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RHINOLOGY

Pleomorphic adenoma in the nasal cavity: a clinicopathological study of ten cases in Finland

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Abstract The objective of the study was to investigate the nationwide occurrence of sinonasal pleomorphic adenoma in Finland. A retrospective study was conducted at The Departments of Otorhinolaryngology—Head and Neck Surgery, and Pathology at the five university hospitals in Finland. Data were obtained by searching for sinonasal pleomorphic adenoma cases in the clinical and histopathological registries at these institutions for the past two to four decades. All patients who had had a histologically proven pleomorphic adenoma in the sinonasal area were included as participants. Ten cases with pleomorphic adenoma of the nasal cavity were found. The majority of these tumours originated in the septum, and there were no malignant transformations. Pleomorphic adenomas of the nasal cavity were found to be extremely rare in this nationwide investigation.

Keywords Sinonasal · Nasal · Pleomorphic adenoma · Salivary gland

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Introduction

Salivary gland tumours are uncommon and constitute about 3 % of all neoplasms [1]. Minor salivary gland tumours account for 15–25 % of all salivary gland tumours [2, 3]. Seventy-five percent of pleomorphic adenomas locate in the parotid gland and 15 % in the submandibular gland. Only 10 % of pleomorphic adenomas arise from the minor salivary glands [4]. Few cases have been reported in the soft and hard palate, lacrimal gland, lip and external auditory canal [5]. Pleomorphic adenoma is extremely rare in the sinonasal area. Two larger series comprising 40 and 41 patients with a pleomorphic adenoma in nasal cavity have been reported in 1977 and 1990, respectively [6, 7]. Another case series included 39 sinonasal and skull base pleomorphic adenoma patients [8]. In this review the primary pleomorphic adenoma originated from parotid gland in three patients and all the others were located in the sinonasal area [8]. Additionally, most references found in the literature are case reports [5, 9–11].

Even though pleomorphic adenomas are rare in this location, they constitute an important differential diagnostic entity. Further, infrequent malignant transformations have been reported [7, 8, 12–14]. Toluie and Thompson [13] reviewed a series of nine of their patients with sinonasal tract adenoid cystic carcinoma ex pleomorphic adenoma (between 1970 and 2000) and six

patients from the literature (publications in English (MEDLINE 1966–2012) [13]. Most of their patients were treated with surgery ($n = 8$) accompanied by radiotherapy ($n = 5$) and one patient was treated with radiotherapy alone. In 55 % of these patients the tumour relapsed, and they all died of the disease with a mean overall survival of 8.4 years. One out of the six patients in their review, who were reported in the literature, had a recurrence and died of the disease [13]. In the report of Kuan et al. one of their own patients had a large carcinoma ex pleomorphic adenoma in maxillary sinus and this was managed surgically and with adjuvant radiotherapy. At 9 months he developed distant metastases and died of the disease at 1 year after surgery [8]. In addition to their own case, three other cases with a malignancy ex sinonasal pleomorphic adenoma were found in the literature. Myoepithelial carcinomas arising in recurrent pleomorphic adenomas in the maxillary sinus have also been described and this case report was included in the above-mentioned review by Kuan et al. [8, 14].

We undertook a survey of the hospital records in the five Finnish university hospitals, which represent the country's population of 5.5 million people, to investigate the nationwide occurrence of sinonasal pleomorphic adenoma.

Materials and methods

This retrospective study was conducted at the Departments of Otorhinolaryngology—Head and Neck Surgery, and Pathology at the five university hospitals in Finland. The pathology registries at these institutions were searched for the past two to four decades to collect clinical and histopathological data.

An institutional research approval was granted for the study.

Results

Ten patients were identified (eight females and two males, mean age 44 years, range 19–75). The follow-up time after surgery varied between 2 and 55 months (mean, 19).

Two out of the ten patients had had blunt nasal trauma 6 and 24 months prior to diagnosis of their tumours. The duration of presenting symptoms in the whole series varied from 1 month to 2 years. Nine patients had unilateral blockage and three also had external deformity of their nose at presentation (Fig. 1a–c). One patient with external nasal deformity had a tumour protruding from the nostril. In addition to nasal obstruction, one patient had epistaxis, another had sinusitis and one was a snorer.

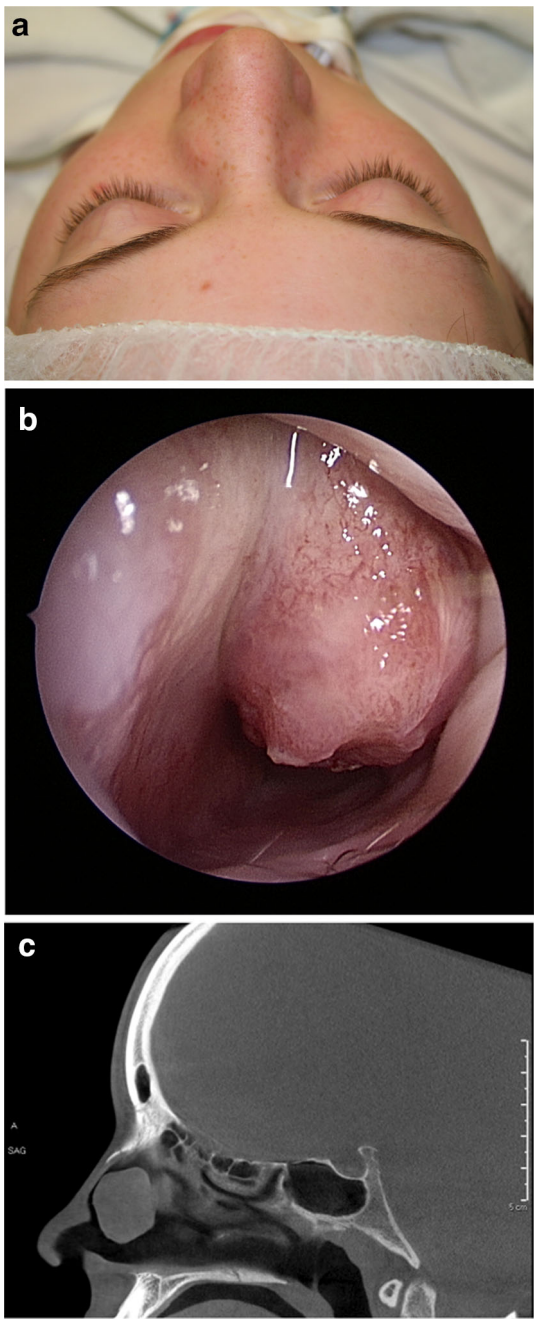

Fig. 1 A 19-year-old patient with nasal pleomorphic adenoma. **a** Nasal deformity, **b** endoscopic view, **c** cone beam computerized tomography image

The tumours originated from the nasal septum in six cases and from the anterior part of the inferior concha in three. One patient had his tumour in the antero-lateral vestibular area.

All tumours were surgically resected and there have been no recurrences or malignant transformations during the various follow-up periods.

Discussion

We report ten cases with pleomorphic adenoma of the nasal cavity. This tumour entity is so rare that it is impossible for single investigators to collect a sizable series from one hospital area or even from one country. However, reporting and centralizing information on rare diseases is one of the current priorities in the strategies for developing European health programmes. More importantly, a national series or a review of existing case reports will provide with useful information on the clinical pattern of these tumours. Our study represents a nationwide series for the past two to four decades of this rare disease in Finland, a country with a current population of 5.5 million people. Therefore, the present report also provides an epidemiological view of this disease entity. Our search may have missed single cases operated on at regional hospitals and consequently not registered in the university hospital data systems. However, this is rather unlikely due to the rareness of the tumour type and the existing pathology consultation system for the diagnostics of these cases.

Histologically pleomorphic adenomas show morphological multiplicity. They are encapsulated and contain myoepithelial and epithelial cells. In addition, mesenchymal or stromal elements are present. The presence and thickness of the capsules vary and the tumours have a tendency to bud into the capsule. The appearance of epithelial and myoepithelial cells is variable. The mesenchymal/stromal component can be myxoid, cartilaginous and hyalinised. Sometimes the stromal component dominates the main bulk of the tumour [15]. Carcinoma ex pleomorphic adenoma comprises 3.6 % of all salivary gland tumours and 12 % of malignant salivary gland tumours and finally, 6.2 % of pleomorphic adenomas actually prove to be carcinomas and most often arise in the parotid gland [15]. The invasive type of carcinoma ex pleomorphic adenoma behaves aggressively while the non-invasive or minimally invasive types behave like pleomorphic adenoma [15].

There are only two large series reporting on pleomorphic adenomas of the nasal cavity. Compagno and Wong in 1977 reviewed 40 cases of intranasal mixed tumours in the Armed Forces Institutes of Pathology [6]. The cases had been referred for consultation from civilian sources, military hospitals and Veterans Administration hospitals from 1949 to 1974. Twenty-three of these patients were females and 17 males and the median and mean age was 42 years for both sexes. Most of the tumours (62 %) originated from the septum and the follow-up data were obtained for 85 % of the cases. Recurrent or persistent pleomorphic adenoma occurred in three of the 34 patients. One patient refused to be treated and was followed up for 11 years. In this period, his tumour involved left maxillary sinus, both frontal sinuses, right orbit and skin over the nose and sinuses. None of the patients had a malignant transformation of their lesion. Another series reported from Japan included 41 patients with pleomorphic adenoma in the nasal cavity [7]. The median age was 45 years and the sex ratio showed female prominence (1:1.18). The tumours originated from the septum in 91 % of the cases. In that patient group both the recurrent and malignant transformation rates were 2.4 % [7]. The results of our patient series are similar to those two earlier reports. The majority of pleomorphic adenomas (60 %) originated from the septum, the mean age at diagnosis was 44 years and there was female predominance (80 %). Further, in a recent case series and a literature review of 32 case reports, 36 cases of pleomorphic adenoma were in sinonasal area. In this report the primary site was nasal septum in ten patients, lateral nasal wall in ten patents, maxillary sinus in seven patients, nasopharynx in seven patients and pterygopalatine fossa in one patient and nasal vestibule in one patient [8]. In this series the reported carcinoma ex pleomorphic adenoma patient was male and all the other three carcinoma patients in their literature review were females [8]. In the study by Toluie and Thompson [13] 80 % (12/15) of patients with malignant transformation were women and in the other two reports all the three patients were also women [12–14]. It seems that a clear gender difference exists among the reported patients with a carcinoma arising from pleomorphic adenoma.

There was no recurrence or malignant transformation of pleomorphic adenomas in our study, but regretfully the follow-up time for six cases was less than 1 year. It is noteworthy that, according to literature, metastasis to a submandibular lymph node, in a patient with recurrent nasoseptal pleomorphic adenoma, has occurred even 17 years after the primary diagnosis [16].

Many theories have been proposed for the origin of intranasal pleomorphic adenomas. They usually arise in the nasal septal mucosa even though the seromucosal glands are mainly located in the lateral nasal wall and particularly in the turbinates [17, 18]. According to Stevenson [19], pleomorphic adenoma can originate from remnants of the vomeronasal organ, an epithelium-lined duct in the septum that regenerates in early foetal life [19]. Matthew et al. have proposed that the aberrant origin of pleomorphic adenomas from the mucous membrane of the septum probably results from misplaced embryonic epithelial cells, derived from the ectoderm and carried via the nasal pits into the septal region [20]. Twenty-four cases of congenital pleomorphic adenomas, mainly referred as congenital salivary

gland anlage tumours have been identified [21]. This tumour involves nasopharynx and a narrow pedicle may be attached to the nasopharyngeal mucosa or to the mucosa of the posterior nasal septum. Obstruction of the nasal airway is a life-threatening condition [21]. However, pleomorphic adenomas are almost universally accepted to be of epithelial origin and to arise from fully developed salivary gland tissue [22].

The pathogenesis of pleomorphic adenoma in the sinonasal area is unknown but viral involvement has been discussed. Epstein–Barr virus (EBV) association with nasopharyngeal carcinoma or Burkitt lymphoma is a well-known factor [23–25]. Malinvaud et al. reported three cases of pleomorphic adenomas of the nasal septum and they all had positive rates of EBV-related blood antibodies and one patient also had positive EBV-DNA in the tumour [9]. In another study, tumour-related viruses such as human papillomavirus (HPV), EBV, human herpes virus 8 (HHV-8) and human cytomegalovirus (CMV) involvement were found by means of polymerase chain reaction (PCR) analysis both in malignant salivary gland tumours and in pleomorphic adenomas [26]. In that study there was one pleomorphic adenoma of the nasal cavity with positive PCR detection for EBV. Two of the ten patients in the present series had had blunt trauma to their noses and had then later developed the presenting symptoms of a nasal pleomorphic adenoma. The importance of these single occasions in terms of a possible etiological factor remains speculative.

Conclusion

Pleomorphic adenomas of the nasal cavity were found to be extremely rare in this nationwide investigation. We emphasize the differential diagnostic importance of this intranasal lesion due to its neoplastic nature, which has to be considered in individual treatment planning. In the present series with a female predominance and a mean age of 44 years at diagnosis, the majority of these tumours originated from the septum, and there were no cases with malignant transformation.

Compliance with ethical standards

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Conflict of interest None.

Ethical approval This article does not contain any studies with human participants performed by any of the authors. No informed consent from the patients or approval by the Research Ethics Board is needed for a retrospective chart review.

References

1. Jassar P, Stafford N, Macdonald A (1999) Pleomorphic adenoma of the nasal septum. J Laryngol Otol 113(5):483–485
2. Auclair PL, Ellis GL, Gnepp DR et al (1991) Salivary gland neoplasms: general considerations. In: Ellis GL, Auclair PL, Gnepp DR (eds) Surgical pathology of salivary glands. WB Saunders Co, Philadelphia, pp 135–164
3. Eveson JW, Cawson RA (1985) Tumours of the minor (oropharyngeal) salivary glands: a demographic study of 336 cases. J Oral Pathol 14:500–509
4. Manucha V, Ioffe OB (2008) Metastasizing pleomorphic adenoma of the salivary gland. Arch Pathol Lab Med 132(9):1445–1447
5. Sciandra D, Dispenza F, Porcasi R et al (2008) Pleomorphic adenoma of the lateral nasal wall: case report. Acta Otorhinolaryngol Ital 28:150–153
6. Compagno J, Wong RT (1977) Intranasal mixed tumors (pleomorphic adenomas): a clinicopathologic study of 40 cases. Am J Clin Pathol 68(2):213–218
7. Suzuki K, Moribe K, Baba S (1990) A rare case of pleomorphic adenoma of lateral wall of nasal cavity with special reference of statistical observation of pleomorphic adenoma of nasal cavity in Japan. Nippon Jibiinka Gakkai Kaiho 93(5):740–745
8. Kuan EC, Diaz MF, Chiu AG, Bergsneider M, Wang MB, Suh JD (2015) Sinonasal and skull base pleomorphic adenoma: a case series and literature review. Int Forum Allergy Rhinol 5(5):460–468
9. Malinvaud D, Couloigner V, Badoul C et al (2006) Pleomorphic adenoma of the nasal septum and its relationship with Epstein. Barr virus. Auris Nasus Larynx 33:417–421
10. Ceylan A, Celenk F, Poyraz A et al (2008) Pleomorphic adenoma of the nasal columella. Pathol Res Pract 204:273–276
11. Baron S, Koka V, El Chater P et al (2014) Pleomorphic adenoma of the nasal septum. Eur Ann Otorhinolaryngol Head Neck Dis 131:139–141
12. Cimini-Mathews A, Lin BM, Chang SS et al (2011) Carcinoma ex-pleomorphic adenoma of the nasal cavity. Head Neck Pathol 5:405–409
13. Toluie S, Thompson LD (2012) Sinonasal tract adenoid cystic carcinoma ex-pleomorphic adenoma: a clinicopathologic and immunophenotypic study of 9 cases combined with a comprehensive review of the literature. Head Neck Pathol 6(4):409–421
14. Gupta A, Manipadam MT, Michael R (2013) Myoepithelial carcinoma arising in recurrent pleomorphic adenoma in maxillary sinus. J Oral Maxillofac Pathol 17(3):427–430
15. Evasion JW, Kusufuka H, Stenman G, Nagao T (2005) Pleomorphic adenoma. In: Barnes L, Eveson JM, Reichard P, Sidransky D (eds) Pathology and genetics, head and neck tumours, World Health Organization classification of tumours. IARC Press, Lyon, pp 254–258
16. Freeman SB, Kennedy KS, Parker GS et al (1990) Metastasing pleomorphic adenoma of the nasal septum. Arch Otolaryngol Head Neck Surg 116:1331–1333
17. Castello E, Caligo G, Pallestrini EA (1996) Case report: pleomorphic adenoma of the lateral nasal wall. Acta Otorhinolaryngol Ital 16:433–437
18. Carriero E, Almandori G, Cadoni G (1997) Pleomorphic adenoma of the lower turbinates: clinical case and review of literature. Acta Otorhinolaryngol Ital 17:377–381
19. Stevenson HN (1932) Mixed tumor of the septum. Ann Otol Rhinol Laryngol 41:563–570
20. Matthew S, Ersner MD, Saltzman M (1944) A mixed tumor of the nasal septum.Report of a case. Laryngoscope 54:287–296
21. Tinsa F, Boussetta K, Bousnina S et al (2010) Congenital salivary gland anlage tumor of the nasopharynx. Fetal Pediatr Pathol 9(5):323–329

22. Evans RW, Cruickshank AH (1970) Epithelial tumors of the salivary glands. In: Major problems in pathology, vol 1. W B Saunders, Philadelphia, pp 281–295
23. Giannoudis A, Ergazaki M, Segas J et al (1995) Detection of Epstein Barr virus and human papillomavirus in nasopharyngeal carcinoma by polymerase chain reaction technique. Cancer Lett 89:177–181
24. Pathamanathan R, Prasad U, Sadler R et al (1995) Clonal proliferatins of cells infected with Epstein-Barr virus in preinvasive lesions related to nasopharyngeal carcinoma. N Engl J Med 333:693–698
25. Ampinder RF, Mann RB (1994) Detection and characterization of Epstein-Barr virus in clinical specimens. Am J Pathol 145:239–252
26. Atula T, Grénman R, Klemi P et al (1998) Human papillomavirus, Epstein-Barr virus, human herpesvirus 8 and human cytomegalovirus involvement in salivary gland tumours. Oral Oncol 34:391–395