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CASE REPORT

Endonasal approach for frontobasal malignant nerve sheath tumor: a case report

Frontal bölge kafa tabanında malign sinir kılıfı tümörü için endonazal yaklaşım

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Malignant peripheral nerve sheath tumors (MPNST) are rarely encountered in the paranasal sinuses and frontal skull base. We present histopathological findings, cytometric DNA measurements, and the preliminary results of comparative genomic hybridization studies of a 46-year-old male patient with a frontobasal MPNST. The tumor was resected via the endonasal approach. No tumor recurrence was detected during a follow-up of three years. Rhinologists are being more frequently involved in endonasal tumor resection.

Key Words: Nerve sheath neoplasms; nucleic acid hybridization; paranasal sinuses; skull base.

Paranazal sinüsleri ve frontal bölge kafa tabanını etkileyen malign periferik sinir kılıfı tümörlerine nadir rastlanır. Bu yazıda, frontobazal bölge malign periferik sinir kılıfı tümörü saptanan 46 yaşındak erkek hastanın histopatolojik bulguları, sitometrik DNA analizleri ve karşılaştırmalı genomik hibridizasyonun ilk sonuçları sunuldu. Tümör endonazal yaklaşımla çıkarıldı ve üç yıllık izlem sırasında nüksle karşılaşılmadı. Rinologlar endonazal tümör cerrahisine giderek daha sık başvurmaktadır.

Anahtar Sözcükler: Sinir kılıfı tümörleri; nükleik asit hibridizasyon; paranazal sinus; kafa tabanı.

Benign neurinomas and even more malignant peripheral nerve sheath tumors (MPNST) are rare within the paranasal sinuses.[1,2] One of the most difficult issues in a paranasal/frontobasal MPNST is to estimate its biological behavior.[3] In general, MPNSTs have been found to show a more aggressive growth pattern in patients with "von Recklinghausen`s disease" compared to those arising without a neurofibromatosis association.[4] While surgery is considered to be the first treatment of choice, the value of additional radiation therapy or chemotherapy for paranasal MPNSTs remains uncertain.[5] This might reflect the difficulty of proper tumor grading in individual cases.

In many tumors and especially in MPNSTs, not only the control of the primary tumor side needs caution, but metastasis also has to be taken into account. In MPNSTs pulmonary metastases are quite common. Pulmonary metastases are diagnosed in 40% of the patients, rising to 90% in autopsies.[5]

We present comparative genomic hybridization analysis as an additional option to support proper grading of a MPNST and the possibility to resect a frontobasal low-grade MPNST endonasally.

CASE REPORT

A 46-year-old male suffering from nasal obstruction and loss of smell on the right side was presented

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with suspicion of chronic rhinosinusitis. Rhinoscopy revealed a space occupying lesion in the right nasal cavity extending from the right middle nasal meatus to the nasal floor. The mucosa covering the lesion was inconspicuous. Palpation of the lesion with a probe proved a firm mass. Any allergic disease or trauma of the otherwise healthy patient were denied.

Computed tomography imaging revealed a shadowed anterior ethmoid complex and frontal sinus on the right side. The cranial part of the bony septum and a circumscript area of the ethmoid roof appeared to be destroyed. As the possibility of a tumor was taken into account, magnetic resonance imaging was performed showing a huge frontobasal tumor extending from the ethmoidal roof to the nasal floor. The tumor itself showed an intense Gadolinium-enhancement. The frontal sinus was not affected by the tumor. Only mucous retention was noted in this sinus (Fig. 1a). A slight extension to the left side below the cribriform plate was observed (Fig. 1b) corresponding to the CT finding of a destroyed bony septum in this region.

An endonasal biopsy of the lesion was taken. Histopathological evaluation revealed a low-grade malignant spindle cell tumor of probable neurogenic origin. No lymph node metastases were noted by ultrasonography of the neck. X-ray of the chest, ultrasonography of the abdomen and bone scintigraphy revealed no evidence of distant metastases. Endonasal tumor resection was accomplished. The tumor was clearly dissected from the lamina papyracea which was still covered by unaffected mucosa. The cranial part of the nasal septum and the middle turbinate were included in the resected specimen. Due to the size of the tumor it had to be removed in different parts. Finally, the anterior skull base with its adjacent dura affected by the tumor were resected. Frozen section analysis from the resection margins revealed complete tumor resection. For endonasal duraplasty fascia lata was harvested from the left leg. In a combined underlay/onlay-technique the closure of the dural defect was accomplished. The postoperative course was uneventful and the inserted nasal packing was removed after 7 days.

Final histopathological evaluation confirmed the diagnosis of a malignant peripheral nerve sheath tumor. An intensive S-100 staining and a proliferation index of 10% (MiB1) were seen. Immunostaining for desmin, alpha-actin and CD 34 were found to be negative in the tumor cells. Cytometric DNA-analysis of 230 cell nuclei found an aneuploid proliferation with a malignancy grade of G 1.23.

Tumor tissue was snap frozen at –80° C immediately after resection, and was available for comparative genomic hybridization (CGH). After isolation of the tumor DNA and control DNA from a male donor, CGH was performed as described previously.[6] We detected a gain of the chromosome X, a loss of the Y chromosome and a deletion on the short arm of chromosome 16 (16p12p13.1).

The interdisciplinary tumor conference suggested no postoperative radiation therapy to the patient. Smell testing confirmed preserved smell on the left side. Careful endoscopic follow-up in 3 months intervals found no evidence for tumor recurrence neither did magnetic resonance imaging at 3 months, 1 year, 2 years, and 3 years (Fig. 1c, d) after endonasal tumor resection. Additional chest X-ray one and two years after tumor resection detected no lung metastases.

DISCUSSION

Our intention in selecting the presented surgical approach was complete tumor resection with least morbidity and mortality. The endonasal approach as the least traumatic approach was in the first place increasingly attractive for the treatment of benign tumors in the nasal cavity, paranasal sinuses and frontal skull base based on the excellent experiences in dealing endonasally with chronic rhinosinusitis and mucoceles. Osteomas, juvenile angiofibromas and inverted papillomas have successfully been resected by the endonasal approach.[7-10] In the meantime, endonasal approach has also been reported for the treatment of various other tumor entities including sinunasal schwannomas.[11,12] In selected cases, endonasal approach has even been successfully used to resect malignant tumors.[13,14]

One prerequisite for considering endonasal approach in resection of low-grade malignancies is their precise neuroradiological delineation. The lateral and caudal tumor borders can be exposed by the endonasal approach micro-endoscopically in tumors located in the midline (nasal cavity, ethmoid). If necessary, nasal septum and lamina papyracea are included in the resected specimen. In

case the tumor is not connected to the frontal skull base and is of considerable size even an en-bloc-resection can be achieved by this approach. However, if the tumor is in contact with the frontal skull base and is of considerable size similar to our case en-bloc-resection is endonasally not achievable. In these cases, the neoplasm has to be divided into pieces for complete tumor resection using the endonasal approach. From our point of view this surgical technique can be considered in a low-grade malignancy as in our case. But it is of utmost importance to us that the adjacent frontal skull base including the attached dura can be resected and reconstructed endonasally without any limitations of leaving tumor tissue along the frontal skull base. Frozen section analysis from the resection margins further support complete tumor resection.

A further advantage of the endonasal approach not used here is the facility of postoperative radiation therapy without any delay as especially no bone is temporarily removed like in osteoplastic procedures. A combination of endonasal tumor resection and postoperative radiation therapy has already been suggested in esthesioneuroblastomas.[15] Experiences of the endonasal approach in resecting malignant tumors are still limited. Increasing experiences in endonasal tumor resection and especially the knowledge of the long-term results will allow to define the appropriate indications for the endonasal approach within the variety of other approaches for dealing with sinunasal/frontobasal malignancies in the future.

Comparative genomic hybridization studies on MPNSTs in various locations have been performed previously, but according to our knowledge we presented the first CGH results from a paranasal MPNST. While in sporadic MPNSTs CGH analysis has found gains most frequently at 5p, 6, 8q, and 20q, in patients with Recklinghausen`s disease most gains were detected at 7q, 8q, 15q, and 17q.[16] In our case none of these chromosomes showed aberrations. On the other hand, gains for the chromosome X in 5 out

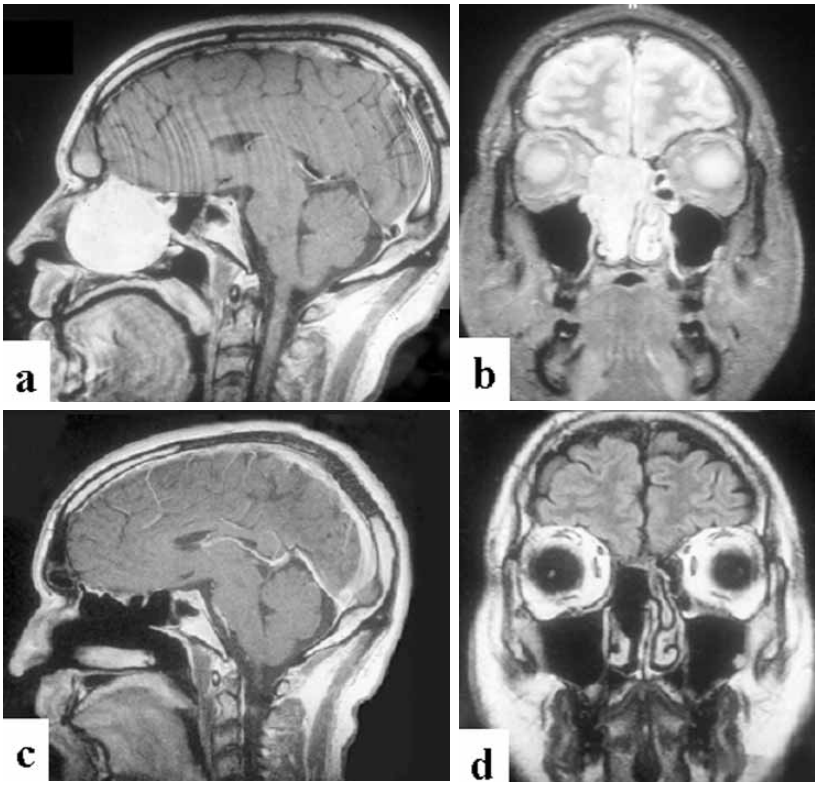

Fig. 1 - ***(a)*** *Preoperative magnetic resonance imaging shows after Gadolinium application tumor extension in the sagittal,* ***(b)*** *coronal plane from the anterior skull base to the nasal floor.* ***(c)*** *Postoperative magnetic resonance imaging 3 years after endonasal tumor resection proves complete tumor resection in the sagittal,* ***(d)*** *coronal plane.*

of 23 MPNSTs and loss of 16p in 1 out of 23 MPNSTs, but no chromosome Y losses in MPNSTs were reported.[16] Chromosomal losses affecting the Y chromosome are quite common in other neoplasms. In 169 CGH studies on 73 different tumor types losses of the chromosome Y were found in 12 % with the minimal overlapping regions Yp and Yq11q12.[17] In further genetic studies on MPNSTs 7p (EGFR), 9p (p16), 17q (NF1,) or 22q (NF2) alterations were suggested to support differentiation between low-grade and high-grade MPNSTs.[18] Thus, our CGH findings give further recognition beyond histopathological grading to classify the presented tumor in accordance with the cytometric DNA-analysis as a low-grade MPNST.

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