Hamartomatous Angiolipoma of the Parotid Gland (Sialoangiolipoma)

Eugenio Maiorano · Saverio Capodiferro · Benito Fanelli · Luca Calabrese · Anna Napoli · Gianfranco Favia

Received: 30 August 2007 / Accepted: 14 December 2007 / Published online: 8 February 2008
© Humana 2008

Abstract Mesenchymal tumors of the salivary glands are rare and mostly localized to the parotid gland. We report on the clinico-pathological features of a distinct parotid tumor occurred in a newborn, showing glandular structures admixed with mature lipocytes and blood vessels in variable proportions. This was a well-circumscribed and slowly growing nodule of the superficial parotid lobe, mostly reddish in color with white-yellowish striations. Microscopically, a distinct lobular architecture was evident, along with normal-appearing acinar and ductal structures with interposed loose fibrous stroma. The latter contained aggregates of mature lipocytes and variably sized blood vessels. The morphological features of the lesion reported herein recapitulate those of sialolipoma but also include the presence of a prominent vascular component intimately admixed with both the glandular and the adipose tissues. At variance with salivary lipoadenoma, the glandular component in the current case distinctly showed all the cellular components of normal salivary (serous) glands. In consideration of the young age of the patient, the minimal

growth rate and the histological features of the lesion, we hypothesize a hamartomatous origin for this lesion and propose the designation of sialoangiolipoma.

Keywords Salivary gland neoplasms · Soft tissue tumors · Lipoma · Angiolipoma · Sialolipoma

Introduction

Mesenchymal tumors of the salivary glands are rare, accounting for 2–5% of all salivary gland tumors [1, 2], the parotid gland being their most common localization. They most frequently are benign, may occur at any age, with prevalence in the 5th–6th decades, with the exception of vascular tumors that occur at a younger age, and affect males more frequently than females. Angiomas, neural tumors (schwannomas and neurofibromas) and lipomas are by far the most frequent benign mesenchymal tumors occurring in the salivary glands, with several distinct subtypes or variants of each group having been reported (e.g., juvenile and cellular haemangioma, hibernoma, lipoblastoma, pleomorphic and spindle cell lipoma, etc.) [1, 3–5].

Combined mesenchymal neoplasms, composed of cells showing different differentiation, though rare may affect many distinct sites, including the skin and subcutis and viscera. These are exceptional in the salivary glands and a single case of intra-parotid angiolipoma has been reported so far [6] composed of an admixture of mature blood vessels and adipocytes.

Such combination of mature mesenchymal tissues may be encountered within hamartomatous proliferations of different organs. Hamartomas of major salivary glands, composed by sero-mucous acini, ducts, myoepithelial cells,

E. Maiorano (✉) · A. Napoli
Department of Pathological Anatomy, University of Bari,
Piazza G. Cesare, 11, Bari 70124, Italy
e-mail: emaiorano@anatopat.uniba.it

S. Capodiferro · G. Favia
Department of Dental Sciences and Surgery, University of Bari,
Bari, Italy

B. Fanelli
Division of Pediatric Surgery, Department of Surgery,
“Giovanni XXIII” Paediatric Hospital, Bari, Italy

L. Calabrese
Division of Head and Neck Surgery, European Institute
of Oncology, Milan, Italy

adipose and lymphoid tissues have been reported very rarely [7]. Very recently, hamartomatous lesions of the tongue containing salivary gland structures, along with vascular, fat and other mesenchymal tissues have been reported, which mostly occurred in young patients of female gender and some of which were congenital in origin [8].

Interestingly, two distinct neoplasms composed of mature adipocytes intimately admixed with salivary structures have been described, namely sialolipoma and lipoadenoma. The former [9–11] is a well-demarcated neoplasm that histologically shows mature adipocytes and glandular structures with distinct ductal, acinar, basal and myoepithelial cells, closely resembling the cellular composition of normal salivary glands. Lipoadenoma and its oncocytic variant [12–15] are well-circumscribed and encapsulated neoplasms comprising mature adipocytes and branching narrow tubules, sometimes without evident lumina formation, lined by columnar cells with interposed scattered basal cells.

The aim of this study was to illustrate the clinico-pathological features of a distinct parotid lesion, occurring in a new-born, composed of blood vessels, mature adipocytes and salivary gland structures, to discuss its differential diagnosis and to speculate on its origin.

Case Report

A female newborn, delivered at term after uncomplicated pregnancy, was hospitalized a few days after birth for the presence of slight facial asymmetry due to a space-occupying lesion in the left parotid region. Clinical examination demonstrated a well-demarcated ovoid mass, medially located to the angle of the mandible, which was mildly hyperechoic and solid at ultrasound examination, with a maximum diameter of 2.7 cm (Fig. 1). Lymph nodes enlargement was detected bilaterally in the neck and interpreted as reactive in nature. Color-doppler examination showed multiple vascular proliferations, possibly arterial in nature, and subsequent CT-scan and NMR examinations confirmed the solid nature of the lesion, which also showed increased signal after contrast enhancement. Anatomically, the mass was sharply defined and in continuity with the postero-inferior area of the superficial lobe of the left parotid. Adjacent osseous and soft tissue structures were mildly compressed, as were the overlying skin and subcutis.

The above data were suggestive for a benign lesion and, in consideration of the age of the patient, strict follow-up was advised with semi-annual clinical and ultrasound examination. The lesion slowly grew over the next 3 years

Fig. 1 Ultrasound examination demonstrated a well-demarcated ovoid mass, medially located to the angle of the mandible, solid and mildly hyperechoic, with a maximum diameter of 2.7 cm

Fig. 2 The surgical specimen consisted in a $3.2 \times 3.0 \times 2.4$ cm red mass containing distinct white-yellowish striations. The mass was well-circumscribed and showed distinct lobular architecture

up to the maximum diameter of 3.1 cm when the patient reached the age of 3 and surgery was recommended.

Subsequently, the patient underwent superficial parotidectomy and remained well and free of disease over the next 2 years.

The surgical specimen consisted of a $3.2 \times 3.0 \times 2.4$ cm red mass containing distinct white-yellowish striations (Fig. 2). The mass was well-circumscribed and showed distinct lobular architecture.

Table 1 List of the antibodies (all raised in mouse, with the exception of S-100 protein, which was raised in rabbit) used to immunohistocharacterize sialangiolioma

Antibody	Clone	Company	Dilution	Positive control
Actin (muscle specific)	HHF 35	Dako ^a	1:150	Leiomyoma
Calponin	CALP	Dako	1:20	Leiomyoma
CD31	JC/70A	Dako	1:30	Haemangioma
CD34	QBE10	Immunotech ^b	1:40	Haemangioma
Cytokeratin 34 β E12	34 β E12	Dako	1:50	Prostate
S-100 Protein	–	Dako	1:1000	Melanoma

^a Dako, Glostrup, Denmark^b Immunotech, Marseille, France

It was fixed in 10% neutral buffered formalin for 24 h, embedded in paraffin, cut and stained with hematoxylin–eosin (H&E) and Gomori's reticulin.

Consecutive sections, collected on poly-L-lysine-coated slides, along with appropriate positive controls (detailed in Table 1), were used for the immunohistochemical detection of the antigens listed in Table 1, with an avidin-biotin peroxidase (ABC) method. All sections were subjected to an epitope retrieval procedure in boiling 0.01M citrate buffer, pH 6.0, under 4 cycles of 5 min. irradiation in a microwave oven, operating at 750 W. All the subsequent incubations with primary antibodies took place for 2 h at room temperature in an automated immunostainer (Autostainer Dako, Glostrup, Denmark).

Negative controls were obtained by substituting the primary antibodies with non-immune rabbit or mouse sera, and consistently lacked any immunostaining.

At low power magnification thin fibrous septa subdivided the lesion in distinct lobules showing similar histological structure (Fig. 3). Variably sized salivary lobules composed of both acinar and ductal structures were evident throughout the mass and were separated from each other by variable amounts of fibrous connective tissue containing blood vessels of different diameter. Groups of mature and mono-vacuolated adipocytes were sparse throughout the lesion. The glandular structures were composed by acinar cells surrounded by a basal layer of spindled and cuboidal cells, morphologically consistent with myoepithelial and basal cells. A structured ductal system departed from the acini, with evidence of intercalated, striated, intra- and inter-lobar ductal differentiation (Fig. 4).

A fibrous stroma was interposed among acinar and ductal structures, containing variably sized blood vessels, that apparently dissociated and replaced the glandular structures to varying extents: some parotid lobes, particularly those peripherally located, were almost entirely

Fig. 3 At low power magnification the lesion shows distinct lobular architecture. Variably sized salivary lobules are evident throughout the mass and are separated from each other by variable amounts of fibrous connective tissue. Groups of mature adipocytes are sparse throughout the lesion (Haematoxylin-Eosin, 1 $\times$) **Fig. 4** The glandular structures are composed by acinar cells surrounded by a basal layer of spindled and cuboidal cells. A structured ductal system departs from the acini, with evidence of intercalated and striated ducts (Haematoxylin-Eosin, 100 $\times$)

Fig. 5 The stromal component interposed among acinar and ductal structures contains variably sized blood vessels. These most frequently are of capillary size but venular, arteriolar and cavernous vessels are present as well (Haematoxylin–Eosin, 100×)

composed by acinar/ductal structures while others, especially in the centre of the mass, were predominantly composed by fibroconnective tissue and blood vessels with evidence of scattered and dispersed acinar/ductal structures.

The blood vessels most frequently were of capillary size but venular, arteriolar and cavernous vessels were present as well and were randomly distributed within the lesion (Fig. 5).

The amount of adipose tissue was extremely variable, from isolated mature lipocytes, sometimes laying in close proximity with the acinar structures, to distinct lobules of mature fat tissue.

Mitotic activity, necrosis or invasive growth were not detected.

Fig. 6 A distinct layer of calponin immunoreactive myoepithelial cells is evident around the acinar structures and striated and intercalated ducts (ABC technique, anti-calponin, 200×)

Immunohistochemistry

A distinct layer of muscle actin- and calponin-immunoreactive myoepithelial cells (Fig. 6) was evident around the acinar structures and striated and intercalated ducts while cytokeratin 34 β E12-positive cells were detectable in a basal location within the acini and the ductal structures.

The vascular component showed consistent CD31 immunoreactivity in the endothelial layer and muscle actin and calponin immunoreactivity in the vessel walls. Adipocytes disclosed consistent S-100 protein positivity.

Discussion

We describe herein the salient characteristics of a novel parotid lesion occurring in a newborn, with indolent progressive growth and an apparently benign clinical course, for which, in view of its typical histological features, we propose the designation of sialoangiolipoma. Its morphology strictly recapitulates that of sialolipoma, [9–11] being composed of normal looking acinar and ductal structures with interposed mature adipocytes. At variance with sialolipoma, the current lesion also included a prominent vascular component, consisting in capillaries, venules, small arteries and cavernous vessels irregularly distributed throughout the mass. The vascular-adipose component was more abundantly represented in the central areas of the lesion and seemed to progressively substitute the glandular component.

The current case also recapitulates some of the features of lipoadenoma. [12, 13, 15] Nevertheless, the latter includes irregularly branching tubules that do not show all the cellular components of normal salivary gland, i.e., acinar, ductal, basal and myoepithelial cells, which are clearly detectable in sialoangiolipoma.

Angiolipomas are uncommon mesenchymal neoplasms that may occur in the head and neck area [16, 17] and occasionally may show aggressive behavior in its infiltrating variant [18, 19] In a single circumstance parotid angiolipoma has been previously reported and its morphological characteristics were identical to those of angiolipomas occurring at other sites, consisting of a proliferation of blood vessels and adipocytes in a collagenous stroma, without evidence of any glandular components.

Furthermore, common benign neoplasms of the salivary glands, namely pleomorphic adenomas, may occasionally include an abundant adipose component (pleomorphic adenoma with lipometaplasia) [20] possibly deriving from metaplastic changes of myoepithelial cells. Such neoplasms, at variance with sialoangiolipoma, demonstrate at least focal typical features of pleomorphic adenoma including neoplastic ductal structures, myxochondroid differentiation, plasmacytoid, spindle or clear cells.

Due to the lack of residual normal salivary tissue around the lesion we were not able to ascertain whether sialoangioliipoma involved the whole superficial lobe of the parotid or was limited to a restricted part. The presence of residual parotid tissue, in fact, would have pointed to a focal outgrowth of possible neoplastic nature while the extension of the lesion to the entire glandular parenchyma would have favoured its disontogenetic or hamartomatous origin. Nevertheless, in consideration of the very young age of the patient, the minimal growth rate of the mass and the intimate admixture of mesenchymal and glandular components within the lesion we tend to favour the hamartomatous nature of this peculiar lesion. It is not uncommon, in fact, that hamartomas may present at birth even if, due to their slow growth, they may not become manifest until late, when deeply located. In the current case, the occurrence of the lesion at a superficial site facilitated its early detection. This hypothesis is supported by the detection of a similar hamartomatous lesion occurring in the thymus (thymohaemangioliipoma) composed by an intimate admixture of thymic tissue, medium-caliber blood vessels and adipose tissue, in a 18-year-old woman [21]. The deep location of the neoplasm might have delayed its identification though it could have arisen long before its clinical detection.

It is worthwhile to emphasize that lipomatous tumors, breast adenoliipoma and pleomorphic adenomas may share common cytogenetic abnormalities involving chromosome 12 (q13–q15) at the Multiple Aberration Region (MAR) [22, 23]. Though we could not prove such aberrations to be present in the current case, it may be worth to investigate future cases on this issue due to the morphological similarities between sialoangioliipoma and the above neoplasms in which such abnormalities were detected.

As to the biologic behavior, our patient did not experience tumor-related events after surgical excision and, similarly to other salivary gland lesions with similar morphology, such as sialoliipoma and lipoadenoma, a completely benign clinical course may be anticipated.

References

- Gnepp DR. Soft tissue tumors. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. *Histological typing of salivary gland tumors*. World Health Organization classification of tumors. Pathology and genetics of head and neck tumors. Lyon: IARC Press; 2005. pp. 275–6.
- Seifert G, Donath K, Schafer R. Lipomatous pleomorphic adenoma of the parotid gland. *Classification of lipomatous tissue in salivary glands*. *Pathol Res Pract* 1999;195:247–52.
- Calhoun KH, Clark WD, Jones JD. Parotid lipoblastoma in an infant. *Int J Pediatr Otorhinolaryngol* 1987;14:41–4.
- Fregnani ER, Pires FR, Falzoni R, et al. Lipomas of the oral cavity: clinical findings, histological classification and proliferative activity of 46 cases. *Int J Oral Maxillofac Surg* 2003;32:49–53.
- Vinayak BC, Reddy KT. Hibernoma of the parotid region. *J Laryngol Otol* 1993;107:257–8.
- Kelly DR, Reilly JS, Royal SA. Angioliipoma of the parotid: case report and review. *Laryngoscope* 1988;98:818–21.
- Tsuda H, Morinaga S, Mukai K, et al. Hamartoma of the parotid gland: a case report with immunohistochemical and electron microscopic study. *Virchows Arch A Pathol Anat Histopathol* 1987;411:473–8.
- Kreiger PA, Ernst LM, Elden LM, Kazahaya K, Alawi F, Russo PA. Hamartomatous tongue lesions in children. *Am J Surg Pathol* 2007;31:1186–90.
- Hornigold R, Morgan PR, Pearce A, et al. Congenital sialoliipoma of the parotid gland: first reported case and review of the literature. *Int J Pediatr Otorhinolaryngol* 2005;69:429–34.
- Michaelidis IG, Stefanopoulos PK, Sambaziotis D, et al. Sialoliipoma of the parotid gland. *Int J Craniomaxillofac Surg* 2006;34:43–6.
- Nagao T, Sugano I, Ishida Y, et al. Sialoliipoma: a report of seven cases of a new variant of salivary gland lipoma. *Histopathology* 2001;38:30–6.
- Hirokawa M, Bando Y, Tashiro T, et al. Parotid lipoadenoma with sclerotic and polycystic changes. *Virchows Arch* 2002;440:549–50.
- Hirokawa M, Shimizu M, Manabe T, et al. Oncocytic lipoadenoma of the submandibular gland. *Hum Pathol* 1998;29:410–2.
- Kato M, Horie Y. Oncocytic lipoadenoma of the parotid gland. *Histopathology* 2000;36:285–6.
- Yau KC, Tsang WY, Chan JK. Lipoadenoma of the parotid gland with probable striated duct differentiation. *Mod Pathol* 1997;10:242–6.
- Ali MH, El Zuebi F. Angioliipoma of the cheek: report of a case. *J Oral Maxillofac Surg* 1996;54:213–5.
- Ida-Yonemochi H, Swelam W, Saito C, et al. Angioliipoma of the buccal mucosa: a possible role of mast cell-derived VEGF in its enhanced vascularity. *J Oral Pathol Med* 2005;34:59–61.
- Hamakawa H, Hino H, Sumida T, et al. Infiltrating angioliipoma of the cheek: a case report and a review of the literature. *J Oral Maxillofac Surg* 2000;58:674–7.
- Sugiura J, Fujiwara K, Kurahashi I, et al. Infiltrating angioliipoma of the mucolabial fold: a case report and review of the literature. *J Oral Maxillofac Surg* 1999;57:446–8.
- Seifert G, Oehne H. Mesenchymal (non-epithelial) salivary gland tumors. Analysis of 167 tumor cases of the salivary gland register. *Laryngol Rhinol Otol* 1986;65:485–91.
- Ogino S, Franks TJ, Deubner H, et al. Thymohemangioliipoma, a rare histologic variant of thymoliipoma: a case report and review of the literature. *Ann Diagn Pathol* 2000;4:236–9.
- Rohen C, Caselitz J, Stern C, et al. A hamartoma of the breast with an aberration of 12q mapped to the MAR region by fluorescence in situ hybridization. *Cancer Genet Cytogenet* 1995;84:82–4.
- Wanschura S, Belge G, Stenman G, et al. Mapping of the translocation breakpoints of primary pleomorphic adenomas and lipomas within a common region of chromosome 12. *Cancer Genet Cytogenet* 1996;86:39–45.