Enigmatic intranodal spindle cell lesion

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Received 22 March 2020
Accepted 21 April 2020
Published Online First 8 June 2020

CLINICAL QUESTION

A middle-aged woman without prior medical history presented with multiple enlarged lymph nodes in the right anterior cervical chain. Excisional biopsy of the affected nodes was performed. Two adherent lymph nodes were received measuring 3×3 cm together. The sample was bisected and submitted for histopathological evaluation. Review the high quality, interactive digital Aperio slide at http://virtualacp.com/JCPCases/jclinpath-2020-206586/ and consider your diagnosis.

WHAT IS YOUR DIAGNOSIS?

A. Fibroblastic reticular cell sarcoma.
B. Follicular dendritic cell sarcoma.
C. Inflammatory myofibroblastic tumour.
D. Interdigitating dendritic cell sarcoma.
E. Intranodal palisaded myofibroblastoma.

The correct answer is after the discussion.

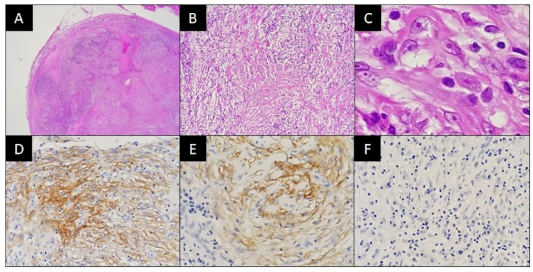

Figure 1 (A) Effacement of the nodal architecture and replacement by a lobular proliferation (H&E, 25×). (B) Spindle cells are intimately admixed with lymphocytes (H&E, 100×). (C) The spindle cells have uniform ovoid vesicular nuclei with distinct single central nucleoli (H&E, 400×). Immunohistochemistry is positive for CD21 (D) and CD35 (E) and S-100 protein is negative (F).

DISCUSSION

The nodal architecture is effaced (figure 1A) by a proliferation of spindle cells which are arranged in a vaguely whorled pattern (figure 1B) and in loose fascicles with conspicuous admixed small lymphocytes and few plasma cells. The neoplastic cells have indistinct cell borders and elongated ovoid nuclei with vesicular chromatin and small central eosinophilic nucleoli (figure 1C). The spindle cells show positive immunohistochemical labelling with CD21 (figure 1D) and CD35 (figure 1E). S100 protein (figure 1F), desmin, AE1/AE3, EMA, CD34, HMB-45, ALK-1 and HHV-8 are negative. Epstein–Barr virus (EBV)-encoded small RNA in situ hybridisation (EBER-ISH) is negative.

Follicular dendritic cell (FDC) sarcoma is rare, but represents the most common dendritic cell neoplasm.[1] Most patients are adults with a mean age of 50 years and there is no gender predilection.[1 2] Rare associations with paraneoplastic pemphigus or myasthenia gravis have been described. Some cases of FDC sarcoma have occurred in association with antecedent or concurrent Castleman disease (usually hyaline vascular variant); however, a causal link remains to be proven.[1] FDC sarcoma behaves like an intermediate grade sarcoma with a moderate risk of local recurrence (28.1%) and distant metastasis (27.2%).[1] There are no characteristic recurrent genetic aberrations. *BRAF* V600E mutations have been reported in 20% of cases.[3]

Extensive immunohistochemical interrogation may be needed to arrive at the correct diagnosis, and tumours metastatic to lymph nodes as well as inflammatory conditions must be excluded. Metastatic spindle cell carcinoma and malignant melanoma should be routinely excluded with broad spectrum cytokeratins and melanocytic markers. The intimate admixture of spindle cells and inflammatory cells may raise consideration of inflammatory myofibroblastic tumour (IMT). IMT would, however, show patchy positivity with smooth muscle actin and ALK (in approximately 40% of cases). Mycobacterial spindle cell tumour is a consideration in certain risk groups and can be investigated with a Ziehl-Neelsen stain. The presence of intermingling inflammatory cells is an important clue to the diagnosis of FDC sarcoma. Positivity with one or more of the FDC-associated markers including CD21 (figure 1D), CD23, CD35 (figure 1E), KiM4p, CNA.42 and clusterin is required to confirm the diagnosis. More recent FDC markers include FDC secreted protein and serglycin.[4] S-100 protein may show focal positivity which helps to distinguish FDC sarcoma from interdigitating cell sarcoma which shows widespread

Take home messages

- Follicular dendritic cell (FDC) sarcoma is rare and has an intermediate prognosis (better than metastatic carcinoma or melanoma, its high-grade mimics).
- High index of suspicion and thorough immunohistochemical interrogation is required to arrive at the correct diagnosis.
- Other tumours in the category of non-Langerhans dendritic cell tumours include interdigitating dendritic cell sarcoma (S100 positive) and fibroblastic reticular cell sarcoma (desmin positive).
- CD21, CD35, KiM4p, CNA.42, clusterin, FDCSP and serglycin are the FDC markers which are useful in establishing the diagnosis.

To cite: Aldera AP, Govender D. *J Clin Pathol* 2020;**73**:e6.

positivity. Desmin is negative in FDC sarcoma but shows patchy staining in fibroblastic reticular cell sarcoma. It is noteworthy that intratumoural lymphocytes is a feature of most dendritic cell tumours; hence, immunohistochemistry is often the final arbiter.

ANSWER

B. Follicular dendritic cell sarcoma.

Handling editor Iskander Chaudhry.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

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