiocytes were negative for EBER (EBV in-situ hybridization), CD15, CD30, HHV-8, CD21, CD23, CD31, CD34, smooth muscle actin (SMA) and S-100. Scattered T-cells and B-cells were positive for CD3 and CD20 respectively. An AFB stain (modified Kinyoun) revealed the presence of numerous acid fast bacilli within the spindle cells and macrophages (see Figure 1). Microbial cultures and polymerase chain reaction (PCR) were performed on the tissue, which returned a positive result for Mycobacterium avium complex in case 1 and 2, and Mycobacterium tuberculosis complex in case 3.

3. Discussion

Mycobacterial spindle cell pseudotumors are a rare entity, originally described in 1985.[2] They usually occur in immunocompromised patients, although rarely they have been reported in immunocompetent patients with predisposing factors.[3,4] They typically present in the lymph nodes, although they can occur in any location. Other reported sites include: skin,[4] brain,[5] nasal cavity,[6] lungs,[7] and spleen.[8] Table 1 summarizes the clinicopathologic features of all reported cases in the literature. The most common etiological agent is Mycobacterium avium complex, while Mycobacterium tuberculosis complex is the second most common organism. Other rare non-tubercular mycobacteria that have been reported to be associated with spindle cell pseudotumors include: M chelonae,[9] M microti,[10] M haemophilum, M simiae,[11] M kansasii, M gordonae, M xenopi,[12,13] M szulgai,[14] M genavense.[15] There are also rare case reports of Bacillus Calmette-Guérin induced MSP.[16–19]

Mycobacterial spindle cell pseudotumors should be differentiated from other mesenchymal neoplasms of the lymph node, most notably Kaposi sarcoma (KS), although there are several conditions that can mimic MSP. These include idiopathic inflammatory pseudotumor, Hodgkin lymphoma, leiomyoma, follicular dendritic cell tumor and intranodal hemorrhagic tumors with amianthoid fibers. Considering all of these entities, the most important and difficult differential diagnosis is Kaposi sarcoma. Both KS and MSP are frequently seen in immunocompromised, HIV positive patients.[12] Involvement by KS can be very focal, showing characteristic vascular proliferation, mitotic figures and

extravasation of red blood cells. The extent of cytological atypia is usually greater in KS than in MSP. KS can also appear with concomitant mycobacterial infection involving lymph nodes, mimicking MSP and necessitating the need for IHC.[20] Kaposi sarcoma is usually positive for vascular markers such as CD31 and CD34. Availability of the antibody for HHV-8 by IHC has also made the differentiation easy. Conversely, spindle and epithelioid cells in MSP are usually positive for CD68 and S100.[21] Predisposition to develop Hodgkin lymphoma in patients with HIV infection and AIDS has been well reported in literature.[22,23] Rare cases of classical Hodgkin lymphoma can show prominent fibroblastic and histiocytic components, and minor populations of Reed-Sternberg cells can be easily overlooked. However, a careful examination of the slide will usually reveal the presence of Reed-Sternberg cells. Hodgkin lymphoma can be easily ruled out with the use of CD15, CD30 and CD45 IHC stains, with the Reed-Sternberg cells staining positive for CD30, CD15 and negative for CD45.

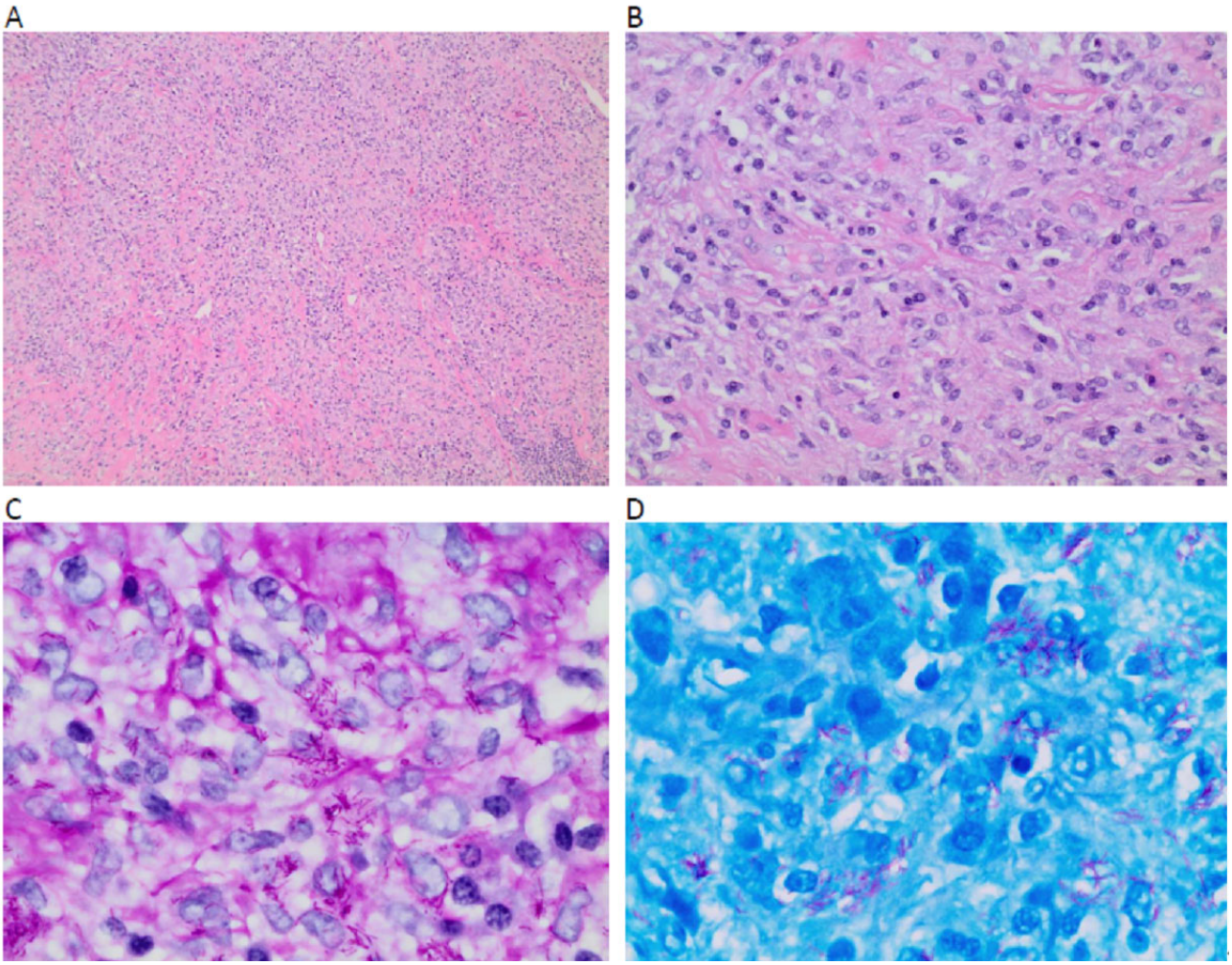

Figure 1. Histology of Mycobacterial Spindle Cell Pseudotumor. A. Low-power hematoxylin and eosin (H&E) picture shows effaced nodal architecture by fascicles of proliferating spindle cells and increased vascular proliferation (x200). B. High-power picture of H&E section shows fibrohistiocytic spindle cells with bland morphology, collagen fibrosis and polymorphic inflammatory infiltrate (x1000). C. High-power PAS stain and D. High-power AFB stain (modified Kinyoun) shows presence of numerous acid fast bacilli within the spindle cells and macrophages.

Follicular dendritic cell tumors can also present with lymphadenopathy. Follicular dendritic cell sarcoma is comprised of a proliferation of spindle to ovoid cells, which take on a storiform or fascicular pattern. The cells usually have distinct cell borders and a moderate amount of eosinophilic cytoplasm. They show positivity for one or more follicular dendritic cell markers such as CD21, CD23 and CD35.[24] Intranodal leiomyomas are very uncommon and can be seen in HIV positive patients and rarely in cases of benign metastasizing uterine leiomyomas. The morphology shows interlacing

fascicles and bundles of bland spindle cells with blunt-ended nuclei. The cells are positive for smooth muscle actin.[25] Intranodal hemorrhagic spindle cell tumors with amianthoid fibers (also known as intranodal palisaded myofibroblastoma) is a very rare benign mesenchymal neoplasm, consisting of smooth muscle cells and myofibroblasts. Histopathological appearance is characterized by spindle cell proliferation with nuclear palisading, intraparenchymal hemorrhage and thick collagen fibers (also known as amianthoid fibers), with the spindle cells being positive for smooth muscle actin and vimentin.[25,26]

Table 1. Clinicopathologic characteristics of all cases of mycobacterium spindle cell pseudotumor

Authors	Age/Sex	Site	Organism	Related Comorbidities
Wood et al. 1985[2]	54M	Skin	MAI*	Solid organ transplant, Immunosuppressive therapy
Brandwein et al. 1990[12]	33M	Lymph Node	No Culture	AIDS
Brandwein et al. 1990[12]	34M	Skin	*M. kansasii*	HIV
Brandwein et al. 1990[12]	25M	Lymph Node	No culture	None
Brandwein et al. 1990[12]	27F	Lymph Node	MAC**	AIDS
Brandwein et al. 1990[12]	35M	Lymph Node	MAC**	AIDS
Umlas et al. 1991[27]	27M	Lymph Node	MAI*	HIV
Umlas et al. 1991[27]	31M	Lymph Node	MAI*	AIDS
Umlas et al. 1991[27]	33M	Bone Marrow	MAI*	AIDS
Chen et al. 1992[28]	59M	Lymph Node	1 Unknown, 1 MAI*	HIV
Apel et al. 1993[29]	30M	Hilar/mediastinal	MAI*	Hodgkin's Lymphoma
Sekosan et al. 1994[30]	32M	Lung	MTB***	Solid organ transplant, Immunosuppressive therapy
Suster et al. 1994[8]	55M	Spleen	No culture	AIDS
Corkill et al. 1995[31]	28M	Lymph Node	No culture	AIDS
Wolf et al. 1995[32]	41M	Lymph Node	MAI*	HIV
Wolf et al 1995[32]	29M	Lymph Node	MAI*	HIV
Morrison et al. 1999[33]	38M	Brain	MAI*	Steroid treated for sarcoidosis
Logani et al. 1999[20]	65M	Lymph Node	MAI*	AIDS
Logani et al. 1999[20]	35M	Lymph Node	No culture	HIV
Logani et al. 1999[20]	26M	Lymph Node	No culture	HIV
Basilio-de-Oliveira et al. 2001[34]	34M	Appendix	No culture	AIDS
Yin et al. 2001[35]	1M	Lymph Node	No culture	BCG vaccine
Yin et al. 2001[35]	1M	Lymph Node	No culture	BCG vaccine
Woodhouse et al. 2002[36]	34M	Skin	MAI*	HIV
McArthur et al. 2003[37]	35M	Lymph Node	No culture	HIV
Liou et al. 2003[38]	37M	Skin	MTB***	HIV
Gunia et al. 2005[39]	76M	Nasal septum	No culture	None
Vaos et al. 2007[40]	9F	Liver	MTB***	None
Shiomi et al. 2007[3]	58F	Skin	*M. intracellulare*	Steroid treated systemic lupus erythematosus
Charnot-Katsikas et al. 2008[14]	36M	Lymph node	*M. szulgai*	DLBCL†, Hodgkin's lymphoma
Manitsas et al. 2008[41]	30M	Colon	MAC**	AIDS
Androulaki et al. 2008[42]	40M	Kidney	MTB***	None
Phowthongkum et al. 2008[11]	40M	Brain	*M. haemophilum*, *M. simiae*	AIDS
Tan et al. 2009[43]	43M	Skin	Atypical mycobacterium	None
Satish et al. 2009[44]	7 months	Lymph node	MTB***	BCG vaccine
McGoldrick et al. 2010[10]	44M	Lymph node (mediastinum)	*M. microti*	Steroid and azathioprine treated oral lichen planus
Ilyas et al. 2011[45]	63M	Nasal cavity	MAC**	Treated DLBCL†
Yeh et al. 2011[9]	55M	Skin	*M. chelonae*	Steroid treated scleroderma
Alves et al. 2012[46]	28M	Liver	MTB***	AIDS
Philip et al. 2012[7]	51F	Lung	MAI*	AIDS
Sideras et al. 2013[47]	42M	Plantar fascia	No culture	HIV
Ohara et al. 2013[6]	83M	Nasal cavity	MAI*	HIV

(Table 1 continued on page 37.)

Table 1. (continued)

Authors	Age/Sex	Site	Organism	Related Comorbidities
Rahmani et al. 2013[4]	79M	Skin	MAC**	Solid organ transplant, Immunosuppressive therapy
Holmes et al. 2014[48]	58M	Skin	*M. chelonae*	None
Ismail et al. 2015[49]	69M	Brain	MAI*	Steroid treated sarcoidosis
Franco et al. 2015[50]	69F	Lung	MAC**	Solid organ transplant (lung), immunosuppressive therapy
Lim et al. 2016[51]	66M	Brain	MAC**	Steroid treated sarcoidosis
Coelho et al. 2017[15]	13M	Lymph node	*M. genavense*	Stem cell transplant, immunosuppressive therapy
Thwaites et al. 2018[52]	88M	Bone	*M. chelonae*	Diabetes
Fonda-pascual et al. 2018[53]	50M	Skin (penis)	MAI*	Combined immunodeficiency
Dhibar et al. 2018[54]	38M	Lymph node	MTB***	AIDS
Boylan et al. 2018[55]	33M	Lung	No culture	AIDS
Boylan et al. 2018[55]	45M	Lung	MAC**	HIV
Boylan et al. 2018[55]	69F	Lung	No culture	None
Taneja et al. 2020[56]	34M	Lymph node	MAC**	AIDS
Furlan et al. 2020[13]	42F	Lung	MTB***, MAC**, *M. kansassii, M. gordonae, M. xenopi*	Solid organ transplant, immunosuppressive therapy
Chesdachai et al. 2020[57]	68F	Lung	MAI*	Solid organ transplant, immunosuppressive therapy

**Mycobacterium avium-intracellulare*

***Mycobacterium avium complex*

****Mycobacterium tuberculosis*

†Diffuse large B-cell Lymphoma

Note. Clinicopathologic characteristics of all cases of mycobacterium spindle cell pseudotumor, presented in order of publication.

Mycobacterial pseudotumors not only cause clinical and diagnostic confusion but can also confound the clinical picture as seen in the second case. This case showed hepatic diffuse large B-cell lymphoma as well as nodal MSP. MSP can also co-exist with other entities in same biopsy such Kaposi sarcoma and lymphomas. Omission of this diagnosis will prevent optimal therapeutic management in these cases. Lymphoma was the main differential diagnosis in all three cases. The third case was more challenging from a clinical and pathologic point of view due to a primary concern for PTLD.

4. Conclusion

This case mini-series aims to not only contribute to the available literature regarding mycobacterial spindle-cell tumors, but reinforces the importance of keeping several diagnostic options in mind when approaching lymphadenopathy in an immunocompromised patient. Mycobacterial spindle cell pseudotumor should be considered in the differential diagnosis of spindle cell and histiocytic lesions of lymph node in these patients. The possibility of MSP co-existing with other lymph node pathology should not be overlooked. A timely and accurate diagnosis can ensure optimal management and avoid unnecessary complications due to delayed/incomplete diagnosis.

Conflicts of Interest Disclosure

The authors declare that they have no conflicts of interest.

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