Plexiform Fibrohistiocytic Tumor Presenting as a Central Neck Mass Clinically Mimicking a Thyroglossal Duct Cyst: An Unusual Case Reported with Histo-cytopathologic Correlation and a Review of the Cytopathology Literature

Giap Hean Goh¹ · Fredrik Petersson¹

Received: 2 January 2019 / Accepted: 4 February 2019 / Published online: 13 February 2019
© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

We present the case of an uncommon example of a plexiform fibrohistiocytic tumor (PFHT) occurring in the anterior central neck region of a 40 year-old female with previous subtotal thyroidectomy. The tumor clinically mimics a complicated thyroglossal duct cyst. On fine needle aspiration cytology, the tumor was composed of sheets of bland spindle cells and nests of plump histiocytoid cells in vaguely whorled arrangements. Occasional multinucleated giant cells were also identified. The excised specimen showed an irregular, highly infiltrative subcutaneous tumor arranged in a nodular/plexiform pattern concentrated to the center of the tumor mass. In addition, the tumor contained numerous tongue-like extensions composed of variably cellular, fibroblastic/fibromatosis-like areas. These fibroblastic/fibromatosis-like extensions reached far from the epicenter of the tumor and were associated with scattered small plexiform nodules of histiocytic cells. These tongue-like extensions multifocally involved the surgical margins. The fibroblastic and histiocytoid cells showed diffuse smooth muscle actin (SMA) expression. The multinucleated giant cells and also the histiocytoid proliferation were positive for CD68. This case illustrates an uncommon both anatomical and demographic manifestation of PFHT and also characterize the fine needle aspiration cytologic features in this tumor, which previously have been reported in a few cases.

Keywords Plexiform fibrohistiocytic tumor · Neck · Thyroglossal duct cyst · Fine needle aspiration cytology

Introduction

Plexiform fibrohistiocytic tumor (PFHT) is a rare mesenchymal neoplasm that was first described by Enzinger and Zhang in 1988 [1]. This tumor most frequently presents as a slow growing painless soft tissue mass in the extremities. PFHT occurring in the head and neck region is uncommon; 10% of the tumors in Enzinger and Zhang's series and 7% in the study by Hollowood et al. [1, 2]. While the histopathologic features of this tumor are well described, to the best of our knowledge, detailed cytopathological characterization of PFHT has only been reported in two previous cases [3, 4]. This is not surprising given that open biopsy and

not fine needle aspiration cytology (FNA) is in most centers the standard approach to the histopathologic diagnosis of soft tissue tumors. However, FNA is commonly utilized as a diagnostic tool in lesions of the head and neck region. Herein we describe the clinicopathological features of a case of PFHT occurring in the anterior central neck region, which clinically simulated a thyroglossal duct cyst, characterize the cytopathological findings and provide a review on the limited literature on the cytopathology of PFHT.

Case Report

A 40 year-old Vietnamese woman presented with a central neck lump of 2 years duration that was progressively increasing in size. The patient had a subtotal thyroidectomy performed overseas 3 years ago for a thyroid tumor that was told to be benign. Prior to her visit to our institution, an ultrasonographic examination of the thyroid performed in

✉ Fredrik Petersson
fredrikpetersson@live.se

¹ Department of Pathology, National University Health System, 5 Lower Kent Ridge Road, Singapore 119074, Singapore

Vietnam showed a calcified nodule over the anterior neck region. She was otherwise well with no other significant past medical or surgical history.

On examination, there was a 2 cm hard, central neck mass that did not move on swallowing. A computed tomography (CT) scan of the neck showed a $1.9 \times 1.7 \times 1.5$ cm, hyperdense, poorly circumscribed focus with irregular radiating tongue-like extensions in the central neck region, below the floor of mouth and deep to the platysma muscle. A remnant small thyroid gland was identified. In view of the midline location, a radiological suspicion of a complicated thyroglossal duct cyst was raised. The patient initially underwent an FNA-biopsy of the lesion and a subsequent excision biopsy.

Materials and Methods

Two passes were obtained from the central neck mass of which four slides were smeared. Two slides were alcohol fixed and stained with Papanicolaou and two were air dried and stained with Hemacolor stain. The tissue was fixed in formalin, embedded in paraffin and 4 μ m thin sections were cut and stained with Hematoxylin and Eosin. An immunohistochemical study was performed using commercially available antibodies cytokeratin cocktail—cytokeratin (CK) AE1/3 (DAKO), CAM5.2 (Ventana), CD68 (DAKO), CD163 (Ventana), SMA (DAKO), p63 (Ventana), HMB-45 (Ventana), S-100 (DAKO), Desmin (DAKO), SOX10

(Cell Marque), CD31 (DAKO), ERG (Ventana), CD35 (Cell Marque), CD21 (DAKO), CD23 (Ventana), HHV8 (Ventana) according to the manufacturer's instructions.

Cytopathologic Findings

Smears showed a cellular yield of plump histiocytoid cells forming loose sheets and vaguely whorled clusters (Fig. 1a). Loosely attached to these cellular groups as well as dispersed singly are spindle cells with ovoid nuclei and longer tapering cytoplasmic processes (Fig. 1b). The nuclear chromatin was fine with occasional small nucleoli. The cells in clusters appear to be admixed with some light purple matrix-like material. Occasional multinucleated giant cells were present (Fig. 1c). The neoplastic cells lacked significant nuclear pleomorphism. No mitotic activity or necrosis was identified. No significant inflammatory cells were present. There was no colloid or amyloid seen.

The diagnosis of a low-grade spindle cell neoplasm, likely of mesenchymal origin was suggested. There was no additional material for cell block preparation and further subtyping was not possible.

Gross Pathological Findings

The resected specimen consisted of the hyoid bone, an ellipse of skin with underlying subcutaneous tissue, which on sectioning, revealed an ill-defined brownish nodule measuring 1.0 cm with several slender, firm gray-white

Fig. 1 **a** Smear showed vaguely whorled clusters of plump histiocytoid cells (x400). **b** Loose sheet of plump histiocytoid cells and dispersed singly occurring spindle cells with long tapering cytoplasm (x200). **c** Osteoclastic type multinucleated giant cell (x400). **d** Low power magnification of the tumor with a nodular to plexiform arrangement separated by dense collagenous stroma. (a, c—HC, b—PAP)

bands extending to the surgical margins. The skin was unremarkable.

Light Microscopic Findings

On low power magnification, the epicenter of the tumor showed a nodular to plexiform arrangement separated by dense collagenous stroma (Figs. 1d, 2b). The subcutaneous tumor was infiltrative with radiating tongue-like fibroblastic bands extending to the surgical margins multifocally (Fig. 2a). The radiating tongue-like extensions extended far from the center of the tumor mass and were associated

with scattered smaller plexiform nodules of histiocytic cells. These tongue-like bands were composed of variably cellular, fibroblastic/fibromatosis-like areas. The tumor also infiltrated skeletal muscle focally. On higher magnification, the tumor was composed of two cell types; (A) histiocytoid cells with round vesicular nuclei and ample pale cytoplasm and (B) fibroblastic-type spindle cells with longer tapering cytoplasmic processes. Numerous interspersed osteoclast-type giant cells were present (Fig. 2c, d). Cellular atypia was minimal. Mitotic activity was up to 5 per 10 high-power fields with no atypical mitotic figures seen. No necrosis was identified. As stated above, the tumor exhibited prominent

Fig. 2 **a** Low power magnification of a poorly circumscribed tumor in the subcutaneous fat with radiating fibroblastic extensions from the center of the mass to the surgical margin (H&E). **b** Center of the tumor with nodular arrangement of tumor cells (H&E x100). **c** Fascicles of fibroblastic-type spindle cells with longer tapering cytoplasmic processes (H&E x200). **d** Osteoclastic type multinucleated giant cells admixed with histiocytoid cells (H&E x400). **e** SMA staining in spindle and histiocytoid cells but absent in the multinucleated giant cells (x400). **f** CD68 staining in multinucleated giant cells and histiocytoid cells (x400)

infiltrative features and involved all the excision margins. No thyroid tissue was identified.

Immunohistochemical Study

Diffuse smooth muscle actin (SMA) expression was seen in the spindle and histiocytoid cells while CD68 was strongly expressed only in the histiocytoid cells and multinucleated giant cells (Fig. 2e, f). There was patchy expression of CD163 in the spindle and histiocytoid cells. The tumor cells showed no expression of cytokeratins (AE1/3, CAM5.2), HMB-45, SOX10 and S-100 protein, desmin, CD31, ERG, CD21, CD23, CD35 and HHV8.

Based on these features, a diagnosis of a plexiform fibrohistiocytic tumor was made. The surgery was uneventful and the patient returned to Vietnam. The patient was lost to follow-up post-discharge.

Discussion

Plexiform fibrohistiocytic tumor is an uncommon low-grade malignant mesenchymal tumor that was first described by Enzinger and Zhang in 1988 [1]. PFHT has a predilection for young female patients. In the series of 65 cases by Enzinger and Zhang, the average age of occurrence was 14.5 years of which approximately 70% of the patients were younger than 20 years [1]. The tumor most frequently involved the extremities in both proximal and distal locations in 91% of Remstein's series of 22 cases [5]. The tumor is usually centered in subcutaneous adipose tissue but dermal extension may occur [5]. Less frequently, these tumors extend/infiltrate into skeletal muscle. This tumor, unlike many other soft tissue tumors, is frequently diploid and is not known to have any recurrent cytogenetic abnormalities [3].

PFHT occurring in the head and neck region is distinctly uncommon with seven out of sixty-five (10%) cases reported in Enzinger and Zhang's series, one out of fourteen (7%) cases reported in Hollowood's series and none in Remstein's series of 22 cases [1, 2, 5].

We are only aware of three previous case reports with cytopathologic features of PFHT described, of which comprehensive cytological characterization of PFHT was

presented in two of these cases [3, 4, 6]. Redlich et al. described a tumor composed of a mixed population of fibrohistiocytic, fibroblastic and multinucleated cells with a myxoid background. The fibroblastic cells tended to occur singly and the multinucleated giant cells occurred in small clusters. In the case described by Chou et al., the very cellular smears contained large branching cellular fragments and within these fragments, the cells showed a vaguely whorled arrangement [3]. The background contained colloid-like material and occasional cells showed intranuclear inclusions. Details of this colloid-like material were not further described in the excision specimen. Our case shared some similar features to the case by Chou et al. in terms of the sheet-like and vaguely whorled arrangement of the cells but lacks the colloid-like material and intranuclear inclusions in the neoplastic cells. Clustering of multinucleated giant cells was also not seen. These differences are reflective of the variable cellular composition seen on histology. PFHT is composed of three distinct cell types: spindle fibroblast-like cells, mononuclear histiocyte-like cells and multinucleated osteoclast-like giant cells. The amount of each cell type varies and based on the predominant cell type, it can be divided into three variants: fibrohistiocytic, fibroblastic and mixed including a rare myxoid variant [5, 7]. The cytologic features described in these cases are summarized in Table 1.

From a differential diagnostic perspective, on fine needle aspiration cytology material, a smear with cellular sheets of spindle cells without prominent nuclear pleomorphism, a whole range of differential diagnoses could be considered, including dermatofibrosarcoma protuberance (DFSP), low-grade variants of leiomyosarcoma (LMS) and malignant peripheral nerve sheath tumor (MPNST) [8–10]. The tumor cells in DFSP tend to be arranged in a storiform pattern while in leiomyosarcoma, the tumor cells tend to be arranged in fascicles [8, 9]. The rare fibroma variant of epithelioid sarcoma and monophasic spindle cell synovial sarcoma may need consideration, but these tumors generally display some expression of cytokeratins and EMA positivity [3, 11]. Benign mesenchymal neoplasms that can display a plexiform growth pattern include plexiform variants of neurofibroma and schwannoma. The lack of Verocay bodies and absence of S-100 protein expression strongly argue against

Table 1 Previously reported Plexiform fibrohistiocytic tumors that have cytologic descriptions

Reference	Patient gender, age	Site	Cytologic description
Chou et al. [3]	Male, 19 years	Left arm	Cellular smears with large branching fragments, vaguely whorled cellular arrangement, colloid-like material, multinucleated giant cells, cells with intranuclear inclusions
Redlich G et al. [4]	Male, 8 mths	Posterior chest wall	Mixture of fibrohistiocytic, fibroblastic and multinucleated cells in a myxoid background. Clustering of multinucleated cells
Angervall et al. [6]	Female, 7 years	Abdominal wall	Fibroblastic-histiocytic features with bi- and multinucleated giant cells

a peripheral nerve sheath tumor. PFHT can present with a predominant fibroblastic pattern with an inconspicuous histiocytoid component and this can mimic fibromatosis but unlike PFHT, this tumor displays generally a more diffuse infiltration and lacks the nodular/plexiform aggregates of histiocytoid cells. Nuclear immunoreactivity for beta-catenin is helpful for establishing a diagnosis of fibromatosis especially in deep seated lesions.

Other tumors that may come into the differential diagnosis include spindle cell melanoma, spindle cell carcinoma, follicular dendritic cell sarcoma and Kaposi sarcoma. However, all these tumors generally exhibit significantly more pronounced nuclear atypia. Moreover, the lack of epidermal involvement and the absence of HMB-45, SOX10 and S-100 essentially exclude a melanoma proliferation. The absence of cytokeratin expression and endothelial markers (CD31, ERG) and absence of HHV8 excluded a carcinoma and Kaposi sarcoma. The nodular arrangement of histiocytoid mononuclear cells with admixed giant cells may suggest the possibility of a granulomatous process. However, close inspection will reveal osteoclast-like rather than Langerhans-type giant cells. Central necrosis is also not a feature of the histiocytic and giant cell-rich nodules of PFHT. Another possible diagnosis to be considered is nodular fasciitis. Nodular fasciitis contains loose, immature stroma whilst in PFHT, the stroma is mature and collagenous. Nodular fasciitis is also relatively small, and lacks nuclear hyperchromasia, pleomorphism and atypical mitoses. A clinical history of rapid lesional growth will also support nodular fasciitis.

The lack of clinical detail and incomplete clinical history, i.e. unknown histologic diagnosis of the previous subtotal thyroidectomy added to the diagnostic challenge in this case. Given the site of a central neck mass and a history of a previously excised thyroid lesion, the possibility of a recurrence of a malignant thyroid tumor were raised. With the exception of a few well-described entities, spindle cells are not commonly encountered in the context of thyroid pathology. The cytologic yield of a mixture of histiocytoid, spindle and multinucleated giant cells at this site raise differential diagnoses ranging from benign conditions such as de Quervain's granulomatous thyroiditis to neoplastic conditions such as spindle cell metaplasia in follicular adenoma/papillary thyroid carcinoma, medullary thyroid carcinoma and a spindle epithelial tumor with thymus-like elements. The plump histiocytoid and spindle cells in our case do not resemble the classical slipper shaped epithelioid cells in granulomas. The spindle cell component in papillary thyroid carcinoma and follicular adenomas tend to be focal and is usually admixed with the conventional forms of the epithelial component, which is not seen in our tumor. Our tumor cells lacked stippled or salt and pepper chromatin of medullary carcinoma. The extremely rare monophasic variant of spindle epithelial tumor with thymus-like differentiation of the thyroid is also

conceivable but the majority of the reported cases are truly biphasic with a distinct epithelial component [12].

Cellular neurothekeoma (CNT) is an important close histologic mimic to consider in cases where subcutaneous adipose tissue infiltration is seen [13]. PFHT shows similar demographic and anatomic distributions as CNT. CNT and PFHT can potentially show overlapping histologic features when both are predominantly composed of histiocytoid cells. As a result, some authors believe that these two entities might be closely related [13]. However, CNT is generally poorly margined, micronodular or lobulated whereas a more well-defined nodular and plexiform arrangement is generally seen on low magnification in PFHT, especially the fibrohistiocytic variant. CNT also tends to differ in cellular composition and lacks the presence of multinucleated giant cells. The tumor cells also tend to exhibit greater cytologic atypia and higher mitotic activity. MiTF may be a reliable marker for distinguishing CNT from PFHT as it is found to be strongly and diffusely expressed in CNT and not PFHT [14]. Based on observations made by Hornick et al. NKI-C3 and NSE are not reliable as these may also be expressed in PFHT [13].

Given the range of differential diagnoses and the differences in prognosis, an accurate diagnosis of PFHT is important. Surgical resection is the primary treatment for this tumor. The role of chemotherapy and radiation therapy appears to be limited. PFHT is locally aggressive and is prone to recur locally if complete surgical excision is not achieved. Reported local recurrence rate range from (12.5%) in the series by Remstein et al. to (40%) in the series by Hollowood et al. [2, 5]. Complete surgical clearance can be potentially difficult as microscopic infiltration into subcutaneous tissue and skeletal muscle at the periphery of the lesion may not be apparent on pre-operative radiological imaging. A correct pre-operative diagnosis of PFHT will thus aid in choosing an appropriate surgical approach. It is important to recognize that, although uncommon, this tumor is capable of regional lymph node metastasis, as reported in 6% of the cases in Enzinger and Zhang and Remstein's series [1, 5]. This tumor is also capable of producing systemic metastasis, which may be present at the time of the initial diagnosis or may develop subsequently [5].

Conclusion

In conclusion, we present an unusual case of plexiform fibrohistiocytic tumor presenting as a central neck mass in a 40 year-old woman. Clinically, the tumor mimicked a complicated thyroglossal cyst. Awareness that PFHT may rarely occur in the head and neck region and also in adults should facilitate establishing the correct diagnosis. In addition, familiarity with findings on a fine needle aspiration

cytology-biopsy from PFHT would aid the diagnostician. Finally, PFHT may exhibit a prominent infiltrative component, which is only detected on close histopathological examination. Hence, if the correct diagnosis is made preoperatively, the knowledge of the infiltrative nature of PFHT, should aid the surgeon in choosing an appropriate surgical approach.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval It is our institution's policy not to require formal ethical approval for reports on up to two patients.

References

1. Enzinger FM, Zhang RY. Plexiform fibrohistiocytic tumor presenting in children and young adults. An analysis of 65 cases. *Am J Surg Pathol*. 1988;12:818–26.
2. Hollowood K, Holley MP, Fletcher CD. Plexiform fibrohistiocytic tumour: clinicopathological, immunohistochemical and ultrastructural analysis in favour of a myofibroblastic lesion. *Histopathology*. 1991;19:503–13.
3. Chou S, Howle J, Chandraratnam E, Achan A. Fine-needle aspiration cytology features of a recurring plexiform fibrohistiocytic tumor in the upper limb and review of the literature. *Diagn Cytopathol*. 2011;39:49–53.
4. Redlich G, Bocklage T, Joste N. Fine needle aspiration cytology of plexiform fibrohistiocytic tumor. A case report. *Acta Cytol*. 1999;43:867–72.
5. Remstein ED, Arndt CA, Nascimento AG. Plexiform fibrohistiocytic tumor: clinicopathologic analysis of 22 cases. *Am J Surg Pathol*. 1999;23:662–70.
6. Angervall L, Kindblom LG, Lindholm K, et al. Plexiform fibrohistiocytic tumor. Report of a case involving preoperative aspiration cytology and immunohistochemical and ultrastructural analysis of surgical specimens. *Pathol Res Pract*. 1992;188:350–6.
7. Cho S, Chang SE, Choi JH, et al. Myxoid plexiform fibrohistiocytic tumour. *J Eur Acad Dermatol Venereol*. 2002;16:519–21.
8. Domanski HA, Gustafson P. Cytologic features of primary, recurrent, and metastatic dermatofibrosarcoma protuberans. *Cancer Cytopathol*. 2002;96:351–61.
9. Kljanienco J, Caillaud JM, Lagace R, Vielh P. Fine needle aspiration of leiomyosarcoma: a correlative cytohistopathologic study of 96 tumors in 68 patients. *Diagn Cytopathol*. 2003;3:119–25.
10. Kljanienco J, Caillaud JM, Lagace R, Vielh P. Cytopathologic correlations of 24 malignant peripheral nerve sheath tumor (MPNST) in 17 patients: the institute Curie experience. *Diagn Cytopathol*. 2002;27:103–8.
11. Mirra JM, Kessler S, Bhuta S, et al. The fibroma-like variant of epithelioid sarcoma. A fibrohistiocytic/myoid cell lesion often confused with benign and malignant spindle cell tumors. *Cancer*. 1992;69:1382–95.
12. Tong GX, Hamele-Bena D, Wei XJ, O'Toole K. Fine-needle aspiration biopsy of monophasic variant of spindle epithelial tumor with thymus-like differentiation of the thyroid: report of one case and review of the literature. *Diagn Cytopathol*. 2007;35(2):113–9.
13. Hornick JL, Fletcher CD. Cellular neurothekeoma: detailed characterization in a series of 133 cases. *Am J Surg Pathol*. 2007;31:329–40.
14. Fox MD, Billings SD, Gleason BC, Moore J, Thomas AB, Shea CR, et al. Expression of MiTF may be helpful in differentiating cellular neurothekeoma from plexiform fibrohistiocytic tumor (histiocytoid predominant) in a partial biopsy specimen. *Am J Dermatopathol*. 2012;34(2):157–60.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.