LETTERS TO JCP

Mediastinal mixed dendritic cell sarcoma with hybrid features

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This report describes a recurrent sarcoma involving the soft tissues of the posterior mediastinum with features of both follicular dendritic and interdigitating dendritic cells. Histologically, the tumour, which was a recurrent neoplasm 19 years after the initial removal, was composed of bland spindle shaped cells with interspersed inflammatory cells, predominantly lymphocytes. Immunohistochemically, the spindle cells were positive for S100 protein, CD45, CD68, and vimentin, but negative for CD21 and CD35 (markers of follicular dendritic cells). The immunophenotype was in keeping with interdigitating dendritic cells. However, ultrastructural examination demonstrated elongated cell processes joined by desmosome-like junctions—features in keeping with follicular dendritic cells. Follicular dendritic cell sarcoma and interdigitating dendritic cell sarcoma are rare neoplasms and a high index of suspicion is required to make a correct diagnosis. Immunohistochemistry and/or electron microscopy are required for a definitive diagnosis. This case shows that hybrid neoplasms can occur, which have features of both follicular and interdigitating dendritic cells.

Follicular dendritic cell (FDC) sarcomas are rare neoplasms. They most often involve lymph nodes but may arise at a variety of extranodal sites, including the oral cavity, tonsil, gastrointestinal tract, and liver.^{1–10} Particularly in cases with an extranodal location, an erroneous diagnosis is often made, and a high index of suspicion is required with unusual spindle cell lesions that cannot otherwise be readily categorised. The small number of cases reported to date may be explained in part by under recognition of the entity. Histologically, FDC sarcoma is usually composed of spindle, ovoid, or polygonal cells arranged in a whorled, fascicular, or storiform pattern. The tumour cell population is often accompanied by an inflammatory infiltrate, chiefly lymphocytes and plasma cells. Tumour cells have abundant eosinophilic cytoplasm and poorly defined cell borders. Definitive diagnosis invariably requires confirmation by immunohistochemical and/or ultrastructural studies. Interdigitating dendritic cell (IDC) sarcoma is an even more rare neoplasm,^{11–14} and there are no specific morphological features that distinguish this neoplasm from FDC sarcoma. Rather, the distinction is made by immunohistochemical and/or ultrastructural studies.

“There are no specific morphological features that distinguish interdigitating dendritic cell sarcoma from follicular dendritic cell sarcoma”

FDC sarcomas are, in general, low grade neoplasms. They may recur, sometimes many years after surgical removal, and some tumours metastasise.⁸ IDC sarcomas tend to be more aggressive, often presenting with disseminated disease. In this report, we describe a dendritic cell sarcoma showing features

Figure 1 Lesion composed of bland spindle shaped cells.

of both FDC and IDC sarcoma and involving the posterior mediastinal soft tissues. This was a recurrent neoplasm 19 years after excision of what was initially thought to be a “neurogenic tumour”.

CASE REPORT

A 65 year old woman presented with a posterior mediastinal mass, which was excised. The histological diagnosis at that time was a neurogenic tumour. Nineteen years later she re-presented with a left sided posterior mediastinal mass. There was no radiological evidence of disease elsewhere. The mass was removed surgically via thoracotomy. The initial pathology could not be traced and therefore was not reviewed.

PATHOLOGICAL FINDINGS

The recurrent tumour comprised a well circumscribed mass measuring 10 × 6 × 5 cm and weighing 270 g. On sectioning, the cut surface was firm and yellow/white in colour.

Histological examination revealed a cellular lesion composed of spindle shaped cells with a moderate amount of eosinophilic cytoplasm and indistinct cell borders (fig 1). Cells often contained small central nucleoli. There was only a mild degree of nuclear pleomorphism and occasional mitotic figures were identified; a formal mitotic count revealed 1–2 mitoses/10 high power fields. There was a lymphoplasmacytic infiltrate throughout the tumour (fig 2), which was pronounced in some areas and mild in others. No areas of haemorrhage, necrosis, or vascular invasion were seen.

The spindle cells stained positively for S100 protein (Signet, Ontario, Canada), CD45 (leucocyte common antigen; Dako, Ely, UK), CD68 (Dako), and vimentin (Dako). There was no staining of the spindle cells for CD21 (Dako), CD35 (Dako),

Abbreviations: EBV, Epstein-Barr virus; FDC, follicular dendritic cell; IDC, interdigitating dendritic cell

Figure 2 There is an infiltrate of small lymphocytes and plasma cells within the tumour.

desmin (Dako), α smooth muscle actin (Sigma, Poole, UK), AE1/3 (Dako), epithelial membrane antigen (Dako), CD34 (Serotec, Oxford, UK), CD20 (Dako), CD3 (Dako), or CD5 (Novocastra, Newcastle upon Tyne, UK). Immunohistochemistry for Epstein-Barr virus (EBV) latent membrane protein (Novocastra) was negative.

Ultrastructural examination showed spindle shaped cells characterised by long tapering interweaving cytoplasmic

processes (fig 3). Desmosomes or desmosome-like attachments were frequently formed between the closely opposed cell processes (fig 3). In some areas, a discontinuous external lamina appeared to separate the cells from the intervening stroma, although it did not envelope individual cells. Cell nuclei displayed a smooth contour with marginal heterochromatin and occasional nucleoli. Fine 10 nm thick cytoplasmic filaments were scattered throughout the cytoplasm, which contained few organelles apart from a few lysosomes. No neuroendocrine or Langerhans granules were identified.

DISCUSSION

Since Monda *et al* first described an FDC tumour in 1986,¹⁵ several other individual cases and small series have been reported.¹⁻¹⁰ The preferred term is FDC sarcoma because it is apparent that these are low grade malignant neoplasms. It is probable that FDC sarcoma is not as rare as was previously thought, but that this is an under recognised lesion. FDC sarcoma occurs predominantly within lymph nodes, but, as stated previously, has been described in many extranodal locations. Although these neoplasms can occur at any age, they most often arise in young adults.⁵ The sex distribution is equal.

FDC sarcoma is traditionally viewed as an indolent low grade tumour, with a tendency to local recurrence, but little risk of metastasis. However, as already stated, these tumours should be regarded as low grade malignant neoplasms

Figure 3 Spindle cells with long entwining cytoplasmic processes joined together by desmosomes (arrows). Original magnifications, $\times 12\,000$ (main figure); $\times 50\,000$ (inset).

because distant metastasis has been described.⁵ More aggressive behaviour has been associated with an intra-abdominal location (because tumours arising here may grow larger than their counterparts elsewhere without detection), large size, a high mitotic rate, pronounced cellular atypia, and tumour cell necrosis.^{5–10} It has been suggested that intra-abdominal lesions or neoplasms with a malignant histological appearance should be treated with adjuvant chemotherapy following complete surgical excision.⁵

The differential diagnosis depends, in part, on the tumour location and may include thymoma, large cell lymphoma, peripheral nerve sheath tumour, leiomyomatous tumour, malignant melanoma, gastrointestinal stromal tumour, meningioma, true histiocytic lymphoma, Langerhans cell histiocytosis, spindle cell carcinoma, and a variety of other mesenchymal lesions. Chan and colleagues have provided a comprehensive review of these differential diagnoses.⁵ IDC sarcoma is much more rare than FDC sarcoma and is a more aggressive neoplasm, often with a high stage at presentation. As with FDC sarcoma, the neoplasm most commonly involves lymph nodes, although extranodal tumours have been described.

The tumour in our present patient was a recurrent neoplasm 19 years after removal of what was thought to be a neurogenic tumour. The original pathology was not reviewed, but it is probable that the diagnosis of neurogenic tumour was based on the location of the tumour in the posterior mediastinum, the histological appearances of a spindle cell lesion, and the positivity for S100 protein. However, in the recurrent lesion the positivity for CD45 and CD68 initially raised suspicion that this was not a neurogenic tumour. Ultrastructural examination showed long tapering cell processes joined by desmosomes, features characteristic of follicular dendritic cells. However, tumour cells were negative for CD21 and CD35, markers of follicular dendritic cells, and the immunophenotype (S100, CD45, CD68, and vimentin positive) was characteristic of interdigitating dendritic cells. CD45 positivity is often found in IDC sarcoma but usually not in FDC sarcoma. Most of the aforementioned differential diagnoses were excluded on the basis of the immunohistochemical and electron microscopy findings.

“Our present case illustrates the value of electron microscopy in demonstrating dendritic cell differentiation when CD21 and CD35 are negative”

Once the possibility of a dendritic cell sarcoma has been considered, firm diagnosis requires the application of ancillary techniques, such as immunohistochemistry and electron microscopy. Antibodies to CD21, CD23, and CD35 are commercially available and are relatively specific markers for follicular dendritic cells. However, many diagnostic laboratories do not stock these antibodies routinely. As already stated, in our present case tumour cells were negative for CD21 and CD35. Although occasional cases of FDC sarcoma have been reported to be negative for CD21 and CD35, it is possible that these represent hybrid neoplasms, similar to the case we describe. Interestingly, a lymph node dendritic cell sarcoma has recently been reported with mixed dendritic and fibroblastic features.¹⁶

Our present case illustrates the value of electron microscopy in demonstrating dendritic cell differentiation when CD21 and CD35 are negative. The presence of desmosomes and the extensive interweaving processes ultrastructurally excluded a neural tumour. In addition, the focal basal lamina did not envelop individual cells, but separated them from the accompanying stroma. In our present case a spindle cell thymoma was also a diagnostic possibility, but the neoplasm was located in the posterior rather than the anterior mediastinum and there was no staining with AE1/3 or CD5, which would be expected to be positive in a thymoma. Moreover, the ultrastructural appearances were not those of a thymoma.

Take home messages

- We describe a recurrent sarcoma involving the soft tissues of the posterior mediastinum with features of both follicular dendritic and interdigitating dendritic cells
- We wish to raise awareness of dendritic cell sarcomas, which may occasionally show mixed differentiation
- Immunohistochemistry and/or electron microscopy are required for a definitive diagnosis

The aetiology of FDC sarcoma and IDC sarcoma is poorly understood, and to date the only predisposing factor identified has been hyaline vascular Castleman's disease in the case of FDC sarcoma. The Castleman's lesion may be identified either before or concurrent with the development of FDC sarcoma. Such an association appears to be present in only a minority of cases. It has been proposed that FDC sarcoma arising in Castleman's disease develops through a hyperplasia–dysplasia–neoplasia sequence. However, it is also possible that the characteristic Castleman's disease lesion is a reaction to FDC sarcoma rather than a precursor lesion.¹⁷ Rare cases of FDC sarcoma are associated with EBV infection. This association is seen almost exclusively in the liver and spleen, usually in cases with an inflammatory pseudotumour-like appearance.^{4–6} This is an unusual morphological variant of FDC sarcoma. In our present case, EBV was not detected immunohistochemically within the tumour cells. No association with herpesvirus 8, which is implicated in the pathogenesis of hyaline vascular Castleman's disease, has been established.¹⁸

The neoplasm in our present case exhibited an indolent behaviour with recurrence 19 years after surgical resection. This may suggest that the behaviour of these hybrid neoplasms is more akin to FDC sarcoma, because IDC sarcoma often exhibits a more aggressive behaviour. However, recognition and reporting of additional cases will be necessary to define the behaviour of these neoplasms more accurately.

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