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Primary midbrain germinoma

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Abstract
Intracranial germinomas arising primarily in the midbrain are extremely rare and only one case has been reported in the literature. A 15-year-old boy presented with headache, diplopia, unsteadiness and personality changes. Brain MRI showed a heterogeneous lesion in the midbrain. The pineal body region was free. The preoperative diagnosis included brain-stem glioma, metastasis and lymphoma. Stereotactic biopsy was permitted in order to take a specimen and the diagnosis of germinoma was established. The patient responded well to chemotherapy and radiotherapy. Germinoma should be included in the differential diagnosis of midbrain lesions. Preoperative diagnosis is difficult and biopsy is still needed for such lesions.

Key words: *Germ cell tumour, germinoma, midbrain*

Introduction

Primary germ cell tumours of the central nervous system are rare malignancies. They appear mainly in the supra-sellar and pineal region of male children, adolescent and young adults.[1] They represent 50% of all the pineal tumours (20–40% in west Europe and 40–70% in Japan). Few publications have reported unusual locations of intracranial germinomas in areas other than the pineal and supra-sellar regions.[2–9] There was only one case report of a germinoma involving the midbrain.[2] We report a new case of midbrain germinoma without concomitant location in the pineal region. Stereotactic biopsy established the diagnosis and allowed appropriate treatment.

Case report

A 15-year-old boy had a history of headache, diplopia and blurred vision. The headaches were mainly bifrontal, their frequency and duration increased progressively, and were not relieved by conventional analgesics. He noted episodes of double vision. Four months before his admission the patient developed unsteadiness. The family also reported recent personality changes and fluctuating mood. The patient was initially managed in another institution where a ventriculo-peritoneal (VP) shunt was inserted and dexamethasone (4 mg TID) started. Neurological examination demonstrated a right hemiparesis and a wide-based gait. He had left sixth cranial nerve palsy with bilateral upward gaze paralysis and impaired papillary reaction to accom-

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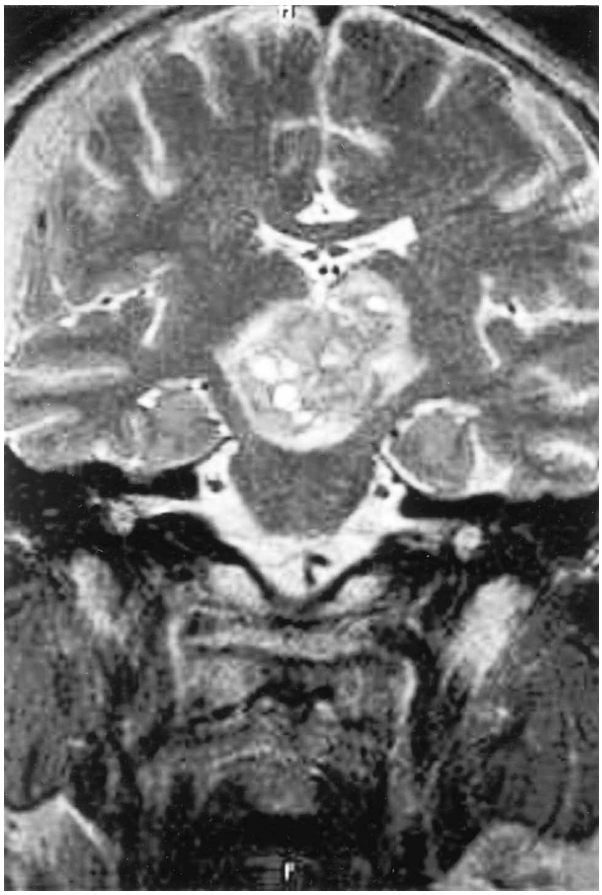

FIG. 1. T2-weighted MR. The lesion is partly cystic. Note the chronic subdural haematoma post-VP shunting.

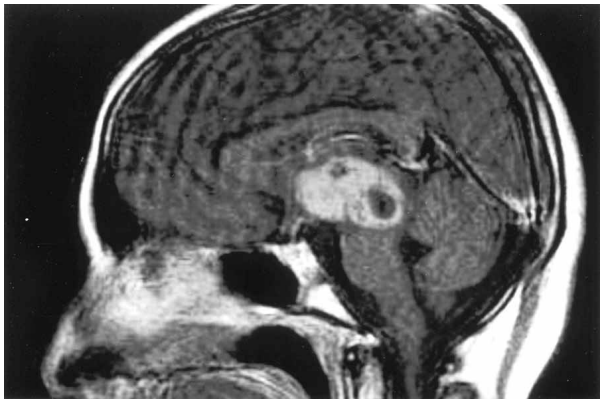

FIG. 2. T1-weighted MR. Axial view post Gd-DTPA: the tumour is heterogeneous involving the midbrain. The pineal region is free.

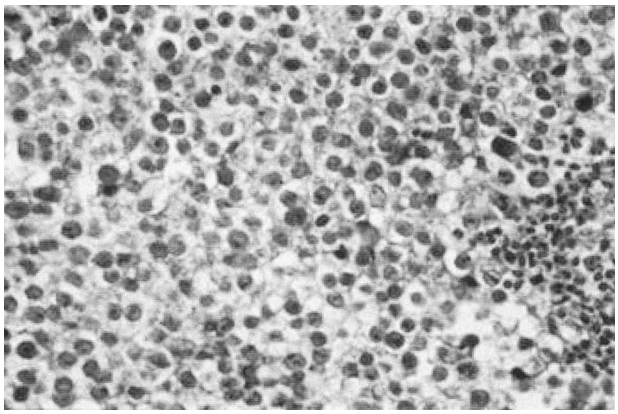

FIG. 3. Photomicrograph of the biopsy specimen. Typical two cells pattern germinoma.

modation. There was evidence of bilateral papilloedema.

MRI showed a mass in the midbrain with significant compression on the third ventricle. It had heterogeneous low intensity on T1-weighted images and a bright signal within it in T2-weighted images consistent with cystic degeneration (Fig. 1). The postgadolinium T1-weighted MRI revealed that the enhanced mass extended to the pons. The pineal body was totally free (Fig. 2). There was also a right hemispheric chronic subdural haematoma following VP shunting. Considering the location, the age of the patient and the MRI aspect of the lesion our preoperative working diagnosis included a tectal glioma, lymphoma or less likely a primitive neuroectodermal tumour. Stereotactic biopsy was performed and two specimens were obtained from the mass. Postoperative period was uneventful. The pathological diagnosis of germinoma was confirmed by H&E staining (Fig. 3) and immunohistochemistry. This showed positivity of the neoplastic cells for placenta alkaline phosphatase and negativity for HCG and AFP.

Biological investigations revealed normal levels of HCG and AFP in both serum and CSF. The patient received four cycles of systemic chemotherapy with cisplatin and etoposide. He received then 45 Gy of local radiotherapy. He tolerated well his treatment with some episodes of headache. Follow-up MRI 3 months later showed no enhancing lesion in the midbrain, but small residual hypointensity (Fig. 4).

On the last examination 1 year after treatment, the patient was headache-free and able to walk with some ataxia. There were no changes of his personality instability and aggressiveness.

Discussion

Primary germinal tumours of the central nervous system appear mainly in the pineal or the suprasellar region. These tumours are more frequent in Japan where they account for 3% of all intracranial tumours.[3] They are thought to arise from remnants of primitive germ cells that have failed to migrate to the genital crest during embryonic life. They show a striking predilection for sites along the midline.[10] The incidence of germinomas in the thalamus and basal ganglia was previously estimated to be 4–10% of all intracranial germinomas.[11] Very uncommon locations have been also reported: optic nerve,[9,12] primary intrasellar[7,8] and spinal cord.[3,4] Recently, Pao-Sheng Yen *et al.*[13] reported a case of primary medulla oblongata germinoma in a 16-year-old girl. Midbrain location of germinoma is extremely rare

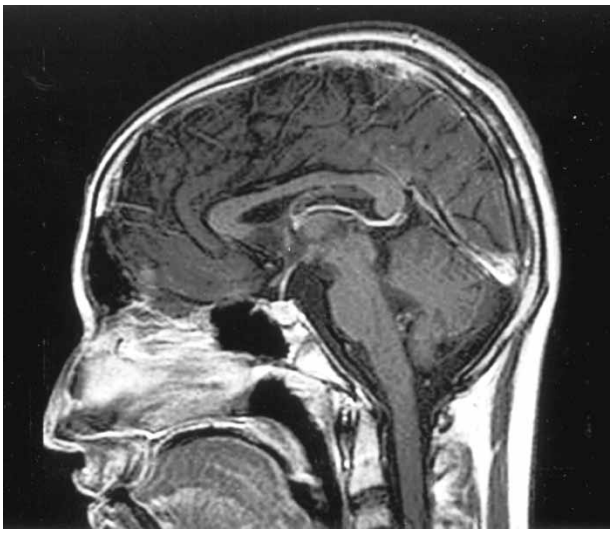

FIG. 4. T1-weighted MR. Sagittal View post-Gd-DTPA: post-chemotherapy and radiotherapy.

and only one previous case has been reported from Japan.[2]

Matsumoto *et al.*[2] reported the case of a 27-year-old man with a 5-year history of diplopia. His symptomatology was dominated by visual disturbance: Parinaud's syndrome and nystagmus. The diagnosis was not possible preoperatively and a stereotactic biopsy led to the diagnosis. The time from onset of symptoms to diagnostic biopsy was protracted in Matsumoto's case (5 years) contrasting with the interval in our case (4 months). Tumour size appeared more important in our case.

Hydrocephalus with intracranial hypertension was present at the time of diagnosis. Personality changes and mood instability noted in our patient may be related to the midbrain tumour itself or to distant effect on the limbic connections. The hydrocephalus could be involved although the symptoms persisted after CSF diversion. Of interest, Coffey[14] reported a case of hypothalamic and basal forebrain germinoma presented with worsening anterograde amnesia and hyperphagia despite having a patent ventriculo-atrial shunt. Behavioural changes have been reported in 12–23% of brainstem tumours. They may even precede the appearance of neurological signs and lead to delay in the diagnosis.[15]

On Matsumoto's patient the brain MRI revealed an iso-intense lesion on T1-weighted and T2-weighted images with homogeneous enhancement after gadolinium injection. In the present case, the lesion was more heterogeneous on T1-weighted postgadolinium and T2-weighted images due to concomitant cystic and solid portions. This pattern is thought to be more common in parenchymal germinoma.[16] The MRI confirmed in our case that the lesion is primary and not metastatic from any other location in the brain. At this stage the clinical and radiological findings were substantially indistinguishable from those of midbrain glioma. The histological aspect of the tumour was typical and did not show any specificity.

That was also the case of germinomas involving uncommon locations.[2–10] Brain-stem tumours constitute a heterogeneous group. Choux *et al.*[17] attempted to classify them according to their anatomical locations and MRI appearance. Focal tumours (type II) are localized in one brain-stem compartment mainly in the medulla and the midbrain.

Most of these tumours were solid and histologically benign astrocytomas. Some authors defined a subgroup of intrinsic brain stem tumours with relatively benign course originating in the upper midbrain.[17] Our patient did not fit in this category. The lesion seemed to extend to the peduncles and partly to the thalamus. The enhancement was heterogeneous and the borders ill defined. These reasons led to the decision to take a biopsy before attempting any debulking. Stereotactic biopsy is currently safe and highly diagnostic. Steck & Friedman[18] reported their experience stereotactically biopsying 24 brain stem mass lesions. Seven of them had a lesion in the midbrain. Their morbidity and mortality were low (respectively two cases and one case). Friedrich *et al.*[19] concluded that a stereotactic approach to pineal region is a relatively safe procedure. The histopathological diagnosis obtained by CT-guided stereotactic biopsy was a valid basis for treatment decision. In the present case, the diagnosis of germinoma could not be made preoperatively. The presumed differential diagnosis included brain stem glioma, lymphoma and metastasis. In their series of midbrain lesions Steck & Friedman[18] reported a heterogeneous histopathological diagnosis in their adult population. The lesions were, however, uniformly astrocytic ones in their paediatric patients. Lymphoma of the midbrain has been rarely reported; most of the cases[20] originate from the basal ganglia and extend to the midbrain. Radiotherapy is a very efficient treatment regardless of the location of the germinoma. Matsutani *et al.*[21] reported an excellent 20-year survival rate up to 80%. Chemotherapy with etoposide and cisplatin was given in our case viewing the encouraging recent published results.[22] Follow-up brain MRI showed total disappearance of the tumour (Fig. 4). Late recurrences are possible and close observation is still mandatory.

Conclusion

Germinoma of the midbrain is a rare entity. It should be included in the differential diagnosis of midbrain tumours. The diagnosis can be established safely by stereotactic biopsy. The prognosis is probably as good as the classical pineal region germinomas with excellent response to radiotherapy and chemotherapy.

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