Recurrent Pleomorphic Adenoma

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History

A 29-year-old male presented for evaluation of an enlarging 4.5 cm firm but mobile mass of the left cheek. He additionally desired revision for a scar that resulted from a prior surgical procedure wherein the patient described undergoing surgery 12 years earlier for a “cyst” in the same region of the face. The patient stated that the surgery was terminated mid-procedure due to concern for the surrounding salivary gland.

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Radiologic Features

Magnetic resonance imaging (MR) of the upper neck revealed a well-defined, lobulated mass that likely represented a venolymphatic lesion predominantly involving the subcutaneous fat with involvement of the superficial lobe of the left parotid gland. The lesion measured approximately 4.3×2.4 cm (axial dimensions) $\times$ 3.7 cm cranio-caudad and was shown to be hypointense on the T1-weighted image (Fig. 1 left) and markedly hyperintense following contrast administration (Fig. 1 right). Curvilinear hypointensities within the lesion, which likely represented septations, were also noted (Fig. 2). The remaining soft tissue structures of the neck were unremarkable.

Diagnosis

The gross tissue specimen showed numerous individual and coalescing islands of firm, white tumor with a smooth, glossy appearance that contrasted with the surrounding yellow adipose and salivary gland tissues (Fig. 3). The hematoxylin and eosin stained slides revealed large islands of tumor surrounded by thick fibrous septae. The tumor nodules varied in size and shape but demonstrated a smooth outline (Fig. 4). Sheets and islands of bland plasmacytoid cells were distributed throughout the loose, pale blue-gray myxoid background stroma (Fig. 5). A proliferation of large and small caliber ducts, some containing an eosinophilic product, were also a prominent component. The degree of cellularity, abundance of ducts and amount of myxoid stroma varied throughout individual tumor islands. Cytologic atypia and true cartilaginous islands were not identified. The combined histologic and radiographic features coupled with the anecdotal clinical

Fig. 1 The *left* image depicts a coronal T-1 weighted MR image with a multi-lobulated mass originally thought to represent a vascular tumor. The *right* coronal T-1 MR image shows the lesion as hyperintense following contrast administration

Fig. 2 This axial T-2 post-contrast image shows a hyperintense lesion also revealing curvilinear hypointensities within the lesion representing septations

Fig. 3 The gross specimen reveals numerous separate and coalescing tumor nodules contained within parotid tissue as well as peri-parotid adipose tissue

Fig. 4 Numerous islands of tumor within peri-parotid adipose tissue showing a bland ductal proliferation in a myxoid stroma separated by fibrous septae

Fig. 5 The myxoid stroma contains thin, anastomosing strands of myoepithelial cells and ducts which contain an eosinophilic product

history were consistent with recurrent pleomorphic adenoma.

Discussion

Pleomorphic adenoma is a benign salivary gland tumor composed of proliferating ductal and myoepithelial elements in a variably myxoid to chondroid background stroma which may demonstrate an infinite number of architectural configurations [1]. It is the most common salivary gland tumor and primarily involves the parotid and minor salivary glands [2]. Pleomorphic adenoma demonstrates a slight predilection for females and occurs in patients of all ages with the highest incidence in the fourth to sixth decades [1].

Magnetic resonance imaging is considered the method of choice for evaluating pleomorphic adenomas [3–5], as MR allows for visualization of the capsule in almost all cases [4]. Additionally, MR is superior for soft tissue differentiation, including deep tissue extension and facial nerve visualization [5]. Typically, imaging studies will reveal a lobulated mass with post-contrast enhancement and a bright T2-weighted signal without local tissue invasion [6]. The bright signal on T2-weighted images corresponds to myxoid areas and is distinctive for pleomorphic adenoma [7]. Alternately, a hypointense signal on T2-weighted or STIR (short tau inversion recovery) images is indicative of hyalinization [8]; when in combination with an ill-defined or infiltrative border [5] the findings are suggestive of degeneration and subsequent malignant change. Recurrent pleomorphic adenomas frequently present on T2-weighted imaging as multiple small nodules [3, 9]. The differential diagnosis on MR image would include carcinoma *ex* pleomorphic adenoma, chondroid syringoma, and metastatic disease.

Grossly, the tumor demonstrates a tan-to-white cut surface with semi-translucent, glistening regions corresponding to chondromyxoid tissue [1]. A capsule of variable thickness and continuity may be present [10]. Histologically, the epithelial component is usually composed of plasmacytoid or spindled myoepithelial cells and ductal structures, however, a wide variety of cell types can occur including cuboidal, basaloid, squamous (with subsequent keratin pearl formation), oncocytic cells and clear cells. Rarely, mucous, sebaceous and serous acinar cell types are present [11]. Tyrosine crystals, oxalate crystals and crystalloids composed of radially-arranged collagen fibers are occasionally present [12]. Immunohistochemically, the luminal (ductal) epithelial cells are reactive for cytokeratins 3, 6, 7, 10, 11, 13 and 16 [11]. Abluminal (myoepithelial) cells are reactive for smooth muscle actin (SMA), calponin, S-100 protein, p63 and glial fibrillary

acidic protein (GFAP) [13], but will demonstrate variable reactivity with these markers based on whether they differentiate as classical myoepithelial cells or modified myoepithelial cells [14]. The histologic differential diagnosis includes polymorphous low grade adenocarcinoma, chondroid syringoma and myoepithelioma.

Pleomorphic adenomas are characterized by recently discovered recurrent chromosomal rearrangements, most commonly t(3;8)(p21;q12) which results in promoter swapping between *PLAG1*, a novel developmentally-regulated zinc finger gene [15] recently characterized as a proto-oncogene [16], and *CTNNB1* which encodes for beta-catenin [15]. The activation of *PLAG1* is considered a frequent genetic event occurring in all major cytogenetic sub-groups of pleomorphic adenomas and is also demonstrated in certain mesenchymal tumors [17]. *PLAG1* is also involved in the second most common translocation of pleomorphic adenomas, t(5;8)(p13;q12) which again results in increased expression of *PLAG1*, except under control of the *LIFR* (leukemia inhibitory factor) promoter region, which is active in a wide variety of fetal and adult tissues, including normal salivary gland tissue [18]. This reinforces the theory that pleomorphic adenoma cells originate from a single pluripotent cell type capable of differentiation into a variety of somatic phenotypes [19].

Due to several features, pleomorphic adenoma, although benign, has a propensity for recurrence if not initially completely excised. Pseudopodia, or microscopic fingerlike projections of neoplastic cells which may extend beyond the tumor, are considered a significant risk factor for recurrence [20]. Spurs, ridges, depressions, and tumor budding can be present on otherwise smooth-surfaced appearing tumors [10]. Although recurrent pleomorphic adenomas may grossly appear to be a single mass, microscopically they typically prove to be multi-nodular with satellite islands present [21]. Furthermore, extensive variability in tumor capsule thickness and completeness is well-documented [10] and thus, a clear resection margin may not guarantee complete removal and cure [21]. Neutron radiotherapy has been advocated for complex recurrent cases to ensure complete tumor removal, as well as to reduce the possibility of surgical damage to the facial nerve. Its use is purported to avoid the adverse effects of traditional radiotherapy [22].

As most tumors do not involve the deep lobe of the parotid gland, the treatment of choice for primary pleomorphic adenoma is superficial parotidectomy with preservation of the facial nerve where possible; recurrence rates are low and incidence of morbidity (most commonly Frey syndrome) is greatly reduced [23]. Because these tumors become more aggressive after each procedure with subsequent increased risk of malignant transformation [21], early diagnosis, treatment and routine follow up are

essential. The current patient underwent a superficial parotidectomy with wide soft tissue margins and has had an uneventful follow-up period.

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