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Endoscopic surgery reveals that woodworkers' adenocarcinomas originate in the olfactory cleft*

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SUMMARY

The olfactory cleft is a narrow chamber located under the cribriform plate and between the turbinate wall of the ethmoidal labyrinth and the corresponding nasal septum. Nasal adenocarcinomas are mostly described as originating in the ethmoid sinus and operated via external approaches. We designed a prospective study on twenty consecutive woodworkers' adenocarcinomas without intracranial extension to determine the precise site of origin of the tumour. All patients were operated under endoscopic endonasal control according to a methodical surgical procedure as follows:

1) debulking of the tumour and identification of the middle turbinate or conchal lamina,

2) exenteration of the ethmoidal labyrinth according to the nasalisation procedure, and

3) exenteration of the olfactory cleft.

Endoscopic endonasal surgery showed that woodworkers' adenocarcinomas constantly originated in the olfactory cleft, appearing as polyp-like neoplasms with well-defined bodies. Over a long period of time, they do not invade, but just displace and push out the surrounding structures, i.e. the nasal septum and the turbinate wall. More than the volume of the tumour, the precise location of the pedicle and especially its connection to the cribriform plate could be of major prognosis value.

Key words: nasal adenocarcinoma, woodworkers, ethmoïd tumours, olfactory cleft, endoscopic endonasal surgery

INTRODUCTION

Woodworkers' adenocarcinomas are most often described as originating in the ethmoid sinus [(1-11)] or in the nasal cavity with no precision on the actual site of origin [(12-16)]. Transfacial approaches through lateral rhinotomy, combined with bifrontal craniotomy in cases of intracranial extension, have been the traditional surgical procedures to remove these tumours [(1-11)].

However, endoscopic endonasal surgery can now be considered as a viable alternative to external approaches for the resection of malignant neoplasms of the nose and sinuses [(17-20)], and notably endoscopic craniofacial resections without the need for open craniotomy have been performed recently and successfully in selected cases [(21-22)].

The principal aim of our prospective study was to localize the site of origin of woodworkers' adenocarcinomas with the use of endoscopic surgery in twenty consecutive patients.

METHODS

Anatomical terminology

The olfactory cleft is a narrow chamber opening anteriorly and inferiorly into the nasal fossa; closed laterally by the turbinate wall of the ethmoidal labyrinth [(23)] and medially by the corresponding nasal septum (Figure 1); closed superiorly, from anterior to posterior, by the nasal and frontal bones, the cribriform plate and the anterior process of the sphenoid roof; closed posteriorly by the anterior wall of the sphenoid sinus.

The turbinate wall of the ethmoidal labyrinth is made of the conchal lamina and the attached middle and superior (and supreme) turbinates (Figure 1); it separates the olfactory cleft from the ethmoidal labyrinth. The ethmoidal cells close to the turbinate wall are called "medial", the one close to the orbital wall "lateral ethmoidal cells".

Since the cribriform plate lies more caudal than then the ethmoidal roof, the turbinate wall of the ethmoidal labyrinth is

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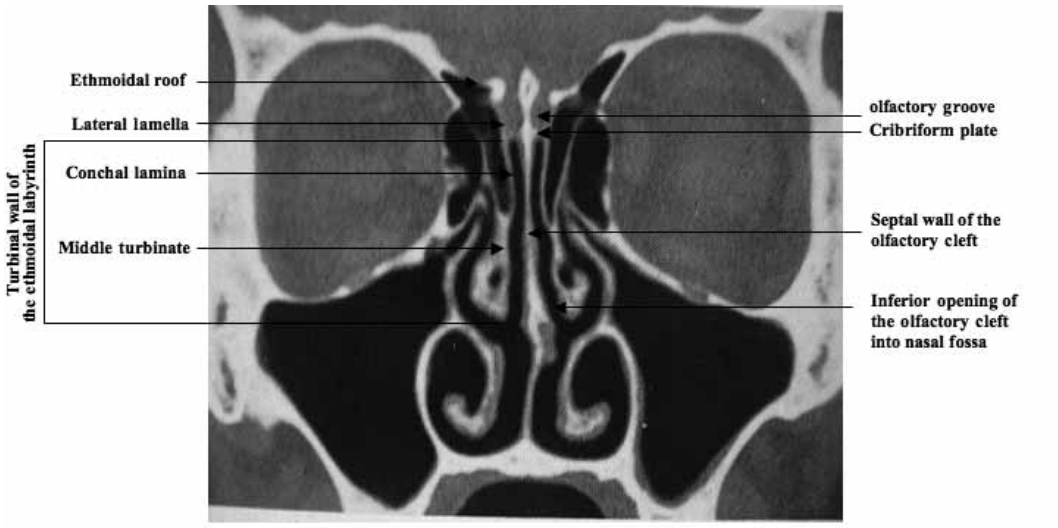
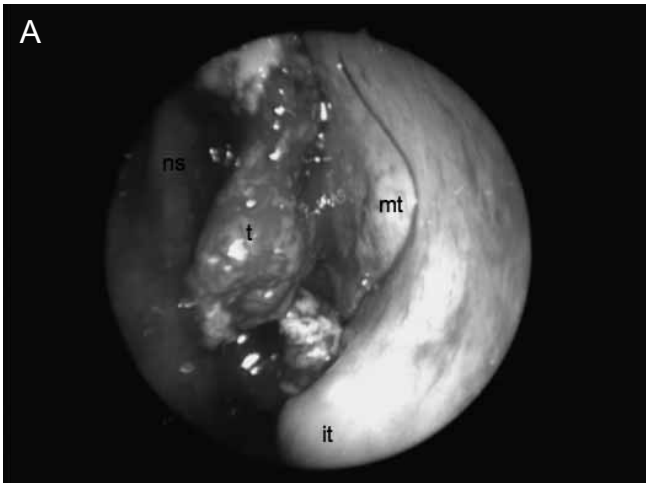


Figure 1. Anatomy of the olfactory cleft in coronal plane.



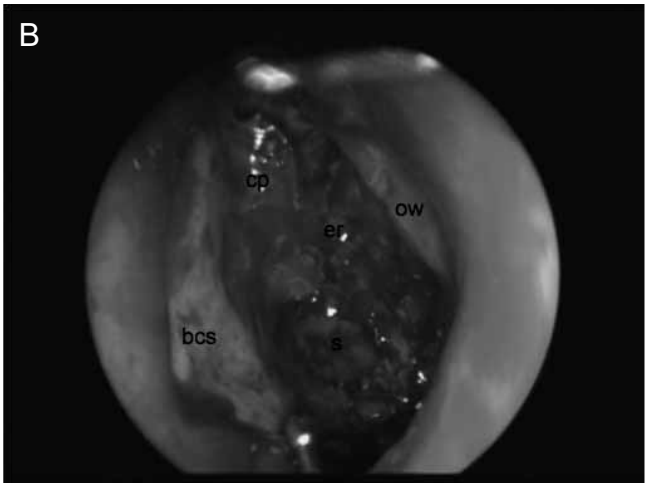


Figure 2. Surgery of a left olfactory cleft adenocarcinoma.
(A) After debulking of the tumour, the middle turbinate can clearly be identified (ns=nasal septum; mt=middle turbinate; t=tumour; it=inferior turbinate). (B) Exenteration of the olfactory cleft is finished (bcs=bony-cartilaginous septum; cp=cribriform plate; er=ethmoidal roof; ow=orbital wall; s=sphenoidotomy).

attached to the ethmoidal roof thanks to the lateral lamella of the intracranial olfactory groove (Figure 1).

Surgical procedure

Our first cases of adenocarcinomas were operated endoscopically in 2000. Since 2004, our surgical procedure was standardized as follows:

- the operation begins with the *debulking of the tumour* until the middle turbinate can clearly be identified (Figure 2A),
- the second step is *dissection of the medial wall of the orbit*; it starts with a large middle meatal antrostomy, that allows clear identification of the maxillary sinus roof, i.e. the inferior orbital wall; ethmoidal cells along the medial orbital wall are successively opened antero-posteriorly from the ascending process of the maxillary bone to the anterior wall of the sphenoid and infero-superiorly from the inferior orbital wall to the ethmoidal roof; the bony medial orbital wall is completely exposed by removing the mucosa or, if necessary, can also be resected,
- the third step is *resection of the middle turbinate*, leaving in place the conchal lamina,
- the fourth step is dissection of the ethmoidal roof, from the frontal sinus ostium to the sphenoid sinus, which is opened trans-ethmoidally, and from the medial orbital wall to the lateral lamina,
- the fifth step is *elevation of the nasal septum mucosa* in the sub perichondrial / periosteal plane; the septal mucosa is incised parallel to the nasal floor one centimetre below the macroscopic margin of the tumour, starting posterior on the free border of the vomer bone; a second perpendicular incision is made anterior to the macroscopic margin of the tumour, starting as high as possible under the nasal bone, and reaches inferiorly the previous incision; this square of septal mucosa is then elevated in anterior to posterior and inferior to superior directions to reach the cribriform plate and anterior wall of the sphenoid bone; elevation of the mucosa can be replaced, if necessary, by a full-thickness resection of the nasal septum,

- the sixth step is the *initial dissection of the cribriform plate*; the mucosa of the nasal vault is incised anterior to the cribriform plate on the horizontal process of the frontal bone, which is hard bone; the mucosa is elevated in the sub periosteal plane and the dissection progresses posterior until the first olfactory fibres are reached,
- the seventh step is *exenteration of the olfactory cleft* (Figure 2B); the conchal lamina is in-fractured from anterior to posterior by pushing it medially with the suction tube ,; the olfactory fibres, which are contained in the conchal lamina, are gradually sectioned at their emergence from the cribriform plate with a cutting Blakesley forceps from anterior to posterior, allowing easy elevation of the mucosa covering the cribriform plate; medially the elevation of the cribriform plate mucosa joins the septal mucosa dissection plane; the nasal portion of the anterior sphenoid wall, which is the posterior limit of the olfactory cleft, is resected starting through the formerly performed trans ethmoidal sphenoidotomy; the olfactory cleft can then be removed in one piece,
- finally, the cribriform plate and ethmoidal roof are covered with fibrin glue and hemostatic sponges, and this ends the procedure; no packing is used.

Patients

Adenocarcinoma diagnosis was based on pre-operative biopsies. Radiology evaluation was based on CT scan and MRI imaging. Patients were selected for endoscopic surgery with multidisciplinary agreement involving surgeons, radiotherapists, medical oncologists, and radiologists. Contraindication to endoscopic surgery was intracranial, intraorbital, or facial skin invasion. All patients were planned to receive post operative radiotherapy.

RESULTS

Twenty men with the diagnosis of nasal adenocarcinoma, who were all woodworkers, were operated by means of endonasal endoscopic surgery between July 2004 and December 2006. Mean age was 68 years (range: 54-79).

Endoscopic examination with the patient under general anaesthesia found no tumour extension in the contralateral nasal fossa in nineteen patients. There were ten left, nine right and one bilateral tumours.

Debulking of the tumour was easily achieved with the use of suction tubes and Blakeslay forceps by piecemeal removal. Tumours were in all cases soft or friable. Debulking was started centrally and after shrinkage of the tumour, we observed that in all cases the periphery of the tumour's body was not invasive, but had only displaced and compressed the surrounding structures. Depending on its size, the tumour was filling the nasal fossa and extending more or less into the surrounding spaces: the tumour prolapsed into the nasopharynx in five cases, into the nasal vestibule in two cases, and into the maxillary sinus in two cases; the tumour was limited to the olfactory cleft in three cases.

The middle turbinate could clearly be identified in eighteen cases, because in all these cases, it was displaced laterally by a polyp-like tumour originating inwards and enlarging the olfactory cleft. In these eighteen cases, the ethmoidal labyrinth was squeezed more or less strongly onto the orbital wall. In two cases, the middle turbinate was not recognizable, being entrapped by a tumour that still was involving the olfactory cleft.

At this stage, in the twenty patients, the next step of the surgery was dissection of the medial orbital wall. In one patient (#5) with exophthalmos and diplopia, the tumour was compressing the orbital content without invading the periorbita; erosion of the posterior bony orbital wall was associated with sphenoid involvement and erosion of its lateral wall was associated with meningeal exposure; a tumourfree dissection of the periorbita and dura was however possible under endoscopic control. In a second patient (#14), a centimetric erosion of the anterior bony orbital wall was found behind the lacrimal duct. In these two patients, the rest of the orbital wall was dissected free of ethmoidal cells and mucosa, which appeared macroscopically healthy. In the remaining eighteen cases, the bony orbital wall was found intact, covered with healthy ethmoidal cells and mucosa. In our twenty cases, the endoscopically healthy ethmoidal cells and mucosa removed on the orbital wall were confirmed histologically.

Dissection of the ethmoidal roof showed healthy mucosa covering the bone in nineteen cases, from the frontal to the sphenoid sinus roofs and in between the orbital wall and the lateral lamella. In one case (#5), erosion of the bony ethmoidal roof was found starting behind the anterior ethmoidal artery and reaching the anterior limit of the sphenoethmoidal or Onodi cell (which was covered with healthy mucosa); the dura however, was not invaded and could be dissected free of the tumour.

At this stage of the procedure it was obvious that the olfactory cleft was the site of origin of the tumour in our twenty cases (Table1).

In two cases (#1,#2), a well defined pedicle could clearly be identified on the *posterior septal mucosa*, staying at a millimetre distance below the cribiform plate and in front of the anterior wall of the sphenoid. In one case (#12), a similar pedicle was reaching and abutting the anterior wall of the sphenoid, whereas in another case (#13), it was reaching the cribriform plate. In two cases (#18,#20), the pedicle was developed on the posterior septal mucosa, on the anterior wall of the sphenoid, on the posterior conchal lamina mucosa, and on the adjacent cribriform plate mucosa, i.e. involving all the walls of the *posterior olfactory cleft.*

In one case (#3), the pedicle was arising from the septal

Table 1. The origin of the various adenocarcinomas in the olfactory cleft.

Case #	Age (years)	Side	Septal mucosa		Turbinate wall of ethmoidal labyrinth		Mucosa of the cribriform plate		Bony cribriform plate		Sphenoid anterior wall	Exenteration	CSF Leak
			Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior			
1	71	R	0	+	0	0	0	0	NA	NA	0	No	No
2	69	L	0	+	0	0	0	0	0	0	0	Yes	No
3	54	R	+	+	0	0	0	0	NA	NA	0	No	No
4	65	R	0	0	+	0	0	0	NA	NA	0	No	No
5	62	L	+	+	+	+	+	+	+	+	+	Yes	Yes
6	75	R	+	+	+	+	+	+	0	0	+	Yes	Yes
7	79	L	0	0	+	+	0	+	0	+	0	Yes	Yes
8	66	L	0	0	+	+	0	0	0	0	0	Yes	Yes
9	72	L	+	0	+	0	+	0	0	0	0	Yes	Yes
		R	+	0	+	0	0	0	0	0	0	No	No
10	66	R	+	+	+	+	+	+	+	0	+	Yes	Yes
11	63	L	+	+	+	+	+	+	0	0	0	Yes	No
12	75	R	0	+	0	0	0	+	0	0	+	Yes	No
13	58	L	0	+	0	0	0	+	0	0	0	Yes	No
14	73	R	0	+	+	+	0	+	0	0	+	Yes	No
15	71	R	+	0	+	0	+	0	+	0	0	Yes	No
16	73	L	+	0	+	0	0	0	NA	NA	0	No	No
17	76	L	0	0	0	+	0	+	0	0	+	Yes	No
18	59	L	0	+	0	+	0	+	0	0	+	Yes	No
19	55	L	+	+	+	+	+	+	+	+	0	Yes	Yes
20	76	L	0	+	0	+	0	+	0	0	+	Yes	No

NA = non applicable; R = right; L = left; 0 = no tumour; + = tumour

mucosa of the olfactory cleft, mirroring the surface of the ethmoidal turbinate wall, but staying a few millimetres below the cribriform plate and in front of the anterior sphenoid wall, reaching inferiorly and anteriorly the level of the free border of the middle turbinate.

In five cases (#5,#6,#10,#11,#19), the pedicle involved all the main three walls of the *olfactory cleft*, i.e. the septal, cribriform plate and ethmoidal turbinate walls. In case #5, the tumour was invading the sphenoid sinus with erosion of its lateral wall below the optic canal and in front of the carotid artery canal but without invasion of the dura. In case #10, the tumour was penetrating into the sphenoid sinus through the anterior wall, but could easily be withdrawn. In the three other cases the mucosa covering the sphenoid anterior wall looked healthy and this was confirmed histologically.

In one case (#4), a well defined pedicle could clearly be identified on the mucosa of the *anterior part of the conchal lamina* in the olfactory cleft, staying two millimetres below the cribriform plate; this tumour had not invaded the conchal lamina bone as the medial ethmoidal cell in contact was found to be free of tumour. In one case (#16), a similar pedicle on the conchal lamina was associated with a second pedicle located directly opposite on the septal mucosa; these two pedicles looked independent and occurred five millimetres below the cribriform plate.

In two cases (#9,#15), the pedicle presented a horseshoe shape in the *anterior olfactory cleft*, and arose on the anterior conchal lamina, cribriform plate and septum. In case #9, the tumour grew through the septum into the contralateral olfactory cleft, invaded onto a half square centimetre of the contralateral middle turbinate, but stayed at distance of the contralateral cribriform plate. In case #15, the anterior cribriform plate bone was eroded but the dura could be dissected free of the tumour.

In two cases (#7,#8), the pedicle was located on the *conchal lamina*, started a few millimetres behind the head of the middle turbinate, and stayed two millimetres in front of the anterior sphenoid wall. In case #8, the tumour did not reach the cribriform plate. In case #7, the tumour destroyed the mid part of the cribriform plate and was dissected free from the dura, leading to a CSF leak, which was per-operatively closed, but needed a second procedure six days later to be controlled. In one case (#14), an identical pedicle on the conchal lamina extended onto the mucosa of the anterior sphenoid wall, posterior septum and posterior cribriform plate; the sphenoid sinus was not invaded and the cribriform bone could be dissected free of the tumour and preserved.

In one case (#17), a small pedicle involved the posterior conchal lamina and the adjacent anterior sphenoid wall and posterior cribriform plate.

The septal mucosa could be elevated in the subperichondrial-subperiostial plane in fourteen cases. In five cases (#1,#3,#5,#16,#20), we systematically resected the posterior half of the nasal septum. However, in only one case (#9), the tumour was transfixing the septum, which was justification for

a full thickeness septal resection. The septal mucosa was involved by the tumour in ten out of the fourteen subperichondrial-subperiostial elevations. However, in none of these cases did the tumour transgress the periosteumor perichondrium. In three out of these ten cases, the septal bone or cartilage however had disappeared and the dissection had to separate both subperichondrium-subperiostium sheets.

In total, exenteration of the olfactory cleft was performed in only 16 patients, because in four cases preservation of the mucosa covering the cribriform plate was possible. In cases #1 and #3, the pedicle was small and localized on the nasal septum at a safe distance from the cribriform plate and anterior wall of the sphenoid. In case #4, the pedicle was small and localized on the anterior part of the conchal lamina at a safe distance below the cribriform plate. In case #16, two pedicles, each less than five millimetres in diameter, were localised and mirrored on the conchal lamina and septal mucosa at safe distances from the cribriform plate and sphenoid anterior wall.
In five of the sixteen patients with exenteration of the olfactory cleft, the cribriform plate bone was gone and the dura had to be dissected free of the tumour. None of these five patients showed intra-cranial extension on the pre op MRI and CT scan imaging.

A CSF leak was identified in seven patients (Table 1). In four cases the CSF leak stopped spontaneously after a few seconds (cases #5,#6,#9,#19). In three cases (#7,#8,#10), the CSF leak stopped immediately after applying fibrin glue; in case #7, the CSF leak recurred six hours later and could not be controlled with medical treatment. However, it was controlled with a fat graft placed under endoscopic endonasal control six days later. In spite of the trans-section of the olfactory fibers, no CSF leak could be identified in nine of the sixteen patients undergoing exenteration of the olfactory cleft. None of our twenty patients developed meningitis after a follow up of three to thirty months. However, patient #7 (aged 79 years) developed chronic subdural haematoma at four month post op which was operated on three times in three months and finally stabilized thanks to proper medical treatment; the neurosurgeons suspected a chronic CSF leak which could not be demonstrated but the patient is still doing well after a follow-up of two years.

In four cases, the tumour invaded the mucosa on the anterior wall of the sphenoid sinus; in three cases, it prolapsed into its lumen; no difficulty was encountered to resect the small extension of the tumour in these seven cases. In case #5 (see above), the tumour invaded the sphenoid sinus to its lateral wall with meningeal exposure.

In our series of twenty adenocarcinomas of the olfactory cleft, we observed an extension to the ethmoidal cells in only eight cases.

DISCUSSION

This study shows that, in a series of twenty consecutive woodworkers' adenocarcinomas which were operated under transnasal endoscopic control, the tumour constantly originateed in the olfactory cleft. These findings have not yet been the experience of other authors undertaking endoscopic surgery for this disease. This is perhaps because our study is the first one entirely focused on endoscopic resection of nasal adenocarcinomas with the specific aim to localize the origin of the tumour but these findings need to be confirmed by other investigators.

Actually, these observations were made possible thanks to a methodical surgical approach, derived from the nasalisation technique we have proposed for nasal polyposis surgery [(24)]. Nasalisation is a radical ethmoidectomy, which is performed centripetally: the dissection starts and follows the different walls of the ethmoidal labyrinth (orbital wall, ethmoidal roof and turbinate wall) to remove its content. Traditional perception is that woodworkers' adenocarcinomas develop in the ethmoidal labyrinth and the nasalisation technique would thus be appropriate to remove ethmoidal adenocarcinomas. However, we observed by applying the nasalisation principles in our first cases that the ethmoidal labyrinth did not seem to be the site of origin of the tumour, but that it seemed to take its origin in the olfactory cleft. This observation was the genesis of our prospective study.

Debulking of the tumour by piecemeal removal is the first oncological concept to be transgressed in transnasal endoscopic resection of malignant adenocarcinomas. Experience shows, however, that true en bloc resection is only rarely possible in nose and sinus tumour surgery, even with traditional external approaches. In fact, there is no study showing that piecemeal removal increases local recurrences, nor adversely affects survival in nose and sinus tumour surgery [(22)].

Endonasal endoscopic debulking of the tumour shows us, that adenocarcinomas are polyp-like neoplasms with a well defined body, which over a long period of time probably do not invade, but just displace and push out the surrounding structures, i.e. the nasal septum and the middle turbinate.
The ethmoidal labyrinth is progressively squeezed onto the medial orbital wall, but stays in most patients as a surgical landmark that helps to dissect the tumour from the compressed orbit wall. In some patients the tumour may protrude into the maxillary sinus through the middle meatus; even in these cases, debulking of the tumour combined with middle meatal antrostomy allow one to find a dissection plane on the medial orbital wall, which is the result of compression of the inferior part of the ethmoidal labyrinth. In most patients, as the dissection of the medial orbital wall progresses superiorly, healthy ethmoidal cells are found under the ethmoidal roof, at least along the lateral lamella of the olfactory groove, because

the cribriform plate lies more caudal than the ethmoidal roof [25] (Figure 1). Thus, a tumour arising in the olfactory cleft and expanding laterally without invasion, leaves the superior ethmoidal space intact. Careful examination of CT scan and MRI imaging shows retention of mucus in this space, whereas tumour is located under the cribriform plate. In our series, the ethmoidal roof was found intact in nineteen patients; only one patient with a huge tumour (#5) showed a more aggressive growing pattern with erosion of the posterior ethmoidal roof and orbit medial wall, which needed a sharp dissection of the periorbita and dura.

The periosteum-perichondrium of the nasal septum seems to be a resistant barrier to adenocarcinoma invasion. Except in patient #9 whose tumour had transgressed the nasal septum and invaded the contralateral middle turbinate, and except in the five cases with systematic septal resection, it is noted that in all the other cases we were able to elevate the septal mucosal flap from the underlying cartilage or bone, or in three cases, from the contra lateral mucosal flap. In these three cases, the bony-cartilaginous erosion was probably the result of tumour compression, which did not alter the periosteum-perichondrium.

Our experience is that adenocarcinomas originated in the olfactory cleft, and our suspicion is that the relationship between tumour and cribriform plate is a major prognostic factor. The tumour involved the mucosa of the cribriform plate in fourteen cases, whereas it involved the ethmoidal roof in only one case. These findings are not only an argument that supports the olfactory cleft origin, but perhaps also provide an explanation for the recurrences observed after surgical procedures which are more focused on ethmoidal than on olfactory cleft exenteration.

We do not have experience with endoscopic craniofacial resection [21-22], but our observations suggest that this technique could be relevant to treat certain cases of the woodworkers' adenocarcinomas, even when the pre-operative imaging does not show intracranial extension, but rather when surgery uncovers a suspicious relationship between tumour and dura. The tumour involved the mucosa as well as the bone of the cribriform plate in five of our cases, and the question is if these five cases might have been indications for endoscopic craniofacial resection. Among these five cases, patient #10 developed an intracranial tumour without any recurrence in the nose fourteen months after surgery plus post operative radiation therapy; his three monthly endoscopic check ups were all normal as well as the six month post therapeutic MRI control. The intracranial tumour was successfully resected transcranially by neurosurgical colleagues, but the patient died four weeks later from a severe seizure attack that occurred after he returned home. The four other patients have not as yet developed recurrence after a mean follow-up of 17 months (range 3-28 months).

In fifteen of our cases, the bony cribriform plate was found intact and preserved. The mucosa covering the cribriform plate is easy to elevate, once the olfactory fibers are sectioned. Our belief is that there is no need for endoscopic craniofacial resection when the bony cribriform plate is found intact during surgery. In these cases, exenteration of the olfactory cleft may be sufficient and we hope to be able to confirm this in a few years with the follow-up of our patients, and also to show that endoscopic exenteration of the olfactory cleft is more appropriate than exenteration focused on the ethmoidal labyrinth.

CONCLUSION

Traditional craniofacial resection through external approach has been the gold standard for resection of woodworkers' adenocarcinomas. The mortality and morbidity associated with this technique may be quite high and includes significant intracranial, orbital, infectious, cosmetic and systemic morbidities [26-29]. Moreover, nasal adenocarcinomas frequently develop in patients with significant co-morbidities and advanced age. More recently, with advances in endoscopic technology and surgical experience, a few papers suggest that endonasal endoscopic resection may provide an alternative to craniofacial resection with equivalent results.

Our experience is that transnasal endoscopic surgery improves visualization and allows a more precise dissection that follows the adenocarcinoma's limits to the actual area of origin of the tumour. According to our experience, woodworkers' adenocarcinomas develop into the olfactory cleft and grow into the nose. Only a few of them develop intracranial extensions in the early stages. In cases with a preserved bony cribriform plate, their oncologically resection may be focused on endoscopic olfactory cleft exenteration. In cases with intracranial extension, endoscopic craniofacial resection should be considered before traditional craniofacial resection.

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