Ameloblastoma of the Maxillary Sinus 11 Years after Extirpation of Extensive Dentigerous Cysts and Dystopic Wisdom Tooth

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Abstract. We present the case of a 36-year-old patient with ameloblastoma of the maxillary sinus. The history of the patient was extraordinary with respect to the diagnosis of an extensive odontogenic cyst of this sinus with a maxillary wisdom tooth located far from the region of origin. Both cyst and tooth had been completely extirpated more than 10 years prior to the current tumor diagnosis. Diagnosis of ameloblastoma was based on routinely processed specimen and supported by immunohistochemical markers. Localization and extension of both cyst and neoplasm support the assumption that both entities arose from the same area. Long-term follow-up is recommended in the treatment of odontogenic cysts.

Ameloblastoma is a benign neoplasm of epithelial origin with invasive and destructive growth characteristics (1). The recurrence rate of ameloblastoma is high in cases of incomplete surgical resection (2). Whereas distant metastasis of ameloblastoma is a very rare phenomenon (3), the local tumor behaviour of this entity is that of a low-grade malignant tumor (1, 2). The tumor grows very slowly and physical findings resulting in seeking medical advice are discrete, such as a gradually increasing deformity of the jaws and/or face, loosening of teeth, or an unspecified intraoral swelling (4-6). The ratio of mandibular to maxillary ameloblastoma is about 5.8:1 (7). The radiological appearance varies substantially (2, 7-10). A subtyping of ameloblastoma was suggested based on morphological and radiological findings, emphasizing differences in tumor biology delineated from this classification (2, 7). The solid/multicystic subtype is by far the most common type of ameloblastoma. Typically, a multilocular destruction of bone is depicted on adequate radiographs. The tumor replaces the bone by small, radiographically well-defined areas often resulting in a honey comb-like translucency (2). This feature is supported by the insufficient regeneration of bone that might result in osseous expansion of the affected site (8). Association of ameloblastoma with dentigerous cysts is well-documented, in particular the development of ameloblastoma in a histologically proven cyst with the retained tooth inside the bone, and in keratocystic odontogenic tumor (12-14). The amount of tumor inside a dentigerous cyst might vary considerably. On the other hand the association of dentigerous cysts with ameloblastomas was called into question (15). Conventional histological diagnosis based on representative slices allows the clear distinction between dentigerous cyst and ameloblastoma (16). The follow-up examination of patients treated for odontogenic cysts might contribute to the differential diagnosis of odontogenic lesions. The aim of this report is to alert clinicians to the importance of follow-up for patients with dentigerous cysts of the jaws.

Case Report

Medical history and findings. A 36-year-old patient was referred for treatment of a radiopaque tumor of the left maxillary sinus depicted on both an orthopantomographic radiograph and Water’s view. General medical history of the patient was unsuspicious.

Physical investigation of the patient revealed a scar of the left upper vestibule. The patient mentioned that about eleven years earlier, at the age of 25 years, the left maxillary sinus had been surgically involved for extirpation of an extensive odontogenic cyst with a maxillary wisdom tooth lying in the sinus. The patient provided radiographs of the former treatment and a medical report. The report detailed the transantral access to a completely extirpated large dentigerous cyst of the maxillary sinus and a dystopic tooth, the upper left wisdom tooth. The radiographs at that time depict tooth 28 (FDI nomenclature) to be located at the upper medial side of the maxillary sinus, in close proximity to the orbital floor. On lateral and anterior radiographs of the maxillary sinus, this tooth appears to have had a malformed
root. On the panoramic radiograph, the tuber area of the maxilla is not as clearly demarcated as the opposite region. However, osteolysis of this area cannot be determined from this early radiograph (Figure 1 A).

Current diagnostics included a panoramic radiograph (Figure 1 B) and computed tomogram (CT) of the region of interest (Figure 1 C – E). On the panoramic radiograph the left tuber region of the maxilla was enlarged in size and showed irregular borders projecting into the maxillary sinus and to the retromaxillary region. The adjacent molars were in place but were incorporated into the lesion that was depicted by a somewhat oval shape. The CT scans and three-dimensional reconstruction of the bony surface revealed the osseous expansion of the distal parts of the left maxilla, with multiple defects of the cortex leading to a characteristic soap-bubble appearance. Inside the lesion, some areas mimicking a trabecular pattern were isointense to bone (Figure 1 D). The cyst-like lesion filled the sinus to about two-thirds of its volume. Tentative diagnosis was an odontogenic tumor.

Surgery. The left maxillary sinus was opened transantrally and a cyst-like tumor was located in the sinus filling the cavity to more than half of its volume (Figure 1 F). The tumor was extirpated with bone and teeth, and the antrum was closed with adjacent flaps by primary intention. Healing was uneventful. Despite the cyst-like appearance on images, the tumor proved to be macroscopically solid. Initially, the resection specimen was diagnosed as a keratocystic odontogenic tumor. However, careful inspection of the specimen disclosed an ameloblastoma of the solid and multicystic type (2). In order to verify clear surgical margins, the patient underwent surgery for a second time and the margins of the first defect were resected to a distance of 10 to 15 mm. Histology of the specimen revealed no tumor. Healing again was uneventful.

Histology. Tissues were fixed in buffered formalin immediately after the surgery and sent to the histopathologic laboratory. Five-μm thick sections were cut from the paraffin-embedded blocks and stained with hematoxylin-eosin. After deparaffinization, immunohistochemical stainings with calretinin (rabbit calretinin, No.18-0211; Zymed Laboratories, San Francisco, CA, USA) and p63 (mouse monoclonal, clone 4A4; Dako, Hamburg, Germany) were performed. The presence, distribution, and intensity of stained cells was determined using conventional light microscopy, giving a descriptive grading of weak, moderate, or intense staining. The nucleus and the cytoplasm of the stellate reticulum-like cells were moderately stained with calretinin antibody (17-19). The nuclei of virtually all cells (20, 21) were strongly positive for p63, but scattered superficial luminal cells were only minimally stained or the immunohistochemical reaction was completely absent from this layer (Figure 2).

Discussion

This report describes the diagnosis and treatment of a maxillary ameloblastoma. The history of the patient was extraordinary with respect to the diagnosis of an extensive odontogenic cyst of this sinus with a maxillary wisdom tooth located far from the region of origin. Both cyst and tooth had been completely extirpated more than 10 years prior to the current tumor diagnosis. The histological diagnosis of the first space-consuming entity of the maxillary sinus was a dentigerous cyst. The differential diagnosis of dentigerous cyst to ameloblastoma can be made positively on routinely processed slices by experienced pathologists (16). The translocation of the wisdom tooth to the orbital floor is probably the result of the cyst growth into the sinus, taking the path of least resistance.

The odontogenic tumor was quite large at the time of diagnosis. The localization of the region giving rise to the tumor with respect to the extension of the entity at the time of diagnosis has to take into consideration primarily the tuber region of the left maxilla. In due consideration of the radiological center of the lesion, it is reasonable to assume that the tumor originated in the area of the left upper third molar. It is likely that odontogenic epithelium in the tuber region gave rise to the ameloblastoma. The imaging of the tumor and the histogenesis of teeth make it likely that both space-occupying lesions come from the same area. Most ameloblastoma arise inside the bone (2). With respect to the visible expansion of the upper jaw and the remnants of bone inside the intracavitary parts of the lesion, the current case confirms this growth pattern.

The metachronous occurrence of both lesions in the same region might be coincidental. However, it is well recognized that ameloblastoma might arise as a result of neoplastic alterations in the epithelia of dentigerous cysts and transformation of the keratocystic odontogenic tumor (2). The neoplastic change inside a dentigerous cyst might be focal. These findings and the collected data are deduced from surgical interventions and do not necessarily represent the biological profile of ameloblastoma in general. It cannot entirely be ruled out that the initial translatory movement of the retained tooth to the maxillary sinus was caused by neoplastic tissue (eventually in a preliminary stage of tumor development). Indeed, the developmental stage of ameloblastoma at the time of diagnosis varies considerably. Ameloblastoma might be an incidental finding following cyst extirpation (even as a focal neoplastic part inside the cystic lumen), or an expansive tumor with bone resorption and bone extension. Moreover, the variation of ameloblastoma diagnosis related to chronological age, with a preference for the second decade of life, all show that the biological profiles of ameloblastomas do not fit into a single diagnostic system (2, 22). The range of chronological ages of patients with ameloblastoma diagnosis covers the period from early childhood to senility, i.e. the whole lifespan (1).
Therefore, it cannot be excluded that the tumor was already present at the time of cyst extirpation, e.g., in the tuber region of the maxilla. According to Gardner, the mean age of patients with solid/multicystic ameloblastoma is 39 years (23). Based on the evaluation of case reports alone, the mean age was 37.4 years and showed differences between gender (female: 35.2 years, male: 39.2 years) (2). The mean age of diagnosis for maxillary ameloblastoma was higher, at 47 years (2). The
patient was of relatively young age in our particular case of
diagnosis of maxillary ameloblastoma.

Calretinin is a calcium-binding protein abundantly expressed
in neuronal tissues. The biological function of calretinin is as
yet unknown, but it has possible roles as a regulator of
apoptosis, and a calcium buffer. Calretinin has been determined
as a sensitive marker to discriminate ameloblastoma from other
odontogenic tumors (18), including keratocystic odontogenic
tumor (KOT) (19). However, scant positivity of basal epithelia
was found in KOT in another study (24). In the present case,
the immunoreactivity of ameloblastoma was restricted to
stellate reticulum-like neoplastic epithelial cells and widely
expressed throughout the tumor (Figure 2).

P63 expression was found in a variety of ameloblastomas
(21). P63 was also detected in other odontogenic lesions that
share a locally aggressive phenotype (20). However, KOT also
expresses p63 (25). Topographical differences of p63
expression were noted compared to solid odontogenic
neoplasms, e.g. ameloblastoma, and cystic lesions (20), which
should be investigated in more detail.

Conclusion

Extirpation of odontogenic cysts and lesions is an everyday
task for dentists and oral/maxillofacial surgeons. The vast
majority of these lesions are benign and are definitively treated
using adequate surgical technique. This report demonstrates
that follow-up control of patients treated for cystic lesions of
the jaws is recommended and the need for thorough
investigation of the specimen is essential in adequate diagnosis
and therapy.

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