Plexiform fibrohistiocytic tumor—report of one case with regional lymph node metastasis

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KEYWORDS
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Lymph node metastasis
Plexiform fibrohistiocytic tumor

ABSTRACT
A plexiform fibrohistiocytic tumor (PFT) is a rare mesenchymal neoplasm primarily occurring in children and young adults. PFTs have been classified as fibrohistiocytic tumors of intermediate malignancy because of the high local recurrence rate and possible lymph node and distant metastasis. Histologically, PFTs are poorly demarcated dermal-to-subcutaneous tumors composed of small nodules or cellular clusters with a characteristic plexiform arrangement. We report a 17-year-old girl presenting with a nasal root tumor and concurrent cervical lymphadenopathy. Light microscopy and immunohistochemical findings were compatible with a PFT, for both the nasal root tumor and the cervical lymph nodes. Under the diagnostic impression of a PFT with neck lymph node metastasis, the patient underwent wide excision of the primary tumor and cervical lymph node dissection, followed by concurrent chemo-radiotherapy. During a 4-year follow-up, no evidence of recurrence was noted. We also review the previously published cases of PFTs with metastasis.

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Introduction
A plexiform fibrohistiocytic tumor (PFT), first reported by Enzinger and Zhang¹ in 1988, is a rare mesenchymal neoplasm primarily affecting children, adolescents and young adults. Clinically, PFTs present as asymptomatic, slow growing nodules without surface ulcerations. This tumor is preferentially located on the upper extremities, followed by the trunk and the lower extremities, and rarely on the head and neck. PFTs are considered fibrohistiocytic tumors of intermediate malignancy,² and have been further categorized into a subtype that is locally aggressive but rarely has the capacity for distant metastasis.³

Histopathologically, a PFT is mainly located at the dermal-subcutaneous layers with a plexiform growth pattern. This type of tumor is composed of a biphasic admixture of fascicles of proliferative spindle cells as well as multinodular aggregates of mononuclear histiocytes and scattered osteoclasts. On immunohistochemical staining, the histiocytic and osteoclastic cells are positive for CD68, but the surrounding fibroblastic cells are focally positive for smooth muscle actin antibodies. We report here a case of a PFT with an unusual clinical presentation and also review the previously published cases.

Case report
A 17-year-old girl presented with an asymptomatic, slow growing, erythematous nodule on the nasal root for 4 months. She denied a history of trauma or insect bites. She also noted a neck mass without tenderness for 1 month. She had no constitutional symptoms including fever or weight loss.

A physical examination revealed a 1.8 cm × 1.0 cm, irregularly shaped, firm and erythematous nodule with infiltrative borders and telangiectasia on the nasal root, accompanied by two pinhead-sized satellite papules (Figure 1). A 1.0 cm × 1.0 cm nonmovable lymph node was also noted in the area of the left submandible. A biopsy specimen was obtained...
from the nasal root and the pathology showed spindle cell proliferation in the dermis with an infiltrating pattern and occasional mitosis (1/10 high power field). Further management was recommended for confirmation under the impression of a proliferating myofibrohistiocytic cell tumor.

Thus, the patient underwent primary tumor wide excision. The histopathological examination revealed that the tumor, which was primarily located in the lower dermis with extension into the subcutaneous tissue, was characterized by multinodular or plexiform proliferation surrounded by hyalinized collagen (Figure 2A). Under high power magnification, these micronodules had a biphasic appearance that was mainly composed of mononuclear histiocyte-like cells with interspersed multinucleated giant cells in the center, and spindle-shaped fibroblastic cells located at the periphery (Figure 2B). A few mitoses were visible, but little cellular pleomorphism was observed (Figure 2C). An immunohistochemical study of the primary tumor showed positive staining for vimentin and CD68 (Figure 3A) in the histiocyte-like and multinucleated giant cells. Smooth muscle actin stained positively in fibroblastic cells (Figure 3B). The lesions were negative for desmin, keratin, CD34, and S-100 protein. Interspersed positive staining for factor XIIIa was shown within the nodules.

Hematoxylin-eosin staining and immunohistochemical study of the specimen led to the diagnosis of PFT. The patient underwent selective neck lymph node dissection and histology of the cervical lymph nodes revealed large fibrohistiocytic nodules associated with foci of microhemorrhage replacing the lymph node (Figure 4A). The metastatic tumor cells within the lymph node also showed immunoreactivity for vimentin and CD68 (Figure 4B). The patient was referred to the Department of Oncology for concurrent chemo-radiotherapy (weekly cisplatin [75 mg/m² for 4 cycles] and a total dose of radiation to 7000 cGy). There was no evidence of local recurrence or distant metastasis during the 4-year follow-up.

Discussion

A PFT was first described by Enzinger and Zhang¹ in a series of 65 cases. In the latest review by Jafarian et al,⁴

Figure 1 A 1.8×1.0 cm, irregularly shaped, erythematous nodule with infiltrative borders and telangiectasia was observed on the nasal root.

Figure 2 (A) Histopathology revealed a dermal tumor with extension into the subcutaneous tissue, characterized by multinodular or plexiform proliferation surrounded by hyalinized collagen fibers (H&E, 40x). (B) The micronodules were composed of mononuclear histiocyte-like cells with interspersed multinucleated giant cells in the center, and spindle-shaped fibroblastic cells located at the periphery of these nodules (H&E, 200x). (C) Biphasic cell components with few mitoses were observed. Arrowhead indicates fibroblastic cells in the peripheral regions of the micronodules (H&E, 400x).
70% of the 123 patients diagnosed with PFTs were less than 20 years of age and females were predominant with a ratio greater than 2:1. The most common location for PFTs is the upper extremities (55.7%), followed by the trunk (16.3%), lower extremities (16.3%) and the head and neck (11.4%).

PFTs are characterized by a high local recurrence rate, ranging from 12.5% to 40%, because of infiltrative borders and frequent subcutaneous extension. However, distant metastasis is rare and has been reported in only 5 of the 123 patients (4%). Among these five cases, there were two patients diagnosed with lymph node metastases and another two patients with pulmonary metastases. There was a 4-year-old girl who developed sequential lymph node and lung metastases and eventually died 3 years after the initial diagnosis. All lymph node metastases reported thus far developed following local recurrence after resection of the primary tumors. Notably, our patient developed concomitant lymph node metastasis as the initial presentation.

PFTs merit separation from other fibrohistiocytic tumors, not only for the malignant potential in clinical presentation, but also for the distinctive pathologic features. PFTs are mainly located at the dermal-subcutaneous layers with a plexiform growth pattern. PFTs show a biphasic architecture, being composed of micronodules of histiocytoid cells with or without osteoclast-like giant cells in the center, and interconnected by fascicles of spindle cells. In our case, the most confusing differential diagnosis in histology was a cellular neurothekeoma, which shares considerable morphologic overlap with PFTs. However, cellular neurothekeomas usually have less tendency to involve the subcutis, possess varying amounts of myxoid or hyalinized stroma, and lack a biphasic architecture. In addition, cellular neurothekeomas usually show a benign clinical course without metastatic propensity. Other histological differential diagnoses include fibrous hamartoma of infancy, plexiform spindle cell nevus, plexiform schwannoma, plexiform neurofibroma, and plexiform granular cell tumor (Table 1). No studies have shown a clear correlation between histologic features and clinical behavior of PFTs.

Primary surgical excision to achieve negative margins remains the most applicable and important treatment. Local recurrence most often occurs 1–2 years after the primary excision, and Mohs micrographic surgery is the treatment of choice for second operations. In the four cases reported with lymph node metastases, three underwent lymph node...

Figure 3  (A) Histiocytes within the micronodules of the primary tumor show positive staining for CD68 (CD68, 200×). (B) Spindle-shaped fibroblasts in the micronodules were positive for smooth muscle actin (SMA, original magnification 100×).

Figure 4  (A) The lymph node was largely replaced by large fibrohistiocytic nodules. Foci of microhemorrhage were also discernible (H&E, 200×). (B) Histiocytoid cells within the nodules were also reactive for CD68 (CD68, 200×).
Table 1  Histologic differential diagnosis of plexiform fibrohistiocytic tumor.

<table>
<thead>
<tr>
<th>Entity</th>
<th>Age</th>
<th>Predilection sites</th>
<th>Histological features</th>
<th>Positive IHC stain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plexiform fibrohistiocytic tumor</td>
<td>Young adults</td>
<td>Upper extremities</td>
<td>Poorly demarcated, dermal-to-subcutaneous tumor composed of micronodules with plexiform arrangement and biphasic cell pattern</td>
<td>CD68,* SMA†</td>
</tr>
<tr>
<td>Cellular neurothekeoma</td>
<td>Young adults</td>
<td>Head, neck, and upper limbs</td>
<td>Ill-defined dermal tumor consisted of uniform nests and fascicles of epithelioid and spindle-shaped eosinophilic cells with vesicular nuclei</td>
<td>Usually NK1-C3 PGP9.5</td>
</tr>
<tr>
<td>Fibrous hamartoma of infancy</td>
<td>0–2 yr</td>
<td>Shoulder region</td>
<td>Ill-defined lesions in deep dermis, composed of fibrous tissue, fascicles of eosinophilic myofibroblasts, adipose tissue, and small primitive cells</td>
<td>SMA, vimentin†</td>
</tr>
<tr>
<td>Plexiform spindle cell nevus</td>
<td>10–30 yr</td>
<td>Head, upper trunk, and proximal limbs</td>
<td>Wedge-shaped, loosely arranged or plexiform fascicles of spindle or epithelioid nevus cells</td>
<td>S-100, HMB-45</td>
</tr>
<tr>
<td>Plexiform schwannoma</td>
<td>Young adult</td>
<td>Trunk</td>
<td>Classic biphasic pattern with cellular and myxoid areas; presence of Verocay bodies</td>
<td>S-100</td>
</tr>
<tr>
<td>Plexiform neurofibroma</td>
<td>Children</td>
<td>Head and neck</td>
<td>Thin spindle cells with wavy nuclei and collagen bundles arranged in a myxoid matrix</td>
<td>S-100</td>
</tr>
<tr>
<td>Plexiform granular cell tumor</td>
<td>Variable</td>
<td>Head, neck, and upper trunk</td>
<td>Perineurial extension of tumors containing polygonal cells with eosinophilic granular cytoplasm</td>
<td>S-100</td>
</tr>
</tbody>
</table>

*Positive for mononuclear histiocyte-like cells and multinucleated giant cells; †positive for spindle-shaped fibroblastic cells; ‡positive for myofibroblasts; §positive for small primitive cells. IHC stain=immunohistochemical stain; SMA=smooth muscle actin; HMB-45=human melanoma black-45.

dissection. One of these three patients subsequently developed pulmonary metastasis,⁶ and the other two patients, including our case, were disease free during follow-ups.¹⁴ Although the frequency of lymph node metastasis is low, physical examination to detect regional lymphadenopathy is still recommended at presentation and during follow-up.⁴ As in our case, early detection of lymph node metastasis can be treated successfully to achieve disease-free status.

In conclusion, we report a rare case of a PFT with an unusual presentation of a nasal root tumor and concurrent neck lymph node metastasis. The patient received complete treatment by wide tumor excision, selective lymph node dissection, and concurrent chemoradiotherapy. No recurrence was noted during the 4-year follow-up.

References