Chondroid Syringoma

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We present the case of a 25-year-old man who presented with a slowly enlarging nodule on the upper lip. This nodule first appeared after minor trauma to the area. Our original differential diagnosis included foreign body granuloma, mucocele, inclusion cyst, and adnexal tumor. Histopathology results showed an encapsulated tumor consisting of 2 discrete lobules composed of numerous aggregates of cuboid epithelial cells with tubuloalveolar structures and keratinous cysts within a chondroid stroma—consistent with a chondroid syringoma. We compare and contrast the clinical and histologic characteristics of chondroid syringomas (arising from sweat glands) with those of pleomorphic adenomas (arising from salivary glands).

The term *mixed tumor* refers to a neoplasm that has microscopic features of both epithelial and mesenchymal differentiation. Tumors with mixed cell types can arise from either salivary glands or sweat glands and most commonly occur in the head-and-neck region of middle-aged men. As their clinical presentations and histologic appearances are similar, these tumors are often difficult to distinguish.[1-7] Tumors that arise from salivary glands are more commonly referred to as *pleomorphic adenomas*, whereas those that arise from sweat glands are referred to as *chondroid syringomas*.[1] Typically, these tumors present as firm subcutaneous nodules that have been present for several years and that tend to remain stable in size or grow slowly and gradually. The incidence of these 2 tumors varies. More than 5000 cases have been reported of pleomorphic adenomas,[8] whereas only 400 cases have been reported of chondroid syringomas.[3] A history of trauma is occasionally elicited, but trauma is thought to be coincidental rather than causative.[1] Both tumors are benign encapsulated neoplasms, but they can recur if excision is incomplete. Malignant forms of mixed tumors can arise, but these tumors are even rarer than chondroid syringomas. In this article, we report a case of chondroid syringoma that is unusual in presentation and location.

Accepted for publication August 20, 2002.

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The views expressed in this article are those of the authors and do not reflect the official policy or position of the US Department of the Navy, the US Department of Defense, or the US government.

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Case Report

A 25-year-old white man presented with an asymptomatic but slowly enlarging nodule on the right upper lip. The patient stated that 5 years previously he had sustained a laceration to the upper lip after minor trauma and that sutures had not been required. Over the next 2 years, he had developed a fibrous cord in the same area on his lip. Because the area was firm and thickened, suggestive of scar tissue, it was injected with 0.1 cm^3 of 20 mg/mL of triamcinolone acetonide. Over the next 3 years, this area had gradually enlarged and become more indurated, until the patient presented to our dermatology clinic and requested surgical excision of the mass (Figure 1).

Results of a physical examination revealed a single, firm, 2-cm dermal nodule causing an asymmetrical protuberance of the patient's upper lip. The nodule was clearly demarcated from the normal surrounding tissue of the upper lip; however, there were no appreciable epidermal changes. The nodule was nontender and mobile, and there was no appreciable cervical lymphadenopathy.

An intraoral approach was used to extirpate the lesion. On blunt dissection, 2 encapsulated firm gray nodules, each measuring 0.7 cm in diameter, were easily shelled out from the normal surrounding tissue.

Results of microscopic studies showed 2 well-demarcated and circumscribed submucosal nodules. The first nodule was composed predominately of a myxoid stroma with a few ductal and epithelial structures. The epithelial component consisted of small scattered ducts lined by 1 to 2 layers of cuboid cells with some ducts exhibiting decapitation secretion. The predominant feature of the myxoid stroma was that it had numerous plasmacytoid cells (Figure 2), some of which were entrapped within a

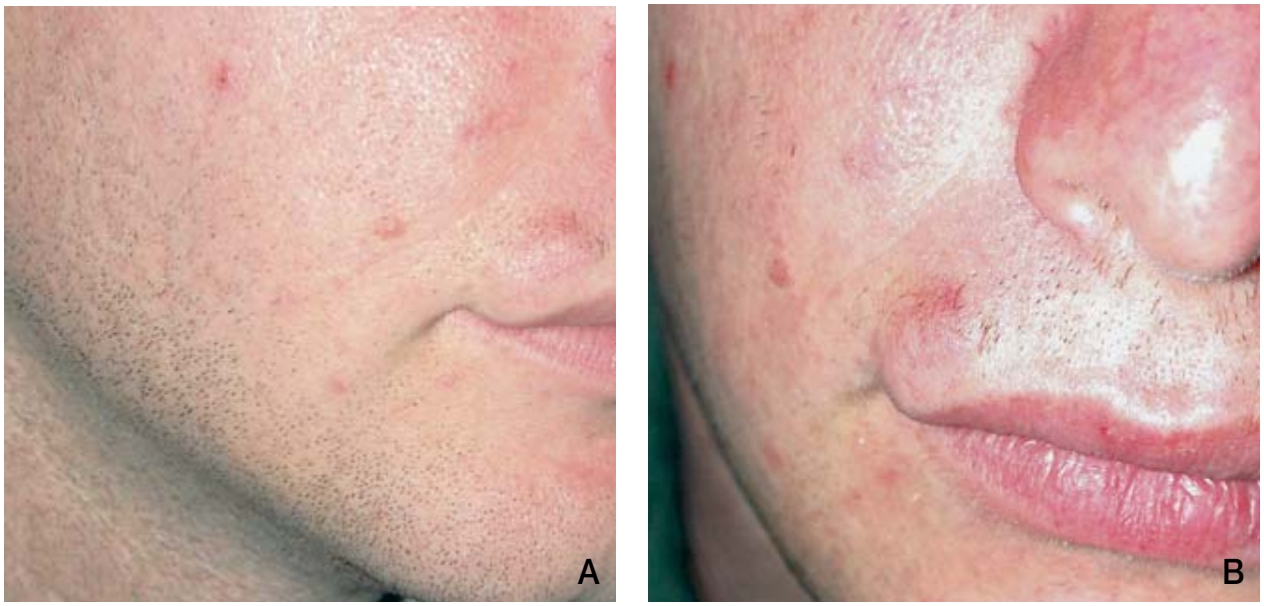

Figure 1. Side view (A) and close-up front view (B) of right upper-lip nodule.

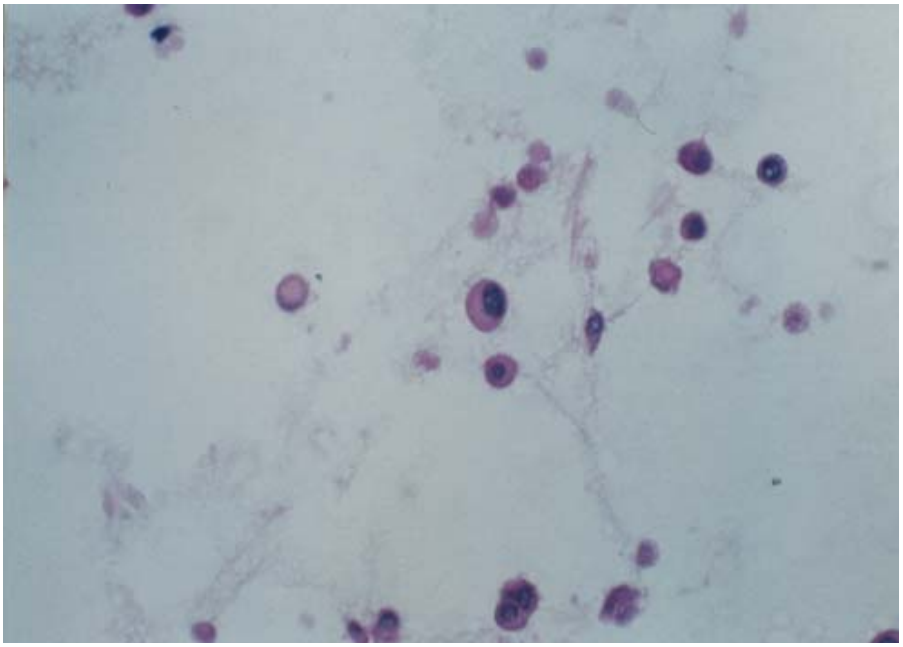

Figure 2. Stroma is myxoid in both lobules but is more so in the first lobule, with a predominance of plasmacytoid cells (H&E, original magnification ×400).

more condensed basophilic stroma forming lacunae-like structures similar to mature chondrocytes.

The second nodule had more of an epithelial component with less of a myxoid stroma (Figure 3). These ducts also were lined with 1 to 2 layers of cuboid cells with decapitation secretion, but the ducts were more extensive and had long interconnecting and branching patterns. Other areas were composed of solid epithelial nests without ducts. Some areas included focal collections of pale eosinophilic shadow cells consistent with matrical differentiation and scattered keratinous cysts. Several areas contained sebaceous glands, and a papillary mesenchymal body, indicative of pilosebaceous-apocrine differentiation, was found (Figures 4 and 5). Given the definitive apocrine-sebaceous-follicular differentiation, the diagnosis of a chondroid syringoma was favored over that of a salivary gland pleomorphic adenoma.

The patient was referred to the otorhinolaryngology department to discuss the option of conservative reexcision. The patient and the surgeons in that department felt that observing the area for recurrence would be best and that, if the tumor recurred,

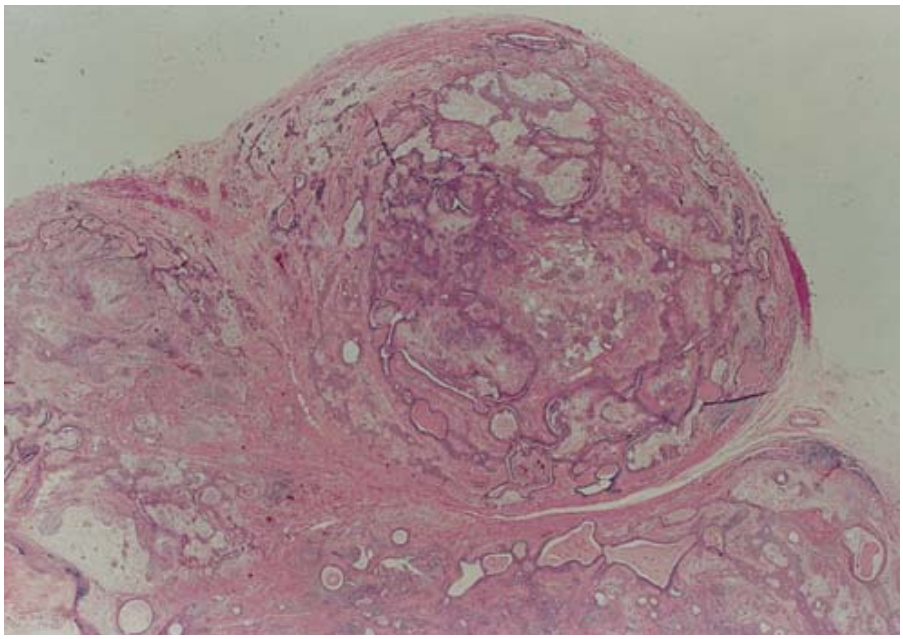

Figure 3. Overall lobular encapsulated architecture of the second, more epithelioid nodule, composed of ducts, eosinophilic collections of ghost cells, and keratinous cysts in a myxoid stroma (H&E, original magnification ×20).

the patient would undergo further surgery. Thirteen months after the original surgery, the patient has yet to experience a recurrence.

Comment

Although chondroid syringomas and pleomorphic adenomas share many clinical and histologic features, their unique cell types and preferential anatomic distributions can readily distinguish these tumors. Both tumors typically present in middle-aged men as painless, slowly growing small encapsulated subcutaneous nodules. The most common presumptive diagnoses include epidermoid cysts, mucoceles, adnexal tumors, or a granulomatous process.[5,6] It is usually not until after the tumor is excised and sent to pathology that the actual diagnosis can be ascertained. Neither the origin of the glandular component nor which cell is responsible for the production of the unique myxoid stroma is known. It is hypothesized that the cells may arise from an abnormal outgrowth of an ectodermal analage or cell rest that has maintained its pluripotent nature.[1,2,7] Results from ultrastructural studies have suggested that the plasmacytoid cell found in the stroma exhibit myoepithelial differentiation and therefore may represent the cell responsible for the production of the myxochondroid stroma.[6,9,10] Other authors have suggested that the myoepithelial cell plays only a minor role in the development of mixed tumors and that it is the filamentous cells, which are derived from the ectodermal analage, that produce the myxochondroid stroma.[7] In either case, because the head-and-neck region is developmentally derived from a series of brachial clefts and pharyngeal pouches, there are multiple opportunities during embryologic development for the entrapment of ectopic cell rests, which can ultimately, once stimulated, have the potential to express various patterns of differentiation.[8]

Pleomorphic adenomas are the most common tumors to arise in the salivary glands. They generally involve the major salivary glands, especially the parotid glands, but they also can arise in the minor salivary glands of the palate, the buccal mucosa, and (least commonly, in <4% of reported cases) the upper lip.[8,11-13] Chondroid syringomas, on the other hand, are thought to arise either from eccrine or apocrine glands. They also occur within the head-and-neck region but are more frequently found on the nose, cheek, upper lip, scalp, forehead, and chin.[1,4] Chondroid syringomas can exhibit 2 separate histopathologic patterns involving the glandular structures. Type I chondroid syringomas, the more common variant, have ducts with lumina that vary sizes, that are lined with 2 layers of epithelial cells, and that exhibit decapitation secretion characteristic of apocrine glands. Type II chondroid syringomas have ducts with lumina lined with a single flattened layer of cuboid cells, some of which have microvilli, and nonbranching ducts more typical of eccrine glands.[4,14]

Histologically, the 2 types of mixed tumors share many features having both mesenchymal and epithelial components.[1,15,16] However, chondroid syringomas can be distinguished from pleomorphic adenomas because the former more commonly

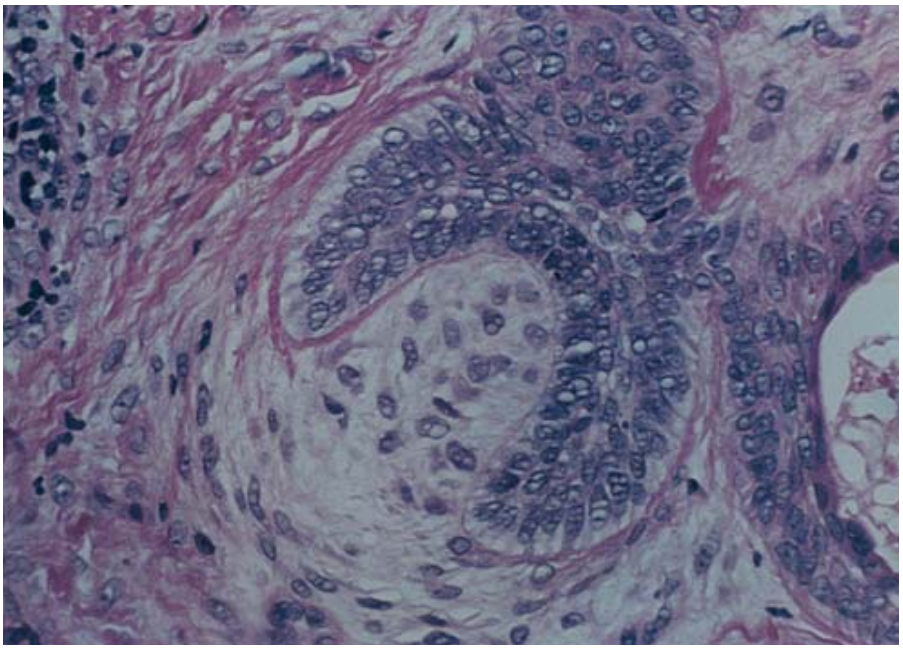

Figure 4. Papillary mesenchymal body (H&E, original magnification ×400).

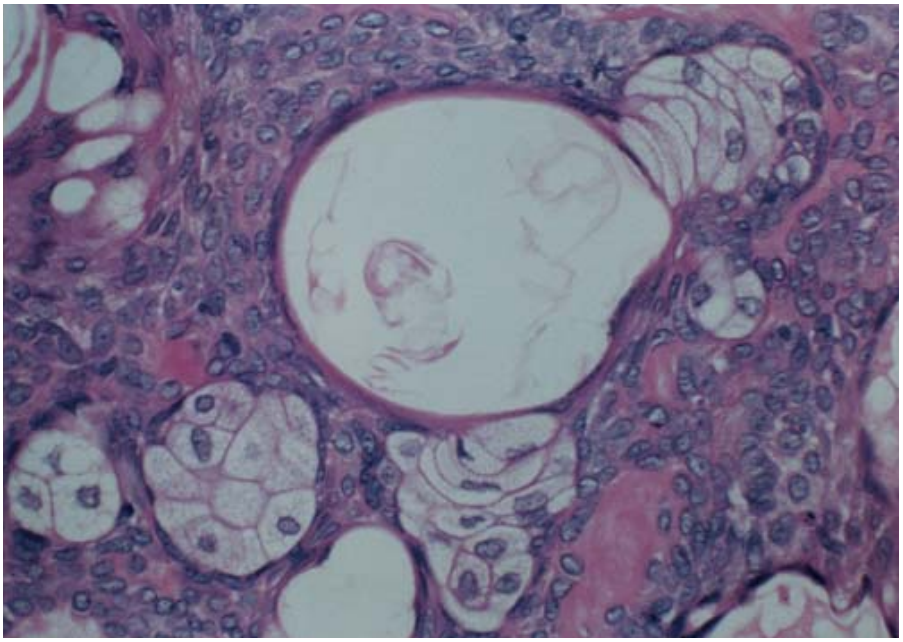

Figure 5. Keratinous cyst centrally surrounded by small clusters of sebaceous cells and solid islands of basaloid cells (H&E, original magnification ×400).

exhibit evidence of pilosebaceous-apocrine differentiation, whereas the latter have salivary gland differentiation. Each type of tumor can be identified as a within-dermis encapsulated proliferation composed of epithelial glands and ducts within a loose myxochondroid stroma. In chondroid syringomas, the tumor nests are composed of cuboid or polygonal cells with abundant eosinophilic-staining cytoplasm forming ducts and trabecular cords. The ducts have 1 or 2 rows of cuboid cells with an occasional taillike protuberance off the duct. The lumina of these ducts vary in size and can contain an eosinophilic secretory material. The stroma is abundant and faintly basophilic with a chondroid or myxoid appearance. As a result of processing, there is a retraction artifact in the myxoid substance, so that the fibroblasts and epithelial cells appear to be surrounded by a halo and therefore are said to resemble mature chondrocytes. Within the stroma are keratinous cysts of various sizes and a unique type of cell that has been referred to as a plasmacytoid cell because of the

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peripheral displacement of the nucleus and large amounts of eosinophilic cytoplasm. Last, chondroid syringomas, especially those occurring on the scalp, can exhibit islands of shadow cells—which is suggestive of pilar differentiation.[1,5]

The staining characteristics of chondroid syringomas and pleomorphic adenomas also are similar. Nests of cuboid cells and keratinous cysts are periodic acid-Schiff stain (PAS) positive before digestion with diastase—an indication of the presence of glycogen. The chondroid stroma also stains positively with PAS, but both with and without diastase digestion; it also stains positively with mucicarmine and Alcian blue at both low and high pH. Also, metachromasia is evident in the stroma stained with toluidine blue O at a pH of 2.5. This staining pattern is suggestive of a sulfated acid mucopolysaccharide similar to that found in normal cartilage.[1,5,8,16-18] Staining of the reticulum shows an abundance of reticular fibers throughout the tumor surrounding the nests and ductal structures.[1,18] Immunohistochemically, the inner cell layer of tubular structures expresses cytokeratin, carcinoembryonic antigen, and epithelial membrane antigen, whereas the outer cell layer expresses vimentin and S-100 protein. Type II collagen, which is found in cartilage, is expressed not only in the chondroid stroma but also within the epithelial portion of the tumor.[6,8,17]

Malignant forms of mixed tumors can arise, but these tumors are even rarer than chondroid syringomas. A lesion that enlarges rapidly—especially a lesion on a lower extremity of a younger patient—indicates possible malignancy. The histologic appearance of malignant mixed tumors also differs in that pleomorphism and necrosis are evident, and the mitotic rate is increased. There is still much debate as to whether malignant mixed tumors arise de novo or from their benign counterparts.[1,3,5-7,15,18]

In conclusion, chondroid syringomas are uncommon skin appendage neoplasms that are of presumptive primitive ectodermal origin and that have maintained their pluripotent ability. As chondroid syringomas have a nonspecific clinical presentation, they are rarely considered in the differential diagnosis, and, histologically, they can be mistaken for pleomorphic adenomas of the salivary glands. Therefore, in the diagnosis of a tumor in the head-and-neck region, consideration should be given both to sweat gland origin and salivary gland derivation. A high degree of keratinization and features of pilosebaceous-apocrine differentiation indicate that a chondroid syringoma is more likely than a pleomorphic adenoma. Both tumors, as a rule, are benign, and recurrence is typically a result of incomplete removal.

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