

Adenomatoid hamartomas of the olfactory clefts

Thomas Georgel¹, MD - Roger Jankowski¹, MD - Jean-Michel Vignaud², MD - Olivier Dugny¹, MD
Nicolas Weinbreck², MD - Béatrice Marie², MD

¹ ENT and cervico-faciale surgery department - Central Hospital CHU - Nancy

² Department of anatomopathology - Central Hospital CHU - Nancy

ABSTRACT

Objective: To describe the clinical, imaging, and pathological characteristics of nasal respiratory epithelial adenomatoid hamartoma (REAH).

Material and Methods: Retrospective study of 10 operated cases observed between 1998 and 2005.

Results: The clinico-radiological picture was typical and permitted a diagnosis to be made before surgery. The clinical presentation mimicked naso-sinus polyposis (NSP), but endoscopic examination showed pinkish polyps with a cerebriform appearance and a pedicle coming from the olfactory cleft on each side. The scan showed characteristic enlargement of the olfactory clefts, although associated ethmoidal opacity could mimic imaging in NSP. Nine patients were operated upon, where in the implantation of a pedicle in the olfactory cleft was confirmed; four patients had associated NSP; in other cases the ethmoidal with opacity corresponded to retained secretion. Pathological examination revealed characteristic features described by Wenig and Heffner in 1995.

Conclusion: Hamartoma should be included in differential diagnosis of NSP; its clinical and imaging characteristics permit pre-operative diagnosis and its removal necessitates a dissection of olfactory clefts and cribriform plates, but not ethmoidectomy.

(Fr ORL - 2007 ; 92 : 274 - 281)

(Presented on October 8-11, 2005 at NOSE congress 2005, Porto (Portugal), and June 10-14, 2006 at the Congress of European Rhinologic Society, Tampere (Finland).)

Key words: Hamartoma, Olfaction, Polyposis, Sinus, Scan.

Submitted for publication: March 2006

Accepted for publication: October 2006

Corresponding author: Roger Jankowski

Service O.R.L. et Chirurgie Cervico-Faciale

C.H.U. – Hôpital Central

29 avenue du Mal de Lattre de TASSIGNY

54035 NANCY CEDEX

e-mail: r.jankowski@chu-nancy.fr

INTRODUCTION

Respiratory adenomatoid epithelial hamartoma (REAH) of the nasal fossae and sinuses is a pathological entity [1], which appears relatively rare. In fact, only about 50 cases have been described in the literature [1-11]. It is a benign tumor, not well recognized by clinicians, radiologists or pathologists; it appears relatively frequently when one knows how to recognize it. The first case came to our attention in 1998. We later realized that this tumor had imaging and endoscopic characteristics that could make it easily identifiable pre and post-operatively. Clinically, it represents the principal differential diagnosis of NSP. However, while there are no data about tumor implantation in the nose or sinuses [1, 5-8, 11], our surgical experience has shown that it has its pedicle consistently in the olfactory clefts. It presents as an enlargement of olfactory cleft on the cross-sectional scans, which allows to strongly suspect the diagnosis pre-operatively. Its implantation in the olfactory cleft modifies the surgical approach: REAH surgery is not intended for lateral ethmoid masses but necessitates a fine, careful dissection of the olfactory cleft and the cribriform plate.

The aim of this study is primarily to describe clinical, imaging and pathological characteristics of our 10 cases, for a better recognition of this new clinical entity that represents a differential diagnosis of NSP and, finally, to underline that the removal of this tumor requires the dissection of the olfactory cleft and not ethmoid.

MATERIALS AND METHODS

Our work is based on 10 hamartomas confirmed by pathological examination of nasal polyps operated between 1998 and 2005. A retrospective analysis of the 10 files was performed, with a review of the medical history (particularly polyposis, asthma, Fernand Widal syndrome and drug history), symptoms, endoscopy, imaging data, diagnoses, therapeutic care, surgical observations and the type of surgery performed, pathological data, and post-operative evolution.

RESULTS

Our series included 6 female and 4 male patients from 52 to 93 years of age (mean age: 71,9 years).

Our first case was an a pathological finding in a patient operated in 1998 for a lesion that appeared to be tumoral a priori, which carried a clinical diagnosis of an inverted papilloma or esthesioneuroma. Five other cases were found in sporadic manner between 1998 and 2004. Three cases were suspected pre-operatively and confirmed histologically over the course of the final three months.

All of these patients presented with chronic nasal symptomatology that developed over 2 to 20 years. This was eventually associated with major nasal obstruction and resistance to different medical therapies (vasoconstrictors, local and systematic corticoids) in 10 cases, anosmia in 7 cases, rhinorrhea in 4 cases, and facial pain in 2 cases. In two patients symptomatology corresponded to a Fernand Widal syndrome.

At the clinical examination, rhinoscopy showed bilateral nasal polyposis stage III-IV in 8 cases, and stage II in 2 cases. Diagnosis of hamartoma was made immediately in three cases with the presence of cerebriform and metaplastic pink polyps, that originated from the olfactory clefts (deep inside of middle concha) and not from the middle meatus of the ethmoid. In one case a malignant lesion was diagnosed because of a clear unilaterality (there were, in fact, bilateral lesions but they were markedly asymmetric) and because of its hard and fibrous appearance.

A CT-scan was performed in all cases. Retrospective analyses of images (Figure 1a, 1b, 1c) found enlarged and opaque olfactory clefts in nine cases (in one case, the images were not found). Complete bilateral opacification of the ethmoid was present in five cases (Figure 1a) and partial opacification in two cases (Figure 1b). The opacities were of different degrees, difficult to globally describe, and inconstantly involved other sinuses. In two cases the lateral parts of the ethmoid and other sinuses were normally ventilated (Figure 1c). The hamartomas in our series were bilateral and originated from enlarged olfactory clefts by depressing turbinal wall of the ethmoid exteriorly.

Biopsy samples were performed during the patients' visits in 5 cases: in 3 cases because of unusual macroscopic aspect and in 2 cases because of enlargement of the olfactory groove.

In 4 cases the pathological report reported an inflammatory benign polyp. In the only case where the pathologist was informed by a clinician, the diagnosis was made with the pathological sample.

Nasal adenomatoid hamartoma

Figure 1: CT-scan appearance of respiratory epithelial adenomatoid hamartoma (REAH) of the olfactory clefts (from left to right: coronal cut passing through the nasal bone; coronal cut passing through the anterior ethmoid; axial cut passing through the superior meatus).



1a: Scan appearance of bilateral pan-sinusitis (endoscopic aspect suggested stage 2 polyposis); enlargement of the olfactory clefts characteristic in REAH with compression of the lateral part of the ethmoid against the orbital wall.



1b: Enlargement of the olfactory clefts characteristic of REAH, associated with partial ethmoidal opacity.



1c: Enlargement of the olfactory clefts characteristic of REAH; absence of ethmoidal opacity highlights the insertion of REAH at the olfactory clefts.

On a therapeutic level, nine patients received medical treatment either temporarily or since the onset of their symptoms, primarily with local corticoids and/or antibiotic-corticoid therapy. These treatments were judged as being poorly effective for nasal obstruction and for hyposmia. One patient did not receive medical treatment because of the clear clinical impression of a malignant lesion.

Five patients underwent endonasal surgery with temporary (several months) or long-lasting (several years)

improvement in nasal obstruction, but without any influence on olfactory disturbance.

For 9 patients we initiated intervention under general anesthesia due to disabling symptomatology and resistance to medical treatment.

One patient could not be operated upon because of his general condition, and the diagnosis was confirmed by biopsy.

In 9 cases, the intervention permitted removal of the tumor with its pedicle inserted under the canopy of nasal

Figure 2: Scan appearance of olfactory clefts in nasosinus polyposis (for comparison).



bone, extending to the posterior part of the olfactory clefts, depressing the turbinal wall of the ethmoid, to which it was often adherent. The extension along the olfactory clefts was to the anterior half or 2/3, apart from one case where it reached the anterior part of the sphenoid.

Tumor removal was performed most often in monoc because of the polyp's fibrous nature. Tumor ablation necessitated a more or less wide opening of the olfactory clefts unilaterally depending on pedicle extension. No CSF leak was noted pre-operatively. None of our patients had CSF rhinorrhea or meningitis during hospitalization.

In 4 cases a nasalisation procedure was performed because of the presence of polyps in the lateral part of the ethmoid (two patients presented with Fernald Widal syndrome). Pathological analyses of ethmoid polyps showed characteristic features of naso-sinus polyposis with eosinophilic infiltration. In one case anterior ethmoidectomy revealed retention of secretions. In 4 cases anatomic integrity of ethmoidal labyrinth was preserved, endoscopic exploration discovered only retained secretions, which were aspirated.

Pathological examination found characteristic features of a hamartoma in all cases. The first case was difficult to interpret pathologically; this lesion was not recognized earlier by our team. This case diagnostic required the assistance of an external team (Dr. Wassef, Laboratoire Jean Roujeau, Service d'anatomopathologie Hôpital Lariboisière, Paris).

Surgical treatment allowed the removal of nasal obstruction in all patients. This nasal obstruction was the principal purpose for visiting our clinic and an indication for surgical intervention in 9 operated patients. Two patients reported olfactory recovery.

No recurrence was observed after radical removal over a follow-up period of 8 months to 7 years (mean 2.5 years).

DISCUSSION

Respiratory adenomatoid epithelial hamartoma is a seemingly rare benign tumor. Only about 50 cases have been described in the literature [1-3]. Our experience spurred us to think that this tumor could be more frequent and possibly underdiagnosed because of its clinical presentation, mimicking the clinical picture of NSP, and due to unawareness of the pathological diagnosis. Hamartomas usually affect the elderly [8] (mean age 71.9 years in our series), however, a case of congenital hamartoma has been described [12].

Symptomatology showed different degrees of nasal obstruction, hyposmia, cacosmia, ageusia, anterior and posterior rhinorrhea [4, 11, 13]. These signs are not specific and do not allow the diagnosis to be made. In our series nasal obstruction with severe alteration of sleep or nutrition, and a minor degree of anosmia dominated naso-sinus dysfunction. Clinical examination revealed highly developed bilateral, often asymmetric polyposis of stage III-IV, with polyps that could be seen on the surface of the threshold of the nares. Indeed, examination showed these polyps to have a pink colour and cerebriform surface, in contrast with smooth and translucent appearance of common polyps, which helps to suggest the diagnosis. Attentive endoscopic examination occasionally permits tracing of the pedicle, which proceeds from the olfactory clefts and not from middle and superior meatus.

CT-scan is indispensable for investigating the diagnostic suspicion (Figure 1). In absence of corticoid treatment, the CT-scan can show images compatible with NSP, i.e. more or less extensive opacification of the sinuses. After medical treatment with antibiotics and corticoids, the CT scan can show disappearance of sinus opacity, in particular showing well ventilated ethmoid labyrinths (one case in our series – Figure 1c) [14]. Only opacity of the olfactory clefts remain, which

Nasal adenomatoid hamartoma

appear enlarged due to suppression of laminae of the conchae [15] to the exterior (in contrast to the situation with NSP (Figure 1d) where the concha can be compressed against the septum from outside or within). On an axial cut (Figure 1) : enlargement of olfactory clefts is generally evident, especially at their anterior half, where the middle concha appears dislocated outwards onto the anterior ethmoid cells, which are crushed by the orbital wall. Occasionally the nasal bones appear outspread under the pressure of this opacity, giving a distended appearance to the nasal base comparable with that observed in Woakes syndrome [16-18].

The hamartoma presents a bell or pear shaped appearance under the roof of the olfactory groove on coronal cuts (Figure 1c). Attentive examination of cribriform plate does not show osteolysis, which permits expansion of cerebrospinal origin (for example meningocele) to be eliminated. MRI could be performed in doubtful cases. We did not use MRI for the patients in our series, but it remains interesting to fully define the MRI features of this lesion, which will be the subject of a future study. While the diagnosis may be indicated clinically and radiologically, biopsies can confirm the diagnosis (including extemporaneous examination). It is suggested to inform the pathologist in order to decrease the risk of false negatives.

It is suggested to inform the pathologist in order to decrease the risk of false negatives. Medical treatment with antibiotics and corticoids can attenuate the symptomatology but it appears less effective than in the case of common polyposis, notably the effect on nasal obstruction and olfactory problems. On the other hand, medical therapy allows associated NSP to be treated, and may reveal the hamartoma by reducing ethmoid opacity. Surgical treatment like polypectomy offer relief of nasal obstruction but there is a risk of possible recurrence. When general anaesthesia is possible and the patient has invalidating symptomatology, the treatment of choice is surgical and complete removal of the hamartoma is recommended [1, 4-6, 8-9, 11]. Some teams select surgery via the paralateral approach due to the differential diagnosis of adenocarcinoma and inverted papilloma [6].

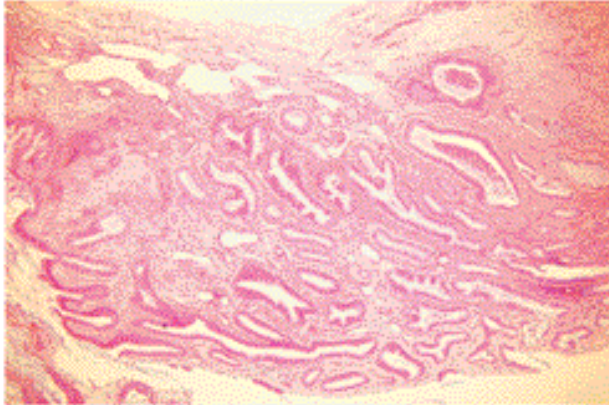
In fact the majority of these tumors were operated by endonasal approach. We were surprised not to find the description of the tumor pedicle implantation in the literature, although it was characteristically at the level of the olfactory clefts. It could be improbable that we found this implantation of the 10 cases at the olfactory

clefts as the result of random. In addition, this implantation was authenticated mainly pre-operatively on CT-scan, which allows us now to suggest an early diagnosis rather than after surgical removal as in previous series.

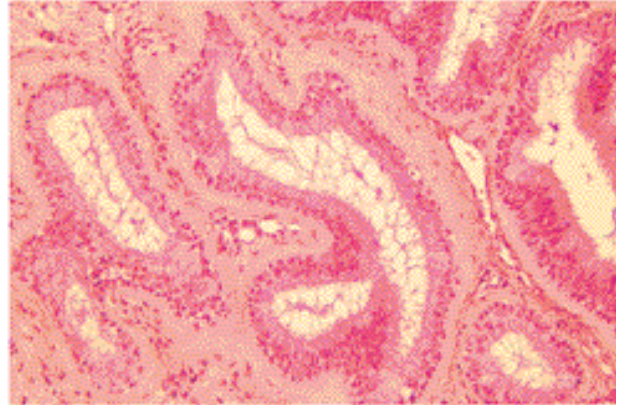
Complete removal of implantation of pedicle of this tumor opens a new era of endoscopic endonasal surgery, concerning surgery of the olfactory cleft. In our experience it was possible to cut several fibers of the olfactory nerve without observing CSF leak pre- or post-operatively, and without meningitis during a 2.5 year interval (2 months-7 years). When the hamartoma is isolated, there is no advantage to evacuate the ethmoid. When the hamartoma is associated with authentic NSP (2 cases with Freund and Widal syndrome and 2 other cases with NSP in our series), surgical intervention must be two-fold: ethmoidal scraping plus removal of the hamartoma at the olfactory cleft level on both sides. Our experience has shown that ethmoidal opacity can be the consequence of simple secretion retention related to the hamartoma volume, which disturbs the drainage and the ventilation of ethmoidal cells that are compressed against the orbital wall. In the absence of a pre-operative diagnosis of a voluminous hamartoma, ethmoidal opacity due to retention, the challenging surgical access and the particular difficulty in recognizing the middle concha allow us to understand why these tumors have, until now, been confused with polyposis and have been operated by ethmoidectomy [1, 4-6, 8-9, 11]. Different sites of hamartomas in the naso-sinus area have been described in the literature, but only after close reading is it evident that they are often found near the olfactory clefts (middle meatus, nasal bone, frontal sinus, ethmoid sinus, superior concha or posterior part of septum) [1,8]. Perhaps in these observations implantation of the pedicle was also at the olfactory cleft level as in our series of patients. However, insertions at the inferior concha level [6] and maxillary sinus [7] have been reported.

From a histological perspective, it is a benign tumor. Malignant transformation has never been reported. REAH has a relatively typical but unfamiliar pathological appearance. These lesions consist of exclusively or almost exclusively medium sized pseudo-glands, resulting from an invagination of the surface respiratory epithelium (Figure 3a). Pseudo-glands are made of pseudo-stratified ciliary epithelium, sheltering mucosecreted cells (Figure 3c), isolated by thick basal membrane (Figure 3b). The chorion can consist of an inflam-

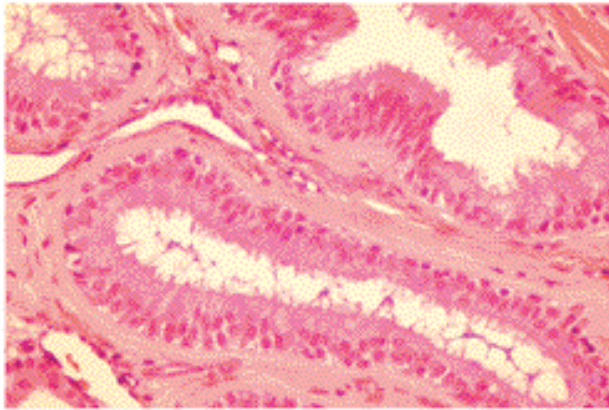
Figure 3: Histo-pathological aspect of REAH



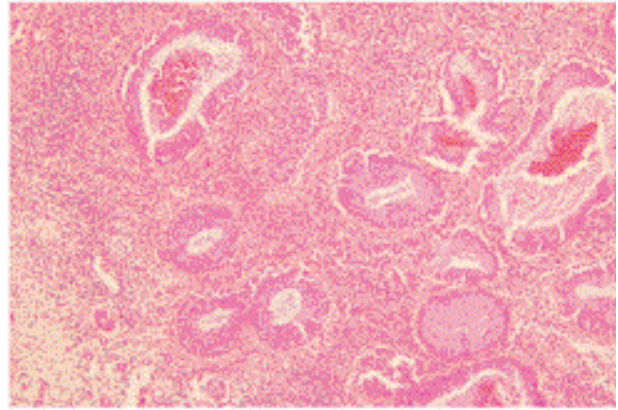
3a: Lesion consisting of invaginations of respiratory epithelial surface in pseudo-glands in the chorion (HES x 20),



3b: Pseudo-glands are surrounded by thickened basal membrane (HES x 40),



3c: Pseudo-stratified cylindrical ciliary respiratory epithelium (HES x 100).



3d: A focus of REAH-like epithelial differentiation also in typical nasosinusal polyposis.

matory infiltrate normally poor in abundance, and comprised of mononuclear cells with rare eosinophils. These data oppose NSP where glands within the chorion are less numerous, are surrounded by a membrane of normal thickness and are without an evident connection to the surface epithelium. While in both cases the chorion can be edematous and somewhat fibrous, the proportion of polynuclear eosinophils within the inflammatory infiltrate is much higher than in NSP.

Making a diagnosis may be difficult for the pathologist that is unfamiliar with this entity. If it is not taken as an inverted papilloma or an adenocarcinoma, it is often classified as NSP by default. Conversely, a diagnosis of REAH must not be raised mistakenly in the setting of NSP consisting of epithelial differentiation focuses

of REAH type. In fact, it is not exceptional to observe invaginations of REAH-like epithelial coating in pseudo-glands in the context of typical NSP (Figure 3d). This architectural differentiation is organized in one or several small foci dispersed in a typical NSP surrounding. At the pseudo-gland level, the basal membrane is not greatly thickened and the neighbouring chorion typically contains an inflammatory cell population marked by numerous eosinophils.

The etiopathogenesis of respiratory adenomatoid hamartoma remains unknown. Delbrouck [9] emphasized their possible association with NSP and suggested the possibility of a secondary lesion induced by inflammation. Our present series is too small to take any stance or to propose other mechanisms.

CONCLUSION

Respiratory epithelial adenomatoid hamartoma of olfactory clefts could be a more frequent lesion than previously thought. It is often isolated and often associated with genuine polyposis. The interesting point in our series is the discovery of the location of its pedicle at the level of the olfactory clefts in 10 cases out of 10. This entity is not well recognized by clinicians, radiologists or pathologists. Greater recognition of this pathology will permit improved treatment.

REFERENCES

1. Wenig BM, Heffner DK. Respiratory epithelial adenomatoid hamartomas of the sinonasal tract and nasopharynx: a clinicopathologic study of 31 cases. *Ann Otol Rhinol Laryngol.* 1995; 104: 639-645.
2. Hager A. [Hamartoma of the nasopharynx.]. *Monatsschr Ohrenheilkd Laryngorhinol.* 1951; 85: 49-51.
3. Majumder NK, Venkataramaniah NK, Gupta KR, Gopalakrishnan S. Hamartoma of nasopharynx. *J Laryngol Otol.* 1977; 91: 723-727.
4. Schneider M, de la Fuente L, Palop JM, Vera F. [Hamartoma of the nasopharynx. Apropos of a case]. *An Otorrinolaringol Ibero Am.* 1987; 14: 447-452.
5. Graeme-Cook F, Pilch BZ. Hamartomas of the nose and nasopharynx. *Head Neck* 1992; 14: 321-327.
6. Endo R, Matsuda H, Takahashi M, Hara M, Inaba H, Tsukuda M. Respiratory epithelial adenomatoid hamartoma in the nasal cavity. *Acta Otolaryngol.* 2002; 122: 398-400.
7. Himi Y, Yoshizaki T, Sato K, Furukawa M. Respiratory epithelial adenomatoid hamartoma of the maxillary sinus. *J Laryngol Otol.* 2002; 116: 317-318.
8. Braun H, Beham A, Stammberger H. [Respiratory epitheloid adenomatoid hamartoma of the nasal cavity--case report and review of the literature]. *Laryngorhinootologie* 2003; 82: 416-420.
9. Delbrouck C, Fernandez Aguilar S, Choufani G, Hassid S. Respiratory epithelial adenomatoid hamartoma associated with nasal polyposis. *Am J Otolaryngol.* 2004; 25: 282-284.
10. Kessler HP, Unterman B. Respiratory epithelial adenomatoid hamartoma of the maxillary sinus presenting as a periapical radiolucency: a case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2004; 97: 607-612.
11. Malinvaud D, Halimi P, Cote JF, Vilde F, Bonfils P. [Adenomatoïd hamartoma of the ethmoid sinus: one case report]. *Rev Laryngol Otol Rhinol. (Bord)* 2004; 125: 45-48.
12. Ladapo AA. A case of benign congenital hamartoma of the nasopharynx. *J Laryngol Otol.* 1978; 92: 1141-1145.
13. Owens D, Alderson D, Garrido C. Nasopharyngeal hamartoma: importance of routine complete nasal examination. *J Laryngol Otol.* 2004; 118: 558-560.
14. Arrarte JL, Franche G, Barra MB, Saffer M. Radiology forum: imaging quiz case 3. Hamartoma of the nasopharynx. *Arch Otolaryngol Head Neck Surg.* 2000; 126: 1032, 1035-1036.
15. Bodino C, Jankowski R, Grignon B, Jimenez-Chobillon A, Braun M. Surgical anatomy of the turbinal wall of the ethmoidal labyrinth. *Rhinology* 2004; 42: 73-80.
16. Pierre M, Bureau H, Louis R. [Correction of nasal deformities secondary to Woakes' syndrome.]. *Ann Chir Plast.* 1962; 7: 35-38.

Nasal adenomatoid hamartoma

17. Busca GP. [The Woakes syndrome. (Etiopathogenetic and clinical considerations with personal case report)]. *Minerva Otorinolaringol.* 1966; 16: 201-205.
18. Kellerhals B, de Uthemann B. Woakes' syndrome: the problems of infantile nasal polyps. *Int J Pediatr Otorhinolaryngol.* 1979; 1: 79-85.