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Sinonasal Schwannoma - a clinicopathological analysis of five rare cases*

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SUMMARY

Schwannoma of the nasal cavity or the sinuses is a rare condition. We report a small series of five consecutive patients; three males and two females, age range 22-81 years, all Caucasian.

Symptoms were typically non-specific, and the tumours were often quite large when diagnosed, being locally infiltrating and even destructive. Histologically, the tumours were remarkable by sparse occurrence of Antoni type B areas and lack of encapsulation. Four cases were benign; however, one case of melanotic schwannoma, exhibited malignant transformation. Two of the patients had intracranial involvement, but with an intact dura. All tumours were treated surgically; only the malignant case received adjuvant radiotherapy. Patients were followed from five months to 15 years, with a median of 57 months. The benign cases have so far shown good prognosis without recurrences; however, in the case of the melanotic schwannoma a fatal malignant transformation was seen 13 years after initial diagnosis.

On the basis of our review early detection and complete surgical removal is recommended.

Key words: Schwannoma, nasal cavity, sinuses, malignant schwannoma, melanotic schwannoma.

INTRODUCTION

Tumours of the Schwann cell are called schwannomas, neurolemomas, neurilemomas or neurinomas, and are derived from the neuroectoderm [1]. They are fairly common neoplasms arising from peripheral, autonomic, or cranial nerves. Between 25-45% of all schwannomas is located in the head and neck region, but of these only 4% are nasal or paranasal [1-5]. Intranasal schwannomas thus are very rare, and less than 100 cases have been described in the literature [2]. These are predominantly benign, and only in isolated cases a malignant transformation has been reported [1,6].

At the Department of Oto-Rhino-Laryngology, Section of Head and Neck Surgery, at Rigshospitalet in Copenhagen, Denmark, a tertiary referral hospital with a population basis of about one million, we have diagnosed five cases of nasal or paranasal schwannomas over the past 25 years.

Given the limited literature on the subject, we report our experience with these tumours. This study will discuss the importance of early diagnosis and primary total surgical excision, as schwannomas of the nasal and paranasal cavities tend to become fairly large before causing symptoms and may be locally aggressive. The histopathological findings will also be described and discussed.

MATERIAL AND METHODS

A retrospective search of our pathology database revealed five cases of nasal or paranasal schwannomas treated at our hospital in the period 1980-2004. The pathological material and the patients' charts were reviewed. New sections were cut from archival paraffin blocks and stained with antibodies against S-100 protein (a marker for the Schwann cells), Ki-67, (a marker for cell proliferation) and Glut-1(a specific marker for perineural cells [7]).

Case 1

A 55-year-old female admitted with complaints of nasal obstruction and a growing mass in the left nasal cavity (Figure 1A). The only symptom was progressive obstruction of the left nasal vestibulum, evolved over less than one year. An ENT specialist performed a biopsy, which rendered the diagnosis of benign schwannoma. Subsequently, the patient was referred to our hospital for surgery. Clinically, the tumour was greyish in colour, polypoid and approximately three-cm in diameter. A transnasal resection was performed. Histology confirmed the diagnosis of benign schwannoma. The patient had an eight-month follow up that showed no recurrence of the tumour.

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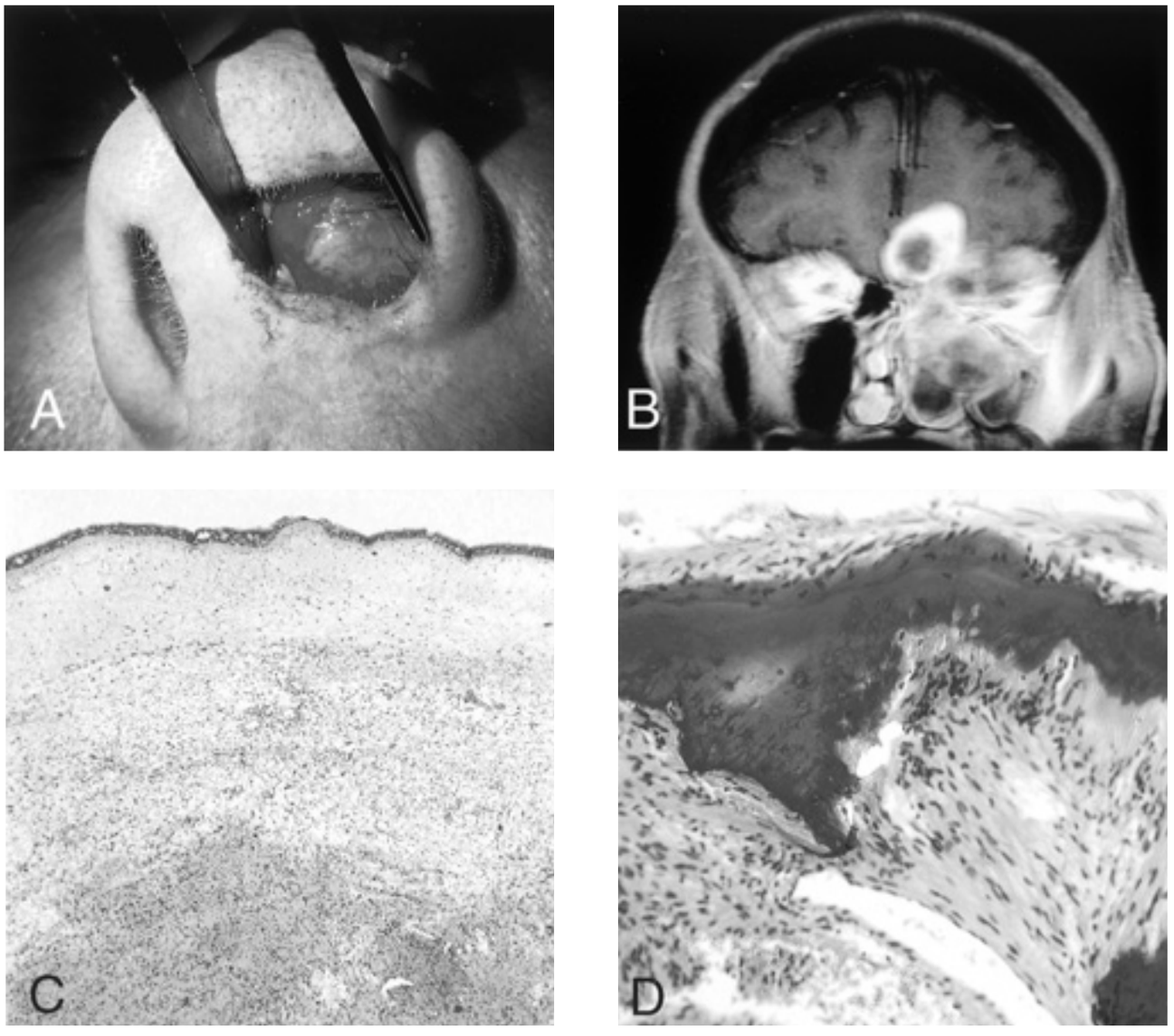

Figure 1. Features of nasal and sinonasal schwannoma.
A: Schwannoma covered by intact mucosa occludes the nasal vestibulum (case 1). B: Coronal, T2 weighted MR scan showing tumour involvement in maxillary and ethmoid sinuses, including protrusion of the tumour intracranially (case 4). C: Benign schwannoma infiltrating nasal mucosa. Note transition without encapsulation from superficial areas towards deeper dense tumour masses (case 4). Haematoxylin and eosin, original magnification x 100. D: Benign schwannoma infiltrating bone, which exhibits irregular resorption, and no demonstrable encapsulation (case 4). Haematoxylin and eosin, original magnification x 200.

Case 2

A 39-year-old male was referred to our ENT department with a sensation of nasal obstruction on the right side, which had been worsening over approximately one year. The patient had had a few episodes of sinusitis two years previously. Examination revealed a visible greyish, soft tumour with a smooth surface in the right nostril. By posterior rhinoscopy, the tumour was visible just inside choana. Coronal CT scans showed the right nasal cavity to be completely obliterated by a solid mass, from the choana to the nostril. The tumour furthermore extended into the left nasal cavity through a defect in the nasal septum. The right maxillary, ethmoid and frontal sinuses were also completely obliterated by hyper dense masses. No visible bony septa remained in the ethmoid region. The right medial wall of the maxillary sinus was displaced, caving inwards towards the sinus itself, although without bone destruction.

Via a lateral rhinotomy a.m. Biller, a complete surgical resection of the tumour was performed. The histology showed benign schwannoma. The patient was followed for six years with regular visits every three to six months, with no signs of recurrence.

Case 3

A 33-year-old female was admitted with complaints of progressive aphasia, memory loss and proptosis of the right eye. The symptoms escalated over the following year. CT scans revealed a large tumour obliterating the right maxillary sinus, involving also the ethmoid region, the sphenoid sinus, and orbit. There was destruction of the orbital floor on the right side and suspicion of intracranial involvement in the medial fossa. A coronal incision gave access to a frontotemporal craniotomy, and a large extradural tumour within the medial fossa was extracted. The tumour, which extended far downwards into the nasal and paranasal structures, was approached by lateral rhinotomy and excised. The patient was re-admitted for follow-up after one year, as she complained of persistent proptosis and diplopia. During subsequent surgery, a large residual cystic tumour in the right maxillary sinus was removed; pathological analysis of the surgical specimen again showed a benign schwannoma. A third operation was planned and conducted, primarily to reconstruct the right orbital floor, and the last ethmoidal part of the schwannoma was extracted. The patient was followed for 26 months with no signs of recurrence.

Case 4

An 81-year-old female was admitted from a county hospital with a diagnosis of benign schwannoma of the nasal and paranasal cavities. Her symptoms included impaired vision and ptosis of the left superior eyelid, left-sided nasal obstruction, a sensation of pressure behind the left eye, and headaches; the symptoms had increased over approximately one year. CT scans showed dense masses in the entire left nasal cavity and the left maxillary sinus. The lesion protruded into the left orbit and ethmoid region, completely obliterating the frontal sinus. A biopsy yielded the diagnosis of a benign schwannoma. A MRI scan revealed the tumour to extend into the anterior fossa (Figure 1B). During surgery, a coronal incision gave access to perform an anterior craniotomy. After the tumour was resected from the anterior fossa, the same access was used to remove the tumour in both frontal sinuses, the left nasal cavity and left maxillary sinus. While the tumour had extended into the anterior fossa via the olfactorial region on the left side, the dura, however, was still intact and the tumour was excised without complications. A subsequent endoscopic examination of the nasal cavity and sinuses revealed an intact mucosa and no residual tumour. The periorbit on the left side was intact and the patient had slight enophtalmus after the operation. Vision was unchanged, but the headaches were gone. The patient is scheduled for regular follow-ups, of which the first one after five months has not shown any signs of recurrence.

Case 5

A 22-year old male was admitted on suspicion of a growing tumour in the left orbit, with minor left sided exophthalmus, developed over three months. The patient underwent an anterior orbitotomy, in which a dark, soft and bleeding tumour was found. Histology demonstrated a most likely benign melanotic schwannoma, with presumed origin from the inferior orbital nerve [8] (Figure 2A). Due to the benign histological diagnosis, and since the patient's vision would be at risk if surgery were to be performed, a "wait and see" approach was opted for. During the following three years, however, the tumour grew and extended into the maxillary sinus and the nasal cavity. The lesion was subsequently surgically removed, without loss of vision. Histology again showed melanotic schwannoma with no signs of malignancy [8]. Ten years later the patient was readmitted on suspicion of recurrence of the tumour. The patient underwent subsequent surgery of which the diagnosis benign melanotic shwannoma of the orbit was re-confirmed. The tumour was only de-bulked to spare the patients vision on the affected left side. The tumour kept recurring, and during surgery approximately 13 years after initial diagnosis, the histology now showed a malignant transformation (Figures 2B and 2C). A radical excision of the tumour, and the orbital floor, fol-

Table 1. Clinical findings in five cases of nasal and sinonasal schwannoma.

Pt. no.	Age (years) /sex	Location (side)	Duration of symptoms	Symptoms	Treatment	Malignant	Follow up	Recurrence
1	55 / female	NC (left)	9 months	NO Visible tumour	Surgery	No	8 months	No
2	39 / male	NC, ethmoid, frontal and maxillary sinuses (right)	1 year	NO "Sinusitis", pain	Surgery	No	72 months	No
3	33 / female	NC, sphenoid, ethmoid, maxillary sinuses. Orbit. Medial fossa. (right)	1 year	Proptosis, diplopia, aphasia, memory loss	Surgery	No	26 months	No
4	81 / female	NC, maxillary, ethmoid, sphenoid sinuses (left)	1 year	NO, Ptosis Headache Impaired vision	Surgery	No	5 months	No
5	22 / male	Maxillary sinus, orbit (left)	3 months	Proptosis, diplopia, pain	Surgery (a) Surgery + radiotherapy (b)	Yes	15 years	Yes

NC = Nasal cavity

NO = Nasal obstruction

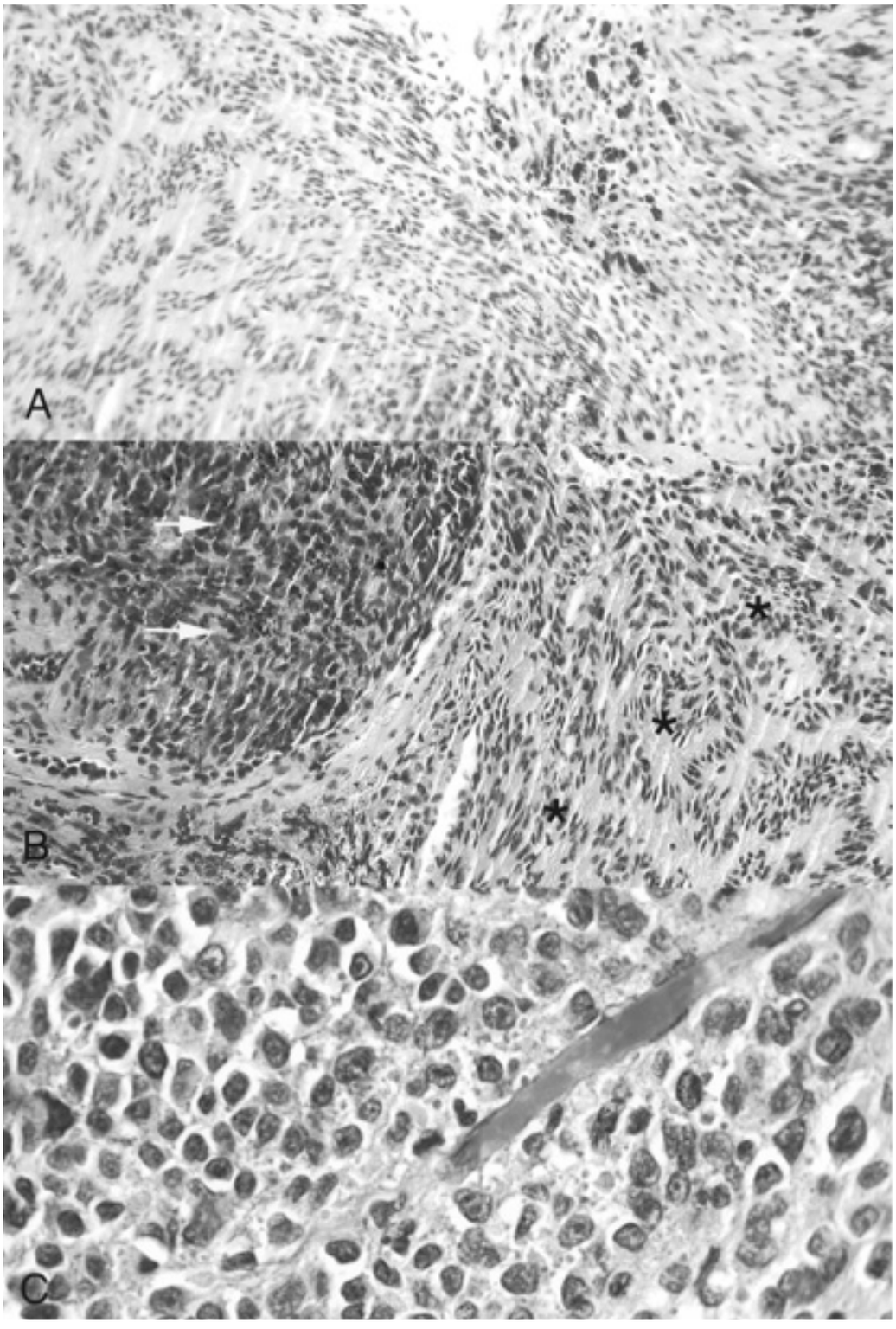

Figure 2. Features of melanotic scwannoma (Case 5)

A: Benign melanotic schwannoma with palisading of nuclei and copious melanin pigment (case 5). Haematoxylin and eosin, original magnification x 200.

B: Sample from 1999 show both areas with benign morphology (*) and areas with malignant morphology (arrow). Hematoxylin and eosin, original magnification x 200.

C: Sample from 2000 demonstrating malignant transformation. The tumour now consists of closely packed malignant epithelioid cells, of which only a few contain pigment. Haematoxylin and eosin, original magnification x 400.

Table 2. Histological findings in five cases of nasal or sinonasal schwannoma.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5-a *)	Patient 5-b *)
Antoni A pattern	+++	+++	+++	+++	+++	epithelioid
Antoni B pattern	0	+	0	+	0	epithelioid
Encapsulation	None	None	None	None	None	None
Pigmentation	0	0	0			
Melanin					+++	++
Haemosiderin				++		
Mitotic activity per 10 HPF **)	2	0	0	3	0	6
Ki67 reactivity	<15%	<5%	<3%	<8%	<8%	25 %
S-100 reactivity	+++	+++	+++	+++	+/++	0/+
Other findings	inflammation	Slight nuclear pleomorphism		Fresh and older bleeding		

*) Case 5 before (a) and after (b) malignant transformation.

**) One HPF (high power field) = 0.3067 ml

lowed by later a total left sided orbital exenteration and maxillary resection, were then performed. Since the tumour was now malignant, the patient was given adjuvant radiotherapy (70 gy/35 fractions). However, the tumour metastasised to the bones over the following two years, and subsequently lead to the patient's death.

RESULTS

The clinical data are summarised in Table 1. The female/male ratio was 3:2, age ranging from 22-81 years at the primary contact, with a median of 48 years, all patients being Caucasians. None of the cases were associated with Neurofibromatosis type 1. Initial symptoms began about one year prior to diagnosis, except for case 5, the patient with melanotic schwannoma, who had had symptoms for three months before admission. Symptoms reflected the location of the tumour, and included obstruction of the nasal cavity, sinusitis and proptosis. In case 3, where the medial fossa was involved, the symptoms were similar to that of an intracranial space-occupying lesion, with progressive aphasia, headache and memory loss.

The relatively unnoticed growth, initially, of the tumour was common for all the benign schwannomas.

The histological findings are summarised in Table 2. The original diagnoses were re-confirmed in all five cases. An Antoni type B pattern was seen only focally, if at all. Encapsulation could not be demonstrated at all; not even with the help of immuno-histochemical staining for Glut-1, which is a sensitive marker of perineural cells [7]. This lack of encapsulation was reflected in a growth pattern that was clearly infiltrative and reminiscent of neurofibromas rather than of conventional schwannomas (Figures 1C and 1D). Degenerative changes were common (haemorrhage, inflammation, slight nuclear pleomorphism). Staining for S-100 protein was generally intense. In case 5 (the melanotic tumour) it was variable, and after malignant transformation only weak and focal. Mitotic activity varied. The proliferative activity, as measured by the percentage of tumour cells positive for Ki-67, varied between three and 15% in the benign lesions; it was 25% in the malignant one.

DISCUSSION

Verocay described the histological aspects of the schwannoma already in the early 1900s, with the characteristic feature of the palisading cell arrangement, also called "Verocay bodies" [5,9]. Macroscopically the tumour is usually well demarcated, greyish to yellowish in colour, fleshy and shiny on the surface. Microscopically, it typically consists of cellular areas (Antoni type A) with spindle-shaped cells often arranged in palisades, together with more loosely structured areas with a myxoid stroma (Antoni type B) [5,8,10]. Some tumours may contain cysts or exhibit other degenerative phenomena; if the tumours are accompanied by a significant nuclear pleomorphism, the term 'ancient schwannoma' may be applied [3].

Sinonasal schwannomas are thought to originate primarily from the ophthalmic and maxillary branches of trigeminal nerve, but could also arise from sympathetic or parasympathetic fibres from the carotid plexus or sphenopalatine ganglion. [1,3,11]. In our case 5, it is reasonable to suggest that the tumour originated in the sensory inferior orbital nerve [8]. In the four other cases the schwannoma originated from nerves in the sinonasal mucosa.

Schwannomas are usually described as being encapsulated, in contrast to the non-encapsulated neurofibromas [10,11]; the capsule is assumed to derive from the perineurium of the nerve of origin. Encapsulation, however, was also not found in a study by Hasegawa et al. [3], consisting of six cases of schwannomas of the sinonasal tract and the nasopharynx, as well as in another pathological study by Buob et al. [2] that comprised of five similar cases. These authors speculate that the tumours derive from sinonasal mucosal autonomic nervous system fibres, which are devoid of perineural cells and therefore lack encapsulation, similar to the case of gastric schwannomas [2,3]. None of our cases were encapsulated or contained perineural cells, which seems to confirm the theory. Encapsulation of schwannomas in this region appears to be the exception rather than the rule, and probably explain the rather aggressive growth pattern compared to schwannomas in other locations. The lack of encapsulation thus does not imply malignancy, but for the clinician the lack of

encapsulation might make the tumour more difficult to define and extract in toto.

Intracranial involvement of a benign schwannoma from nasal or sinonasal cavities has previously only been reported in a very few cases in the literature [3,12]. This may be because patients tend to be diagnosed before the tumour acquires a fairly large size. Since the sinuses are largely comprised of air-filled spaces and cavities, the tumour can grow to a considerable size before symptoms occur. When the patient finally complains of symptoms, tumour has typically reached its maximum within the sinuses and exerts pressure on the surrounding tissue, causing impaired vision or symptoms of intracranial extension.

The feature of bone remodelling due to the pressure of the growing tumour on the bony septa is also distinctive of the benign nature of the schwannoma [2,13,14]. Even in CT scans it may be difficult to determine whether the tumour is invasive in growth or just "pushing" the bone. Most patients had CT scans performed to determine the extent of their tumour. In the sinuses, however, hyper dense areas may well be interpreted as part of the tumour when they in reality only represent fluid in blocked sinuses. In case 3 it was believed that the intranasal schwannoma involved the frontal sinus; however, during surgery this proved to be fluid. A MRI with T2 weighted imaging may differentiate the tumour from for instance fluid [14].

In cases of melanotic schwannoma the most important differential diagnosis was malignant melanoma. Since the two types of tumours carry some of the same histological markers and macroscopically resemble one another, the definitive diagnosis may be difficult or delayed [8,10]. Both tumours exhibit S-100 protein, and even modern immunohistochemical methods using other melanoma markers may not always be able to make a distinction between the two types.

In case 5, the melanotic schwannoma, the most important differential diagnosis is that of malignant melanoma. The two entities exhibit morphological overlap and may express the same immunological markers; a definitive diagnosis may thus be difficult or delayed in some cases, as also discussed in detail in our previous report of the case [8,10]. Both tumours generally exhibit positivity for the S-100 protein and other melanoma markers such as HMB45. In our case, the initial tumour exhibited a clearly benign morphology, with spindle-shaped cells, palisading nuclei, and no pleomorphism (Figure 2A); the diagnosis was further supported by electron microscopy that clearly demonstrated abundant basement membrane material, as described by Jensen and Bretlau [8]. When the tumour recurred after 10 years, the first biopsy still showed foci with spindle cells and palisading (Figure 2B), while the malignant transformation was otherwise characterised by a change in morphology to an epithelioid appearance (Figure 2C), with a higher mitotic frequency, a higher proliferation rate, and a weaker expression of S-100 protein (Table 2). In our opinion, the morphology and the long interval (13 years) between the primary lesion and the recurrence argue for a malignant transformation in a melanotic Schwannoma rather than a malignant melanoma. Melanotic schwannomas are rare, and it has only gradually been realised that they have a high rate of recurrence and metastasis, with about 15% of the patients dying of their tumour [10]. Due to the initial benign diagnosis and the high risk of damaging the patient's vision on the affected side, the patient was not primarily radically operated. Early total surgical excision might have prevented its recurrence with widespread and intracranial infiltration and possibly its late malignant transformation; the current recommendation is surgical excision with tumour-free margins [10].

The present study represents one of the largest series of intranasal and paranasal schwannomas in the recent literature. On the basis of our research we found this to be an extremely rare tumour. Still, our finding of five cases over a period of 25 years in one department covering a population of approximately one million inhabitants may indicate that these tumours are under diagnosed. In its early stages, the tumour may very well be diagnosed clinically as a common nasal polyp, extracted but never sent for pathological examination. Pathologists need also to be aware of this possibility, since the schwannomas may be confused with other spindle cell lesions, especially neurofibromas and leiomyomatous tumours; the main diagnostic difference of the pigmented lesions of course being the malignant melanoma. On the basis of our study we advocate early detection and primary total resection of intranasal and paranasal schwannomas. MRI best determines the extent of these lesions.

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