An update on mesenchymal tumors of the head and neck

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Abstract

The purpose of this review is to offer a brief reappraisal of several soft tissue neoplasms germane to the head and neck region. Specifically, this paper is intended to draw attention to the recently described low-grade sarcoma with neural and myogenic features. In addition, other tumors that are largely specific to the head and neck region, including nasopharyngeal angiofibroma, sinonasal hemangiopericytoma and spindle cell/pleomorphic lipoma, will be reviewed in light of recent advances in our understanding of their pathophysiology and diagnosis.

Keywords glomangiopericytoma; low-grade sarcoma with neural and myogenic features; nasopharyngeal angiofibroma; spindle cell and pleomorphic lipoma

Introduction

Mesenchymal tumors of the head and neck are relatively uncommon,[1] with most entities bearing clinicopathologic semblance to their counterparts arising elsewhere in the body. There are, however, several entities that are largely restricted to the head and neck, which deserve special attention. An appreciation in these cases for subtle morphologic differences is not infrequently all that separates a correct diagnosis from potentially harmful misclassification. The purpose of this brief review is to highlight several mesenchymal neoplasms with a predilection for the head and neck region. In so doing, the relevant clinical, morphologic, immunohistochemical and molecular attributes are discussed.

Low-grade sarcoma with neural and myogenic features

This recently recognized entity represents a distinct neoplasm that, thus far, appears restricted to the superior sinonasal region.[2] Tumors predominate in adults and there is a modest predilection for females (approximately 75% of cases). The most frequent sites of involvement include the nasal cavity and ethmoid sinus, with clinical symptoms typically relating to the sequelae of nasal obstruction. Low-grade sinonasal sarcoma with neural and myogenic features may be locally destructive; however, metastasis has not been reported. Owing in part to difficulty in obtaining uninvolved resection margins, local recurrence is common. While the cell of origin remains to be fully characterized, these tumors are notable for their co-expression of both neural and myogenic markers.

Grossly, tumors are typically received fragmented and may have a polypoid appearance. Histologically, they are poorly circumscribed and characterized by a cellular proliferation of spindle cells with a herringbone-fascicular pattern (Figure 1). The cytoplasm tends to be pale and eosinophilic. The nuclei are ovoid and elongated with minimal atypia and hyperchromasia; mitotic activity, if present, is typically rare. Interspersed between the cells there is often delicate thin bands of collagen. Areas of decreased cellularity may be noted. An interesting characteristic of these tumors appears to be an induced proliferation of the overlying epithelium, which was reported in more than two thirds of cases.[2] The vasculature is largely nondescript; however, a prominent hemangiopericytoma-like pattern may occasionally be observed. Rare cases with rhabdomyoblastic differentiation have been identified. The results of immunohistochemical analysis typically demonstrates diffuse positivity for S100. Generally there is co-expression with smooth muscle actin and/or related muscle markers, with a minority of cases showing focal immunoreactivity for desmin, epithelial membrane antigen and keratin. Interestingly, cytogenetic analysis in two cases was reported to show rearrangement of t(2; 4)(q37.1; q31.3) — with subsequent studies showing a *PAX3-MAML3* fusion product in 75% of cases, and the remaining 25% showing *PAX3* rearrangement only[3]; thereby confirming that this tumor represents a unique entity, rather than an unusual manifestation of schwannoma, malignant peripheral nerve sheath tumor or (myo)fibrosarcoma. Despite its recent recognition and relative rarity, there is evidence this entity was previously reported, largely appearing in the literature under the rubric of fibrosarcoma.[2]

The differential diagnosis for low-grade sinonasal sarcoma with neural and myogenic features includes malignant peripheral nerve sheath tumor, fibrosarcoma, synovial sarcoma, and rhabdomyosarcoma. Admittedly, malignant peripheral nerve sheath tumor can exhibit protean morphologic manifestations. The possibility of a malignant peripheral nerve sheath tumor is, however, made less likely by the combined absence of clinical, morphologic, immunohistochemical and ultrastructural features to suggest neural differentiation.[2] For example, in none of the 28 cases reported by Lewis et al. was there a documented clinical association with type I neurofibromatosis or morphologic evidence of a nerve origin. Ultrastructurally there is no evidence to suggest Schwannian differentiation.[2] The tumors are negative for neurofilament and exhibit only focal immunoreactivity for CD34. So-called adult-type fibrosarcoma, at present, largely remains a diagnosis of exclusion. These tumors are notable for their characteristic null immunophenotype, generally with evidence of only focal myofibroblastic differentiation. Synovial sarcoma can be readily differentiated from low-grade sinonasal sarcoma with neural and myogenic features based on its typically plumper and overlapping cytomorphology, longer fascicles, presence — albeit sometimes only focal — of immunoreactivity for keratins and/or epithelial membrane antigen, and characteristic presence of a t(X; 18) translocation. Rhabdomyosarcoma, namely embryonal rhabdomyosarcoma, may show variable amounts of rhabdomyoblastic differentiation which can be highlighted by immunohistochemistry for desmin, MyoD1 and/or MYF4; it would be unusual to observe diffuse S100 in rhabdomyosarcoma.

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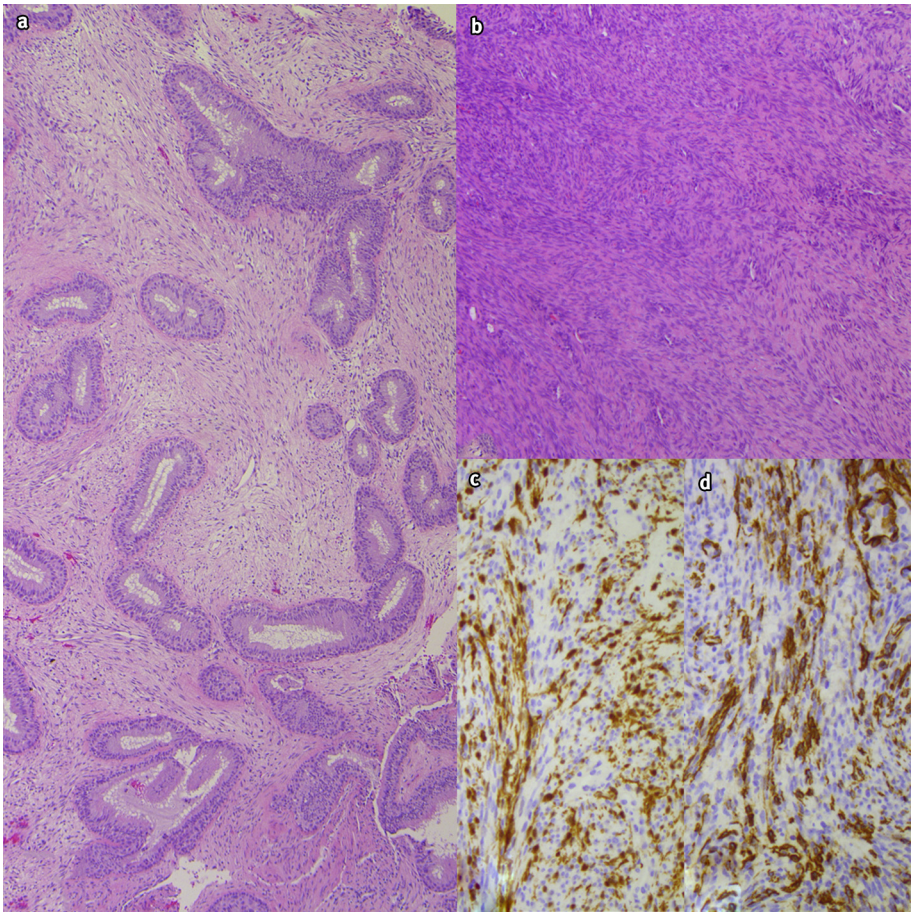

Figure 1 Low-grade sarcoma with neural and myogenic features. (**a**) Low-power photomicrograph showing a monomorphic spindle cell proliferation insinuating around hyperplastic epithelium. (**b**) Higher magnification showing an area of increased cellularity and herringbone pattern of growth. Immunohistochemistry demonstrates patchy immunoreactivity for (**c**) S100, and (**d**) smooth muscle actin.

Nasopharyngeal angiofibroma

Nasopharyngeal angiofibroma (angiofibroma; bleeding fibroma of adolescence; fibroangioma; juvenile angiofibroma; juvenile basal fibroma) represents a benign, albeit locally aggressive, neoplasm that frequently occurs in males during adolescence.[4] The low number of cases makes an assessment of incidence difficult, but it is in the realm of 0.4 cases per million per year.[5] Despite its name, most tumors actually arise from the posterolateral wall of the nasal cavity in the area of the sphenopalatine foramen.[6] Tumors may arise in adulthood[7]; the predisposition for males is so pronounced that female involvement has prompted recommendation that androgen insensitivity syndrome be excluded.[4] Tumors may extend into the paranasal sinuses, soft tissues and cranial cavity. Difficulty in achieving complete surgical resection results in frequent recurrence; however, convincing evidence of metastasis remains the exception.[8] Patients most often present clinically with symptoms of obstruction and/or epistaxis[9]; left unchecked, tumors have the potential to cause sepsis, and marked facial deformity. Malignant transformation has rarely been reported, and appears most often in the context of prior radiation therapy.[9,10] The etiology remains unclear. Nasopharyngeal angiofibroma has been proposed to be an extra-gastrointestinal manifestation of familial adenomatous polyposis[11,12]; however, this assertion has been disputed.[13] An association with the GSTM1-null phenotype has also been proposed.[14,15]

Grossly, tumors tend to be smooth, nodular and unencapsulated with a sessile or pedunculated base; the margins are often infiltrative.[16] On average they are 3–4 cm, but tumors over 20 cm have been reported. Histologically, they contain a proliferation of bland spindle, stellate or round cells, situated in a dense collagenous matrix (Figure 2). The cells have a small amount of pale cytoplasm. The nuclei are ovoid, plump and monomorphic; mitotic activity is uncommon.[16] Multinucleation and scattered nuclear pleomorphism are common. A conspicuous thin-walled vasculature permeates the lesion; vessels may be of variable caliber and density, and range from slit-like to ectatic. Minor histologic differences often reflect the age of the lesion. Myxoid degeneration and infarction is common following embolization. Secondary changes, such as ulceration, granulation tissue, inflammation and hemorrhage can also occur. The stromal cells are immunopositive for vimentin and β-(beta) catenin (nuclear), with variable immunoreactivity reported for smooth muscle actin, androgen receptor and CD117.[17–20]

The differential diagnosis for nasopharyngeal angiofibroma largely includes solitary fibrous tumor and pyogenic granuloma. In contrast to solitary fibrous tumor, the vasculature of nasopharyngeal angiofibroma tends to be thin-walled and lack prominent hyalinization; further, angiofibroma contains more extensive "keloid-like" collagen interspersed between the cells.