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Intracerebral Paraganglioma

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Summary

Paragangliomas of the CNS are relatively rare. Cases of location in the pineal and pituitary glands, cerebellopontine angle, cauda equina and filum terminale are known. In our neurosurgical unit a 42-year-old male patient with a history of vertigo and a generalized seizure underwent an operation for a fronto-temporal tumour. The histological diagnosis was paraganglioma.

Introduction

Paragangliomas are usually benign tumours of the extra-adrenal paraganglia. Despite this, they have a high recurrence rate after surgical resection (10% recurrence rate for paragangliomas of carotid body, 50–60% for other sites) and 10% give rise to metastasis, causing death [3]. Intracerebral locations are very rare: supratentorial paragangliomas have been reported in only ten patients, seven of whom were located in the parasellar area [21]. Possible explanations for an intracerebral location are migration inhibition of neural crest cells and metastasis of an extracerebral paraganglioma. We have identified an intracerebral paraganglioma located fronto-temporally with attachment to the middle cerebral artery (MCA). Current literature is discussed.

Case Report

A 42-year-old male patient had a history of vertigo and a single generalized seizure. Routine clinical and neurological examination on the day of admission exposed no abnormality. However, the neuroradiological investigation, including cranial computed tomography (Fig. 1), magnetic resonance imaging (Fig. 2) and cerebral angiography revealed an irregular contrast medium enhancing pathological structure within the Sylvian fissure extending into the brain. No tumour vessels and no signs of displacement or vessel occlusion due to the lesion were displayed by cerebral angiography.

The patient underwent surgery using the frameless neuronavigation and microsurgical technique. The lesion was approached via the trans-Sylvian route. The tumour was found in the intracerebral zone, encapsulated with a strong attachment to the middle cerebral artery. One small feeder originating from the MCA was completely within the tumour and during dissection it was sacrificed. Finally the tumour was completely removed.

Postoperatively the patient deteriorated clinically, presenting a dense hemiparesis. The postoperative magnetic resonance imaging (Fig. 3) and cranial computed tomography (Fig. 4) confirmed complete tumour removal, but also a caliber reduction of the M1 segment of the MCA. Additionally an infarction was revealed in the area of the basal ganglia.

Histopathological Methods and Results

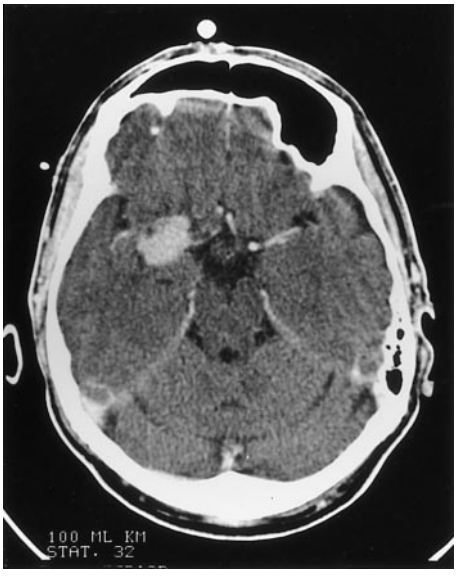
Histological cuts of the neoplasm revealed a rich vasculated tumour composed of lobes. The neoplasma was composed of irregular and lobulated clusters of cuboidal cells (“Zellballen” pattern) separated by thin fibrous septa (Fig. 5). Tumour cells revealed immunohistochemically a strong and diffused reactivity for synaptophysin (Fig. 6) and neuronal specific enolase (NSE). The reaction for S-100 exposed the sustentacular cells more clearly (Fig. 7) and the positive reaction for vimentin indicated the rich vascularization of the tumour. An intracerebral paraganglioma was diagnosed on the basis of these findings.

Discussion

Paragangliomas are tumours derived from the extra-adrenal paraganglia and consist of endocrine cells with the ability to produce catecholamines. As they are neuro-endocrine tumours, paragangliomas belong to the apudomas group. When they are located in the adrenal medulla they are called pheochromocytomas.

They can be most accurately classified as sympathic (e.g. aorticosympathic, most often chromaffin) and parasympathic (e.g. vagal, branchiogenic, most often not chromaffin) forms.

Parasympathic paragangliomas develop from the vessel and nervous system of the branchial arch (bran-



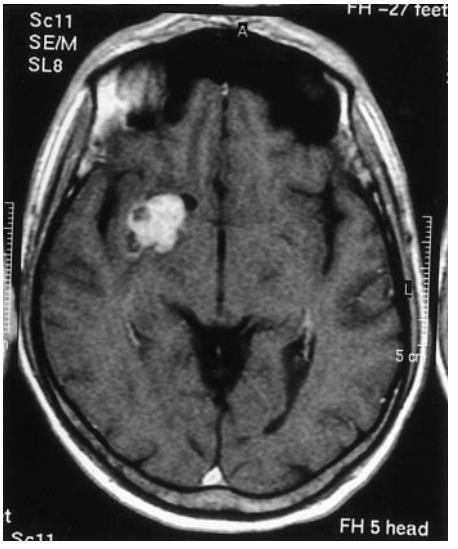
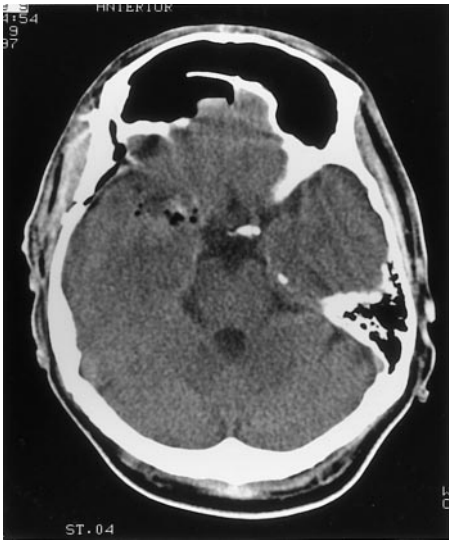


Fig. 1 and Fig. 2. preoperative CCT and axial MRI showing an irregular contrast medium enhancing pathologic structure within the sylvian fissure



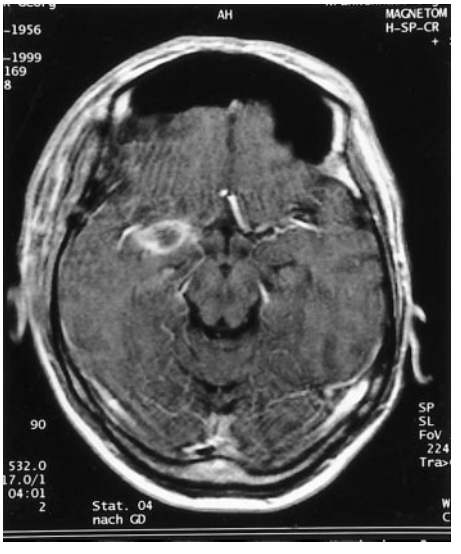


Fig. 3 and Fig. 4. postoperative CCT and axial MRI showing complete tumour removal

chiogenic paraganglias e.g. P. caroticum, P. jugulare, P. tympanicum) or from the peripheral vagus nerve (P. intravagale) and are predominately found in the area of the head, neck and breast. Branchiogenic paragangliomas have chemosensitive receptors which react to oxygen and pH changes in the blood circulation.

Parasympathic paragangliomas are rich vasculated structures and appear intra-operatively, except for the P. jugulare and vagale, as sharply encapsulated structures. Microscopically, the main cells can be separated from sustentacular cells. Important immunohistological markers are chromgranin A, synaptophysin and NSE. S-100 and GFAP indicate the presence of sustentacular cells. Malignant forms are determined by the evidence of metastasis and make up 2–10% of this group [7].

Sympathic paragangliomas develop from the truncus sympathicus and related nerve nets such as Zuckerkandl's organ, and are therefore located intra-abdominally. Sympathic paragangliomas are mor-

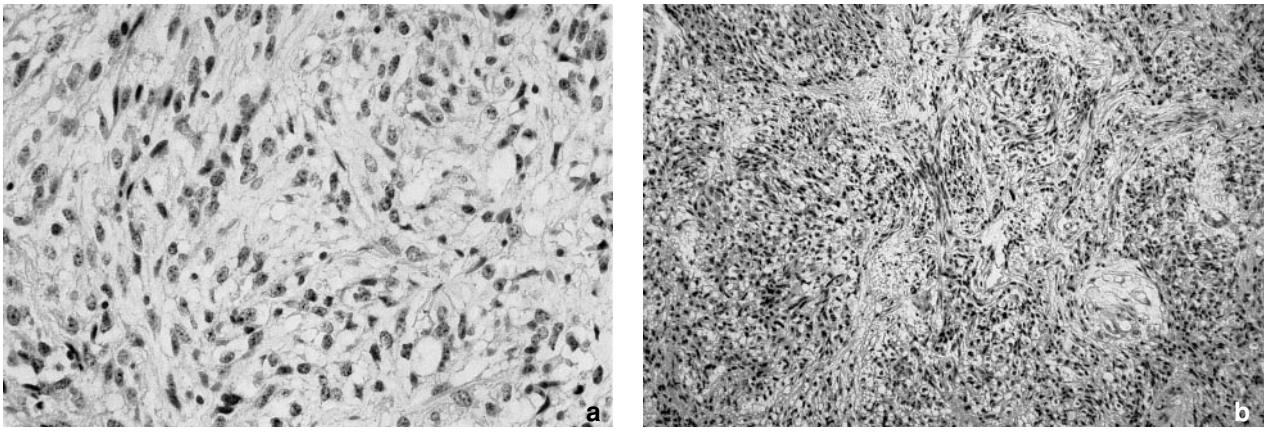


Fig. 5. H & E (a) and PAS (b) stain preparation: lobulated clusters of cuboidal cells (“Zellballen” pattern) separated by thin fibrous septa

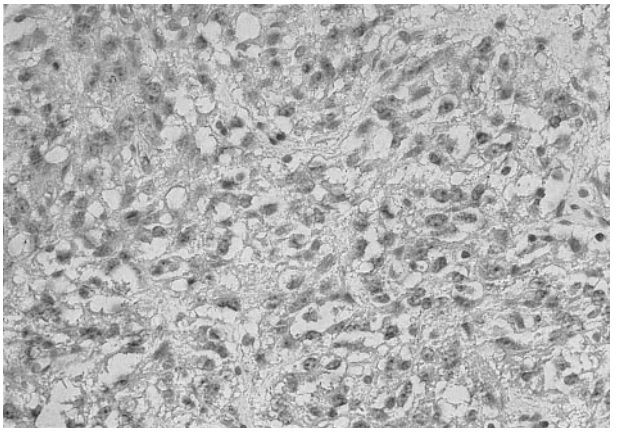


Fig. 6. Immunohistochemical stain preparation: the neoplasma showed a strong reactivity for antibodies against synatophysin

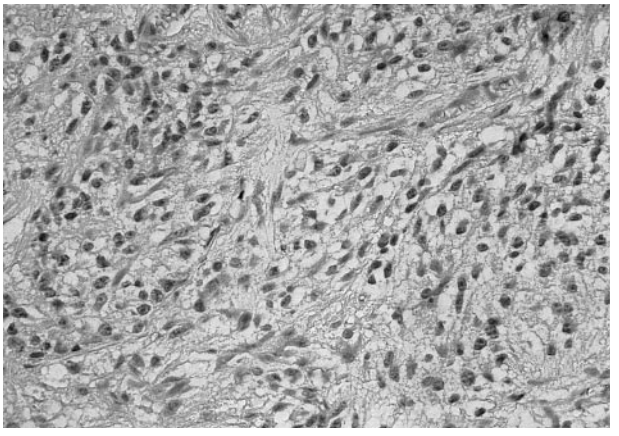


Fig. 7. Immunohistochemical stain preparation: sustentacular cells within the neoplasma stained positive for S-100

phologically identical to pheochromocytomas and can be distinguished immunohistologically from the parasympathic paragangliomas by the absence of GFAP. Malignant forms make up 40% of sympathic paragangliomas (except for the urinary bladder paraganglioma) and are acquired by high mitotic activity, central necrosis, overweight and absent S-100 [7].

The division of paragangliomas into chromaffin and non-chromaffin groups is problematic because the catecholamines responsible for the chromaffin reaction can be found in different concentrations in all paragangliomas and are therefore not a specific marker.

The overall incidence of paragangliomas is very small, with a female predominance of paraganglioma jugulare and vagale. Chronic hypoxia and genetic predisposition promote the formation of paragangliomas.

A clear relationship between the location and frequency of paragangliomas was found by Helpap [5] and Klöppel [7]: P. caroticum 51.9%, P. tympanicum jugulare: 36.6%, P. vagale: 4.4%, intrathoracic paraganglioma: 4.6% laryngeal paraganglioma [9]: 2.5%. They occur very rarely in the P. inferius nodosum, nose and nasal sinus, orbita [19], larynx, para-aortal area, lung [16] and heart [6].

In the lower body they are most often found in the retroperitoneal space [8]. Isolated reports exist of occurrence in the mesentery, mesocolon, stomach [15] and duodenum as well as in the urinary bladder [4].

In CNS the most common location is the cauda equina [10, 13, 14], but paragangliomas have also been reported in the vagal nerve [2, 11], sellar region [17], skull base [12] and filum terminale [1].

But how can an intracerebral location of a paraganglioma be explained? Upon extremely close and careful examination, cell clusters of paraganglias can be found in almost every organ (e.g. urinary bladder,

gallbladder) and so the rare cases of paragangliomas in these organs are understandable.

Two theories exist for the occurrence of paragangliomas in the paraganglia-free cerebral tissue:

a) An intracerebral metastasis of an undiagnosed paraganglioma in an other location [18, 20] must always be considered.
b) A second possibility is that the migration inhibition of cells of the neural crest, which are located in the intracerebral zone, starts to proliferate and in this way an intracerebral paraganglioma is formed.

Before making a definitive diagnosis of an intracerebral paraganglioma, an extracerebral paraganglioma (e.g. P. jugulare, P. vagale, skull base paraganglioma) extended intracerebrally through a foramen of the skull base, must be excluded.

Conclusions

Diffuse bleeding from these rich-vasculated tumours must be anticipated before surgery and as paragangliomas are usually encapsulated, the resection borders are often sharply defined. Annual follow-up cerebral CCT scanning is essential for 10–20 years after resection, as paragangliomas have the tendency to recur and grow very slowly. If an intracerebral metastasis of a paraganglioma is suspected, a further tumour search for the primary tumour location must be undertaken.

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Comment

The authors report the imaging and histopathology of an enhancing temporal lobe lesion which they describe histologically as a paraganglioma.

This is a very interesting case and from the authors description appears to be unique.

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