CASE REPORT

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Neuroendocrine carcinoma of the sphenoid sinus: a case report*

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SUMMARY

The presentation of a neuroendocrine carcinoma in the paranasal sinuses is extremely rare. Until now only 25 cases have been reported in the literature. We report a case of a 65-year-old male with an atypical carcinoid of the sphenoid sinus which seemed to be associated with multiple endocrine neoplasia type 1 (MEN 1). To the best of our knowledge this is the first report on an atypical carcinoid in the sphenoid sinus.

Key words: malignant tumor, MEN I, neuroendocrine carcinoma, paranasal sinuses, sphenoid sinus

INTRODUCTION

Neuroendocrine carcinomas comprise a heterogeneous group of tumors consisting of typical carcinoid tumors, atypical carcinoid tumors and small-cell neuroendocrine carcinomas. The majority of neuroendocrine carcinomas occur in the lungs, however, these tumors can also primarily occur in extrapulmonary sites. In the head and neck area the larynx is the most common site of appearance (Ferlito, 1986).

Neuroendocrine tumors of the paranasal sinuses are extremely rare. Until now 25 cases have been reported in the literature of which only one was located in the sphenoid sinus (Raychowdhuri, 1965). In this paper we present a case of an atypical carcinoid in the paranasal sinuses which is to the best of our knowledge only the second report of occurrence of neuroendocrine carcinoma in the sphenoid sinus and the first report of an atypical carcinoid in this area.

CASE REPORT

A 65-year-old male was referred to the Department of Medical Oncology of our hospital by his rheumatologist as he suffered from progressive pain in his lower back, the back of his head, both upper arms and his right upper leg, which had lasted for 2 years. The complaints had not responded to analgesics prescribed by his general practitioner. X-rays of his upper arms, legs and pelvis showed no abnormalities. However, an X-ray of his spine showed multiple osteolytic lesions in the thoracic and lumbar regions suspicious for malignancy. In addition, a bone scan was made which showed multiple pathological spots in the thoracic and lumbar spine, but also on both sides in the humerus and femur. An iliac crest biopsy was performed and on histopathological examination a metastasis of a neuroendocrine tumor of an atypical carcinoid type was seen.

Except for a small adenoma in the pancreas no abnormalities were seen on a CT-scan of the thorax and abdomen. As the patient had undergone a parathyroidectomy for adenoma of the parathyroid glands 21-years earlier, the possibility of multiple endocrine neoplasia type 1 (MEN 1) was considered. In the search for a coexistent pituitary gland tumor, a MRI-scan of the head was made which indeed showed a microadenoma of 7 mm in the anterior pituitary gland. By coincidence, a tumorous lesion in the left sphenoid sinus was seen. Moreover, multiple skull-bone metastases were found. For further evaluation the patient was referred to our ENT-department. On ENT-history the patient did not suffer from nasal obstruction or epistaxis. Furthermore, he had no swallowing or voice complaints. His family history for malignancies was positive as both his mother and his sister died of pancreas and liver cancer, respectively. None of his family members however, were known with MEN 1 syndrome.

On ENT-examination no abnormalities were seen in the larynx, nasal cavity and in the nasopharynx. No palpable lymphnodes were present in the neck. Examination of the MRI-scan of the head indeed showed, except for the other above mentioned abnormalities, an exophytic lesion in the left sphenoid sinus, which seemed to originate from the sphenoid floor (Figure 1). No clear bone invasion could be seen. An endoscopic removal of the lesion was performed under general anaesthesia and the specimen was submitted for histopathologic examination. The removed tissue showed infiltrating epithelial islands, glands and strands of hyperchromatic cells with polymorphic nuclei and

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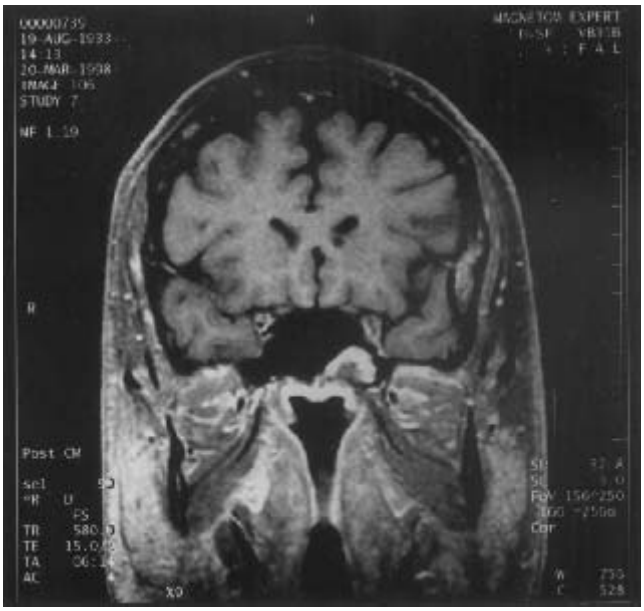

Figure 1. Coronal MRI-scan of the head. There is an exophytic lesion in the left sphenoid visible which extents from the sphenoid sinus floor in the direction of the cavernous sinus.

occasional mitotic activity. No evident necrosis could be noted (Figure 2). Immunohistochemical staining was strongly positive for neuron specific enolase (NSE), Leu 7, and chromogranin. Immunostaining was weakly positive for synaptophysine and negative for epithelial membrane antigen (EMA), keratin and vimentin. Based on these findings the diagnosis of a neuroendocrine tumor was made. The picture was characteristic for an atypical carcinoid comparable with the previously examined iliac crest biopsies. Additional chromosomal examination showed that our patient was a heterozygote carrier of a mutation in exon 7 of the MEN 1 gene on chromosome 11q 13. This finding made the diagnosis of a MEN 1 syndrome likely. The patient was palliatively treated with somatostatine.

DISCUSSION

Neoplasms of the nasal cavity and the paranasal sinuses account for 0.2 to 0.8% of all carcinomas and for 3% of those in the upper respiratory tract. The maxillary sinus is commonly involved (60 %), followed by the nasal cavity (30%), the ethmoid sinus (10%) and the frontal (2%) and sphenoid sinuses (2%) (Osguthorpe, 1994). In the paranasal sinuses squamous cell carcinoma is the most common neoplasm. Furthermore, a spectrum of other tumors like adenocarcinoma, malignant lymphoma, plasma cell tumor, malignant melanoma, olfactory neuroblastoma and neuroendocrine carcinoma have been described (Kameya et al., 1980).

Neuroendocrine carcinoma of the paranasal sinuses is rare. In 1994 Chaudhry summarized the until then known 15 cases in the English literature (Chaudhry et al., 1994). Furthermore, they added one case bringing the total to 16. In 1995 McCluggage reported on a sinonasal neuroendocrine carcinoma arising in a woodworker exhibiting amphicrine differentiation, meaning that the tumor consisted of cells containing both neuroendocrine and exocrine secretory granules (McCluggage et al., 1995). In 1997 Bhattacharyya described 4 more cases of neuroendocrine carcinoma (Bhattacharyya et al., 1997). The most recent report was in 1998 by Perez-Ordonez who described 6 patients with a small cell neuroendocrine carcinoma of the sinonasal tract of which 4 involved the nasal cavity and the maxillary or ethmoid sinuses, bringing the total to 25 cases (Perez-Ordonez et al., 1998).

The different subtypes of neuroendocrine carcinoma exhibit considerable differences in malignant potential. Small cell carcinoma is highly malignant, atypical carcinoid less high malignant, and typical carcinoid low malignant. For all subtypes it applies that, in contrast to presentation in the lungs or in the larynx, the presentation of these tumors in the paranasal sinuses show a propensity for local recurrence and destruction rather than early metastatic spread (Rejowski et al., 1982). Distant metastases of neuroendocrine tumors in the paranasal sinuses are infrequent but when present they predominantly occur in the brain and spine, although bone and neck lymph node metastases have also been described (Silva et al., 1982). Unlike the treatment of neuroendocrine carcinoma of the larynx which demands different treatment strategies depending on the histological type (Gripp et al., 1995), the treatment of neuroendocrine carcinoma of the nose and paranasal sinuses is not clearly established. Until now the most used therapy for paranasal neuroendocrine carcinomas has been surgery or conventional radiotherapy or a combination of both (Janjan et al., 1989). Sometimes additional chemotherapy was used (Weiss et al., 1983). Recently, good results were reported using the combination of cisplatin and etoposide chemotherapy with proton radiation, giving dramatic responses even in bulky tumors (Bhattacharyya et al., 1997). Our patient on presentation suffered already from disseminated disease which made curation impossible. As he did not have any local complaints of his sphenoid tumor radiotherapy was not given. Moreover, the patient renounced from chemotherapy, therefore he was treated with somatostatine as it has been reported that this drug inhibits tumor growth (Lamberts, 1998). The prognosis is determined by accurate histopathological differentiation (Gripp et al., 1995; Ferlito and Friedman, 1989). In the histopathological differen-

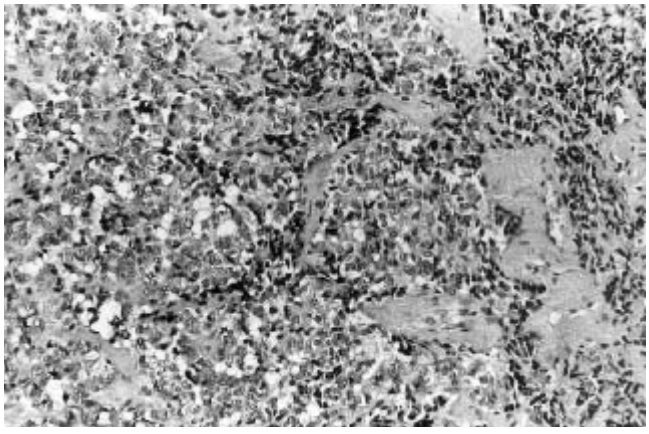

Figure 2. Histopathology (HE, 400x) of the atypical carcinoid tumour of the sphenoid sinus. Infiltrating epithelial islands and strands, composed of hyperchromatic cells with polymorphic nuclei and occasional mitotic activity, are seen. No evident necrosis is present.

tiation electron microscopy but especially immunohistochemistry have been proven to be very helpful. Classically on light microscopy well-demarcated groups of tumor cells surrounded by connective tissue are seen. In primary sites uniform glandular epithelium cells are seen with usually a low mitotic rate and predominantly round or oval shaped nuclei. Focal areas of necrosis are inconsistently found. Characteristically, dense-core membrane bound cytoplasmatic granules are present on electron microscopy (Silva et al., 1982). In addition, monoclonal antibodies against chromogranin A, neuron-specific-enolase, synaptophysin and neural cell adhesion molecule can react positive as neuroendocrine tumors express a great variety of immunoactive peptides (Gripp et al., 1995).

In our patient, on light microscopy the presence of normal glandular tissue, characteristic for primary tumor sites, was not very clear. The definite diagnosis however, could be made on the positive staining of the different immunohistochemical markers. Additional electron microscopy was therefore not performed. As in our patient no other primary tumor site was found it was concluded that the lesion in the sphenoid sinus was the primary tumor.

Multiple endocrine neoplasia type 1 is characterised by the combined occurrence of tumors of the parathyroid glands, the pancreatic islet cells and the anterior pituitary gland. MEN 1 usually inherits in an autosomal dominant manner, however, it can occur sporadically without a family history. It is thought that MEN 1 is caused by a mutation in the MEN 1 gene on chromosome 11q13, a feature also shown in our patient (Pang and Thakker, 1994). The association of MEN 1 syndrome with carcinoid tumors originating from the thymus, the bronchus, the stomach and the duodenum, is well known (Duy et al., 1987). The combination of an atypical carcinoid in the paranasal sinuses with a MEN 1 disorder has, however, to our best knowledge never been described before.

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