Primary Pleomorphic Lipoma of the Parotid Gland with Prominent Myxoid Change: Report of a Rare Case Mimicking Carcinoma Ex Pleomorphic Adenoma on Fine Needle Aspiration Cytology

Giap Hean Goh¹ · Thomas Choudary Putti¹ · Raymond Ngo² · Abbas Agaimy³ · Fredrik Petersson^{1,4}

Received: 4 November 2018 / Accepted: 29 December 2018 / Published online: 4 January 2019
© Springer Science+Business Media, LLC, part of Springer Nature 2019

Abstract

We present a case of a primary 2.5 cm pleomorphic lipoma of the right parotid gland with prominent myxoid change which on FNA displayed features that mimicked a carcinoma or sarcoma ex pleomorphic adenoma. The patient was a 79 year old man with no oncological history or tumor elsewhere. On immunohistochemistry the neoplastic cells strongly expressed CD34. There was no expression of retinoblastoma protein, smooth muscle actin, S100-protein or cytokeratins (AE1/3 and CAM5.2). The Ki-67 proliferation index was low (<2%). Fluorescence in situ hybridization was negative for *MDM2* gene amplification.

Keywords Pleomorphic lipoma · Parotid gland · Carcinoma ex pleomorphic adenoma · Carcinosarcoma ex pleomorphic adenoma · Fine needle aspiration cytology

Introduction

Fine needle aspiration (FNA) cytology is a well established tool in the preoperative diagnostic assessment of salivary gland lesions. Despite the advantages of FNA with regards to salivary gland lesions, both the heterogeneity of salivary gland lesions as well as cytomorphological overlap especially between some benign and low-grade carcinomas often make the task of cytopathological assessment of salivary gland tumors challenging. This is especially true when one is faced with neoplasms that rarely present as primary salivary gland lesions. Herein, we present a case of a pleomorphic lipoma (PL) which displayed features on FNA that initially

were perceived to be suspicious for carcinoma ex pleomorphic adenoma (PA).

Case Report

A 79 year old man with a past medical history of hypertension and hyperlipidemia had noticed a painless, enlarging mass over the right parotid region for the past 2 weeks. On clinical examination, a 2.5 cm soft, well-delineated mass in the parotid region was noted. A FNA cytology biopsy was performed.

Cytopathologic Findings

Smears contained cohesive and individual cells with ovoid to elongated nuclei with no atypia intimately admixed with abundant eosinophilic myxoid stroma. In addition, numerous atypical cells with enlarged, pleomorphic nuclei, and also frequent multinucleated atypical cells were identified (Fig. 1a–c). The combination of the three above mentioned features raised an initial suspicion of a malignant tumor (carcinoma or carcinosarcoma) ex PA. However, on close review of the FNA specimen, no mitotic figures or necrosis was identified. Very focally, vague fat-like vacuoles were seen intermingling with the spindle cells in the stromal component (Fig. 1d). Moreover, the morphological features of the

✉ Fredrik Petersson
fredrikpetersson@live.se

¹ Department of Pathology, National University Hospital, Singapore, Singapore

² Department of Otolaryngology - Head and Neck Surgery (ENT), National University Hospital, Singapore, Singapore

³ Institute of Pathology, University Hospital Erlangen, Friedrich Alexander University (FAU), Erlangen, Germany

⁴ Department of Pathology, National University Health System, 5 Lower Kent Ridge Road, Singapore 119074, Singapore

Fig. 1 **a, b** Smears showed cohesive and individual cells with ovoid to elongated nuclei intimately admixed with abundant eosinophilic myxoid stroma (**a** $\times 400$, **b** $\times 600$). **c** Numerous atypical cells including multinucleated atypical cells were identified ($\times 600$). **d** Fat-like vacuoles (arrows) intermingling with the spindle cells in the stromal component ($\times 400$). Inset: cell block showed atypical cells staining positive for CD34 immunocytochemistry (**a**, **b**, **d**—HC, **c**—PAP)

myxoid stromal component lacked the characteristic/distinct fibrillary appearance with frayed edges that typify the stromal component in a PA.

Immunohistochemical Study on Cell Block

The ovoid/spindled cells as well as the large atypical cells expressed CD34 while myoepithelial markers, smooth muscle actin (SMA), S100-protein and cytokeratins (AE1/3 and CAM5.2) were not expressed. The Ki-67 proliferation index was low ($<2\%$).

The FNA was reported as mesenchymal neoplasm with lipomatous elements and atypical cells. While the possibility of a PL was raised, excision of the mass was suggested.

A computed tomography (CT) scan was performed, and this revealed a heterogeneously enhancing mass in the superficial lobe of the right parotid gland measuring 2.5 cm (Fig. 2a). A superficial parotidectomy was subsequently performed.

Gross Pathological Features

Macroscopically, the tumor appeared as a fairly well delineated yellowish soft tumor and measured 2 cm in fixed state.

Light Microscopical Features

Microscopically, the lesion was bordered by salivary gland parenchyma and consisted of lobules of mature adipose

tissue and spindle cells with several atypical mononuclear cells with large, irregular, hyperchromatic nuclei and also multinucleated floret cells (Fig. 2b). Occasional lipoblasts were identified (Fig. 2c). No atypical mitotic figures, necrosis or areas of prominent vascularity were noted. In addition to a collagenous stroma with focal “ropey structure”, the stroma displayed a variable, but frequently prominent myxoid component. The lesional spindle cells were in some areas present around and also very focally within striated muscle at the periphery of the tumor.

Immunohistochemical Study and FISH on the Resected Specimen

CD34 was diffusely expressed by the tumor cells while no immunoreactivity for the retinoblastoma (Rb) protein or MDM2 was detected (Fig. 2d1–d3). FISH testing was negative for *MDM2* gene amplification (Fig. 2d4).

Discussion

Tumors of the salivary glands containing fat are uncommon and have a predilection for males with a mean age of 50 years [1]. These tumors give rise to a broad morphologic spectrum depending on the intratumoral cellular constituents, which can range from minor scattered adipocytic elements within an otherwise typical salivary gland tumor to predominantly lipogenic salivary gland tumors and pure

Fig. 2 **a** CT scan image showed a heterogeneously enhancing mass in the superficial lobe of the right parotid gland. **b** Low power magnification of the parotid mass surrounded by normal salivary gland parenchyma (H&E). Inset: A lipoblast was identified among variably sized mature adipocytes (H&E $\times 400$). **c1, c2** Proliferation of spindle cells and atypical mononuclear cells with hyperchromatic nuclei and multinucleated floret cells present in a myxoid stroma (H&E $\times 400$).

d1 Positive CD34 expression in the atypical mononuclear and multinucleated floret cells ($\times 400$). **d2** Negative Rb1 staining in the atypical cells with positive staining in the stromal and endothelial cells as internal control ($\times 400$). **d3** Negative MDM2 expression in the atypical cells ($\times 400$). **d4** Negative *MDM2* gene amplification on fluorescence in situ hybridization (FISH)

lipomatous mesenchymal lesions [1]. Salivary gland tumors eg. PA and myoepithelioma are known to contain areas of stromal lipometaplasia. The adipocytic component may range from 20 to 90% of the tumor but unequivocal areas of typical PA and myoepithelioma are usually present with adequate sampling. Sialolipoma is a rare tumor that is composed of normal salivary gland elements admixed with a variable but distinct adipocytic component [1].

Bona-fide lipogenic tumors can, albeit extremely rarely, arise in the salivary gland and are indistinguishable from their soft tissue counterparts. These include lipoma and its variants as well as atypical lipomatous tumor/well differentiated liposarcoma [1]. PL is a benign adipocytic neoplasm, first described by Shmookler and Enzinger in 1981 and is closely related to spindle cell lipoma (SPCL). Most

investigators perceive PL and SPCL to represent two ends of a morphological spectrum and it is not uncommon to see both features of PL and SPCL within one and the same tumor [2]. This similarity is further supported by the genetic finding of loss of Rb expression secondary to chromosome 13q deletion, in both tumors, which thus reinforces their close pathobiologic relationship. On a similar note, cellular angiofibromas, most mammary-type myofibroblastomas, anisometric lipoma and dysplastic lipoma also appear to belong to this group of tumors with 13q deletion [2, 3]. Initial published studies of the very rare lipoblastoma-like tumor of the vulva that has features resembling SPCL reported absent Rb1 expression and suggested possible links to the group of 13q deleted tumors. However, a recent study showed that whilst this rare tumor may resemble SPCL

histologically, they are seem to be genetically different with no demonstrable *Rb1* deletions [4]. *Rb1* is a tumor suppressor protein that plays a vital role in cell cycle progression. Tumors exhibit uncontrolled proliferation when Rb protein and the pathways under it's control are disrupted. Some reports have suggested other functions of the Rb protein, including a role in adipocytic differentiation [2]. In addition to the presence of spindle cells, PL is typified by floret-like giant cells. Moreover, both PL and SPCL frequently display areas of myxoid change which may on occasion be so prominent that the lipomatous nature of the tumor is obscured, so called “fat-free SPCL” [5]. In these instances the tumors may exhibit a pseudolymphangiomatous appearance [5]. Both PL and SPCL usually arises in the subcutaneous tissue of the head and neck region, shoulder and back of men older than 45 years, but these tumors have been described in a wide variety of anatomical sites and over a broad age spectrum. Primary PL and SPC of the major salivary glands are extremely rare with only a handful of cases described in the English literature [6–9].

In the initial workup of the FNA of our case, the spindle cells, which were present admixed with myxoid stromal material, were interpreted as possible myoepithelial cells closely admixed with metachromatic matrix suggesting a PA. In addition, the presence of atypical cells with enlarged, pleomorphic nuclei raised the possibility of a malignant tumor arising on a background of PA, i.e., a carcinoma or carcinosarcoma ex PA. However, other features of malignancy that one should look out for in this context; mitotic figures including atypical forms and granular necrosis (especially when such a degree of nuclear pleomorphism is encountered) were absent. On careful scrutiny of the myxoid matrix, it lacked the fibrillary appearance with frayed edges typically seen in the metachromatic stroma in PA. Moreover, definitive myoepithelial cells were not identified. The absent expression of epithelial and myoepithelial markers also argued strongly against the possibility of a component of PA.

The appearance of the “floret” type giant cells and focal presence of adipocytes with positive expression of CD34 suggested the diagnosis of a PL. The presence of “floret” cells was once considered pathognomonic of PL but it is now known that these cells can occasionally be seen in both SCL and well differentiated liposarcoma. In addition, in contrast to classic text book wisdom, bona fide lipoblasts are not uncommonly encountered in SCL/PL (and may be numerous) [10]. This was also true in our case. Hence, the presence of lipoblasts is not a distinguishing feature from well differentiated, lipoma-like liposarcoma/atypical lipoma, and so far seems to be of no prognostic relevance [10]. Interestingly, some authors have described that atypical mitoses are present in PLs with otherwise classical morphology and hence, this finding does not necessarily indicate malignancy [11]. In view of these morphological overlap of “distinctive” histological features

between liposarcoma and SCL/PL, the negative *MDM2* FISH performed, aided in supporting our diagnosis.

In conclusion, we present a case of a primary parotid PL with prominent myxoid change which on FNA displayed features that mimicked a carcinoma or sarcoma ex PA. Awareness that PLs may rarely occur in salivary glands should facilitate avoiding this mistake. The diagnosis, once suspected, can be substantiated by applying an immunohistochemical panel that should include CD34, Rb protein and *MDM2*. In especially challenging cases a fluorescence in situ hybridization study for amplification of *MDM2* could be considered.

Compliance with Ethical Standards

Conflict of interest The authors state that there are no conflicts of interest to disclose.

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

References

1. Agaimy A. Fat-containing salivary gland tumors: a review. *Head Neck Pathol.* 2013;7:90–96 (**Epub 2013 Jul 3**).
2. Chen BJ, Mariño-Enríquez A, Fletcher CD, et al. Loss of retinoblastoma protein expression in spindle cell/pleomorphic lipomas and cytogenetically related tumors: an immunohistochemical study with diagnostic implications. *Am J Surg Pathol.* 2012;36(8):1119–28.
3. Michal M, Agaimy A, Contreras AL, et al. Dysplastic lipoma: a distinctive atypical lipomatous neoplasm with anisocytosis, focal nuclear atypia, p53 overexpression, and a lack of *MDM2* gene amplification by FISH; a report of 66 cases demonstrating occasional multifocality and a rare association with retinoblastoma. *Am J Surg Pathol.* 2018;42(11):1530–40.
4. Schoolmeester JK, Michal M, Steiner P, et al. Lipoblastoma-like tumor of the vulva: a clinicopathologic, immunohistochemical, fluorescence in situ hybridization and genomic copy number profiling study of seven cases. *Mod Pathol.* 2018;31(12):1862–68.
5. Billings SD, Folpe AL. Diagnostically challenging spindle cell lipomas: a report of 34 “low-fat” and “fat-free” variants. *Am J Dermatopathol.* 2007;29(5):437–42.
6. Thirumala S, Desai M, Kannan V. Diagnostic pitfalls in fine needle aspiration cytology of pleomorphic lipoma. a case report. *Acta Cytol.* 2000;44:653–6.
7. Dundas KE, Wong MP, Suen KC. Two unusual benign lesions of the neck masquerading as malignancy on fine-needle aspiration cytology. *Diagn Cytopathol.* 1995;12:272–9.
8. Graham CT1, Roberts AH, Padel AF. Pleomorphic lipoma of the parotid gland. *J Laryngol Otol.* 1998;112(2):202–3.
9. Rosenthal LS, Garzon S, Setty S, et al. Left-sided facial mass. Spindle cell lipomas of the parotid gland. *Arch Pathol Lab Med.* 2006;130(6):875–6.
10. Michal M, Kazakov DV, Hadravsky L, et al. Lipoblasts in spindle cell and pleomorphic lipomas: a close scrutiny. *Hum Pathol.* 2017;65:140–6.
11. Creyten D, Mentzel T, Ferdinande L, et al. Atypical mitoses are present in otherwise classical pleomorphic lipoma. *Hum Pathol.* 2018. <https://doi.org/10.1016/j.humpath.2018.04.032>.