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A neuroendocrine tumour of the sphenoid sinus and nasopharynx: a case report

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Abstract. *A neuroendocrine tumour of the sphenoid sinus and nasopharynx: a case report.* It is rare for neuroendocrine tumours to originate in the sphenoid sinus and the nasopharynx. Neuroendocrine tumours can be classified into typical carcinoids, atypical carcinoids and small cell neuroendocrine carcinomas. Here we report the case of a 48-year-old man with a typical carcinoid tumour of the nasopharynx and sphenoid sinus. This is a very rare diagnosis, and only a few cases of a typical carcinoid in this region have been described in the literature.

Introduction

Neuroendocrine tumours of the paranasal sinuses and nasopharynx are rare lesions that include typical carcinoids, atypical carcinoids and small cell carcinomas. Of these, typical carcinoid tumours are relatively rare and slow-growing. Several years may pass before symptoms appear and the tumour is diagnosed. Such carcinoid tumours can become aggressive and resistant to therapy. Carcinoid tumours secrete several biologically active substances, including serotonin, kallikrein, histamine, prostaglandins, adrenocorticotropic hormone, gastrin, calcitonin and growth hormones.[1-3]

Carcinoid tumours arise at a number of sites, including the gastrointestinal tract, thymus, lung, kidneys, breasts, testes and ovaries; occasionally, such tumours arise at other anatomical sites. The gastrointestinal tract is the most frequently involved site, followed by the lungs.[1-3]

Carcinoid tumours have a low incidence rate of 1.9 per 100,000, and men and women are affected equally. The age distribution of carcinoid tumours ranges from the second to the ninth decade, with a peak incidence between the ages of 50 and 70.[2,3] This paper describes the second reported case of a typical carcinoid tumour of the sphenoid sinus and nasopharynx.

Case report

A 48-year-old man presented at the ENT department in March 2008 complaining of sudden-onset pain and a sensation of pressure behind his right eye. There were no visual disturbances. The patient had been suffering from bilateral nasal obstruction for two years but had not visited a physician. He had no epistaxis and no headache. The patient had hypertension that was treated with atenolol, amlodipine, moxonidine and a combination of valsartan and hydrochloorthiazide. The patient was a cigarette smoker (20 pack-years). Rhinoscopic examination revealed a bilateral mass in the nasal cavity that originated in the nasopharynx (Figure 1).

Further ENT findings were within normal limits. Neurological examination revealed anisocory, with the right pupil smaller than the left. Light reflexes were present. A multi-detector computed tomography (MDCT) scan of the head revealed a large bilateral soft-tissue mass in the sphenoid sinus with accompanying bone destruction. The tumour completely filled the lumen of the sphenoid sinus and extended bilaterally into the nasopharynx, the posterior ethmoid sinus, the pterygopalatine fossa and the right maxillary sinus. The mass had caused expansion and erosion of the sinus walls, sellar floor and clivus. Magnetic resonance imaging (MRI) confirmed the presence of an expansile nasopharyngeal and sphenoid sinus mass that was slightly hyperintense on T1-weighted images, heterogeneously hyperintense on T2-weighted images and strongly enhanced after intravenous administration of a gadolinium chelate contrast agent (Figure 2). The mass extended into the right maxillary sinus, the posterior ethmoid sinus, and the sella turcica (abutting the pituitary gland); it also extended bilaterally into the cavernous

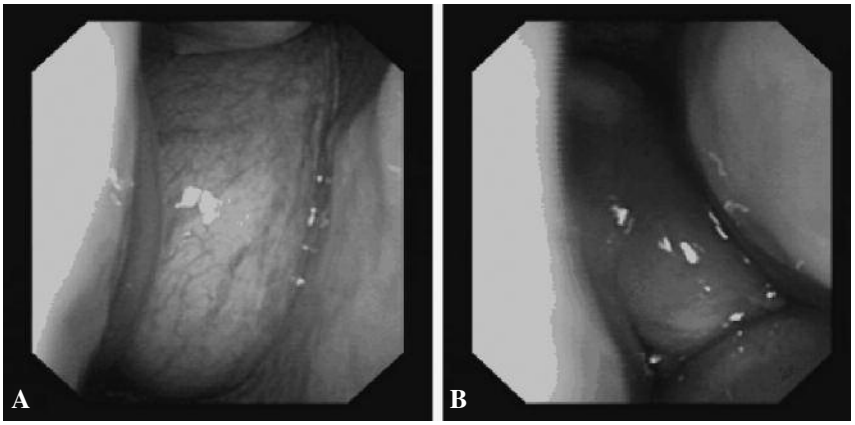

Figure 1
A, B: Endoscopic examination showed a bilateral mass in the nasal cavity that originated from the nasopharynx.

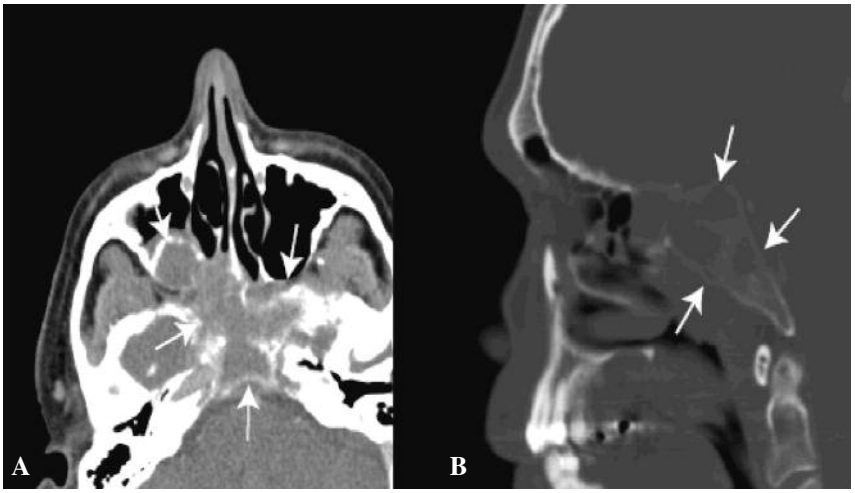

Figure 2
A: An axial contrast-enhanced MDCT scan showed a soft-tissue density mass (arrows) in the nasopharynx, sphenoid sinus, pterygopalatine fossa and in the posterior part of the right maxillary sinus.
B: A reformatted sagittal MDCT image showed that the mass appeared to be expanding and destroying the sphenoid bone (arrows).

sinus, encasing both internal carotid arteries (Figure 3).

Positron emission tomography-computed tomography (PET-CT) with 18-fluoro-deoxyglucose (FDG) was performed for tumour staging. We found a hypermetabolic focus centered on the ethmoid and sphenoid sinuses that extended into the posterior right maxillary sinus. There was no evidence that the mass had spread to the locoregional lymph nodes, nor were there signs of metastatic disease (Figure 4).

A transnasal biopsy was performed under general anaesthesia. Hematoxylin and eosin staining showed that the tumour had an insular growth pattern with focal acinar cell hyperplasia and was composed of uniform tumour cells with round nuclei and typical salt-and-pepper chromatin. Mitotic activity was low (less than one mitotic figure per 1 mm²). There was no cytonuclear atypia and no necrosis. Immunohistochemical examination demonstrated immunoreactivity for chromogranin A and synaptophysin. S100 immunostaining was positive in the sustentacular cells, and Ki-67 staining confirmed the low proliferation rate. The diagnosis of a neuroendocrine tumour (typical carcinoid type) was made based on these histopathological results (Figure 5).

The serum level of chromogranin A was 143 μg/l, within the normal range (40-170 μg/l). The adrenocorticotropic hormone level was 50 pg/ml and normal, the calcitonin level was 3.3 pg/ml and normal, the serotonin level was 0.02 μg/ml and the somatostatin level was normal. At 119 pg/ml, the gastrin concentration was slightly elevated (normal range: 23-114 pg/ml), and glucagon was slightly reduced at 28 pg/ml (normal range: 40-130 pg/ml). The patient's urine level of 5-hydroxyindoleacetic acid was 2.9 mg/d, and the level of vanillylmandelic acid was 2.5 mg/d; these levels were within normal ranges.

Given the histopathological findings, an octreotide scan was performed with 111In-octreotide. Tracer uptake was increased slightly in the central maxillofacial region. No metastasis was observed (Figure 6).

The tumour could not be resected due to intracranial expansion and encasement of both internal carotid arteries. The degree of captation of the tumour on the octreotide scan was insufficient, so tumour-targeted treatment using the radioactive octreotide lutetium-177 was not an option.

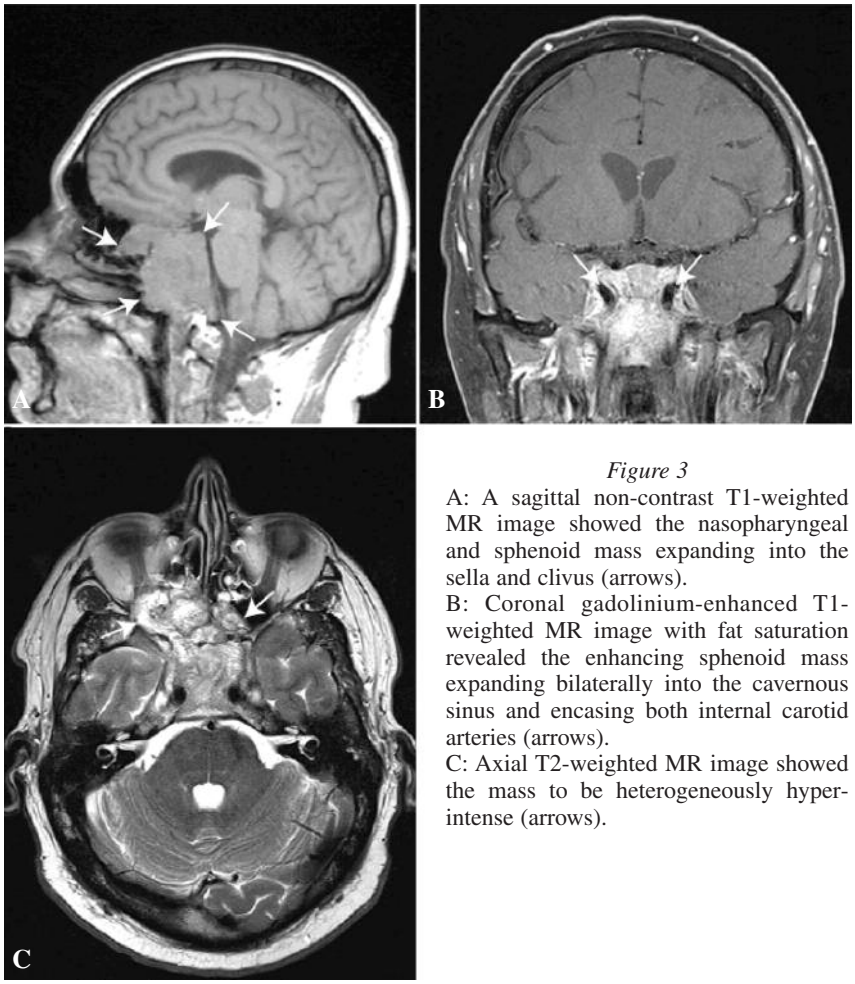

Figure 3
A: A sagittal non-contrast T1-weighted MR image showed the nasopharyngeal and sphenoid mass expanding into the sella and clivus (arrows).
B: Coronal gadolinium-enhanced T1-weighted MR image with fat saturation revealed the enhancing sphenoid mass expanding bilaterally into the cavernous sinus and encasing both internal carotid arteries (arrows).
C: Axial T2-weighted MR image showed the mass to be heterogeneously hyperintense (arrows).

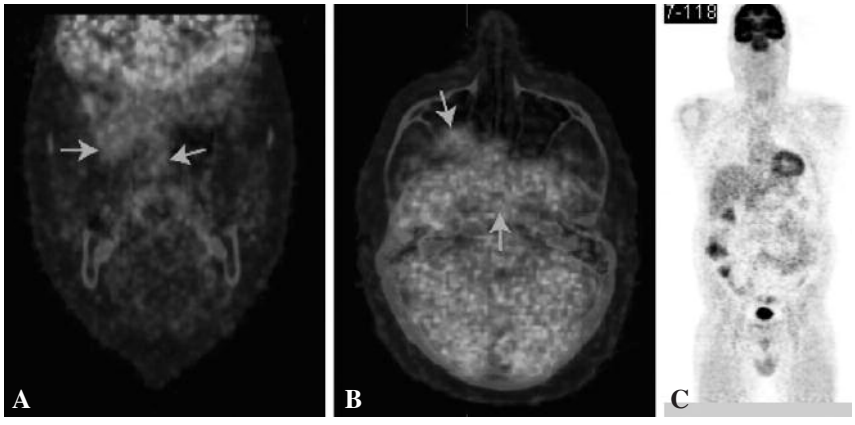

Figure 4
A: Coronal and B: axial PET-CT fusion images showed a hypermetabolic focus (arrows) centered on the ethmoid and sphenoid sinus and extending into the posterior right maxillary sinus.
C, A: coronal FDG-PET image showed no evidence of metastatic disease or spreading to locoregional lymph nodes.

After a discussion with colleagues with broad expertise in ENT diseases and oncology, we decided to perform treatment with neoadjuvant chemotherapy followed by consolidation radiotherapy. The patient underwent chemotherapy with etoposide (150 mg/m²/d, days 1-3), ifosfamide (1500 mg/m²/d, days 1-3) and cisplatin (30 mg/m²/d, days 1-3) every three weeks. After four cycles of chemotherapy, there was a subjective decrease in pain and improved nasal breathing. However, CT and MRI imaging showed no marked reduction in tumour size. Subsequently, radiotherapy was started (68.4 Gy in 38 fractions). The patient's prognosis is poor.

Discussion

Neuroendocrine tumours are rare. In the head and neck region, neuroendocrine tumours are found most commonly in the larynx, where they account for less than 1% of all laryngeal neoplasms. Atypical carcinoid tumours are the most frequent type of neuroendocrine neoplasms of the larynx, followed by small cell neuroendocrine carcinomas, paragangliomas and, finally, typical carcinoid tumours.[4]

There is only one previous report of a neuroendocrine tumour that is a typical carcinoid in the sphenoid sinus and nasopharynx regions; this was reported by Kanamalla *et al*.[5] in 2000. This group also reported on a small cell neuroendocrine carcinoma of the maxillary sinus, which had expanded into the nasal cavity and the nasopharynx with destruction of the hard palate, ethmoid cells and sphenoid sinus; that carcinoma had intraorbital extension.

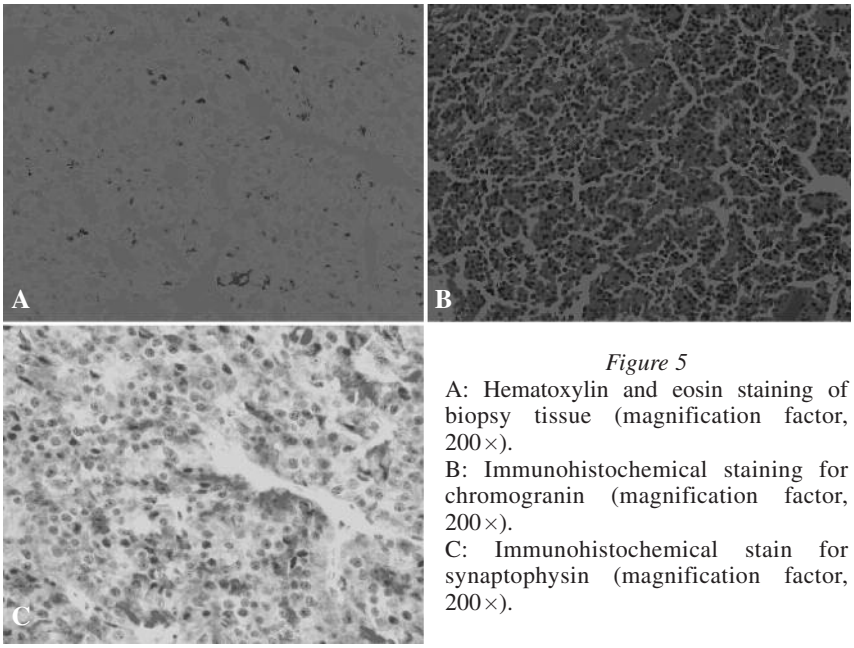

Figure 5
A: Hematoxylin and eosin staining of biopsy tissue (magnification factor, 200×).
B: Immunohistochemical staining for chromogranin (magnification factor, 200×).
C: Immunohistochemical stain for synaptophysin (magnification factor, 200×).

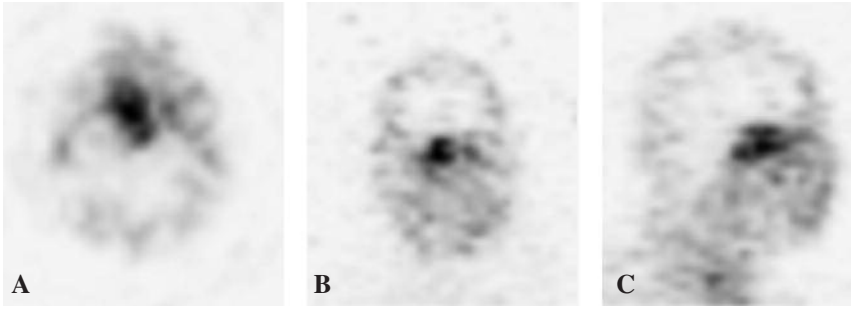

Figure 6
A: Axial, B: Coronal and C: Sagittal octreotide scans show increased tracer uptake in the central maxillofacial region.

Treatment consisted of chemotherapy (VP-16 and cisplatin) and radiotherapy, followed by a radical maxillectomy with bilateral modified radical neck dissection. The patient ultimately died of liver metastases.[5]

Although the tumour described here is very rare, there are some other reports of neuroendocrine tumours in the nasal cavity. The first description of a carcinoid tumour in the nasal cavity was published by Lee *et al.*[6] in 2007. A carcinoid tumour of the nasal septum was reported by Galm *et al.*[7] and Feng *et al.*[8] described a typical carcinoid tumour of the middle ear, an atypical carcinoid tumour of the nasopharynx and a small cell neuroendocrine carcinoma of the nasal cavity. Westerveld *et al.*[9] described an atypical carcinoid of the sphenoid sinus. Esposito *et al.*[10] reported four cases of primary sphenoid sinus neoplasms, of which one was a high-grade neuroendocrine carcinoma. Sriumpai *et al.*[11] reported a carcinoid tumour of the maxillary antrum in 1982.

Radiographic and nuclear imaging play important roles in the diagnosis and management of carcinoid tumours. CT and MRI are used both to determine the precise location and extent of tumours as well as to monitor the response to treatment.[5,12,13] The WHO criteria for histological diagnosis of a typical carcinoid include a carcinoid histological pattern with fewer than 2 mitoses/2 mm² with a lack of necrosis and a diameter greater than 0.5 cm.

Neuroendocrine tumours express somatostatin receptors, which can be demonstrated using a radionuclide coupled to the somatostatin analog, octreotide (indium-111 pentetreotide). The whole body can be imaged to identify metastatic disease. This technique is highly sensitive and specific for carcinoid tumours.[12,14] Chromogranin A (CgA) levels tend to correlate with tumour bulk but not with symptoms. In general, CgA levels are elevated in 85-100% of patients with carcinoid tumours. The specificity of CgA levels is 98.4% and the sensitivity 62.9%.[12,15]

Surgery is the treatment of choice for a localized carcinoid tumour and is the only therapeutic option that offers a real chance of cure. The goal is en bloc resection of the entire neoplasm.[1] In addition, tumour-targeted treatment using radioactive octreotide derivatives (i.e., octreotide lutetium-177) is associated with tumour shrinkage in 20-25% of tumours; therefore, an octreotide scan is useful in planning therapeutic treatment.[12] Notably, external radiation therapy has limited value in the treatment of carcinoid tumours and is recommended only for bone and brain metastases. For patients with more advanced disease, cisplatin-chemotherapy is a reasonable option.[12]

Conclusion

Neuroendocrine tumours that are typical carcinoids of the sphenoid sinus and nasopharynx are very rare. Before this report, only one case was described in the medical literature (Kanamalla *et al*.[5]). In general, the prognosis for a patient with a typical carcinoid tumour is good if the tumour can be resected completely. However, the tumour described here is unresectable, resulting in a poor prognosis for the patient.

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