GLIOBLASTOMA MULTIFORME OF THE PINEAL REGION

Case report

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ABSTRACT - Purpose: pineal region tumors are uncommon, and comprise more frequently three categories: germ cell, parenchymal cell and glial tumors. Most pineal gliomas are low-grade astrocytomas. Glioblastoma multiforme, the most aggressive and common brain tumor, is extremely rare at this location with only few cases reported. Case description: a 29-year-old woman with a two month history of headache, nuchal pain, fever, nausea and seizures and physical examination showing nuchal rigidity, generalized hypotony, hypotrophy and hyper-reflexia, Babinski sign and left VI cranial par palsy. CT scan examination revealed a ill-defined hypodense lesion at the pineal region with heterogeneous contrast enhancement. MRI showed a lesion at the pineal region infiltrating the right thalamic region. The patient underwent a right craniotomy with partial resection of the mass. The histological examination of paraffin-embedded material defined the diagnosis of glioblastoma multiforme. Post-operative radiotherapy was indicated but the patient refused the treatment and died two months afterwards. Conclusion: in spite of its rarity at this location, glioblastoma multiforme should be considered in the differential diagnosis of aggressive lesions at the pineal region.

KEY WORDS: brain tumor, pineal gland, glioblastoma multiforme.

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Received 9 August 2002, received in final form 26 November 2002. Accepted 7 December 2002.

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Pineal region tumors are rare, comprising 0.4% to 1% of adult brain tumors1,2. Despite its small size, the pineal gland is the origin of a surprisingly diverse array of tumor types. The three major categories are germ cell tumors, parenchymal cell tumors, and the supporting tissues neoplasms (glial tumors). Germinomas are the most common histological type, comprising 50-60% of all pineal tumors3,4. Gliomas account for 33% of pineal neoplasms, but are mainly low grade astrocytomas1,4. Pineocytomas and pineoblastomas can also be found. Glioblastoma multiforme (GBM), the most malignant and frequent brain tumor, is rare at this location with only few cases reported1,5-12.
We present a patient with GBM of the pineal region emphasizing the imaging findings and the review of the literature reported cases.

CASE

A 29-year-old woman presented with a two-month history of headache, nuchal pain, drowsiness, fever, nausea, dizziness and seizures. Physical examination revealed nuchal rigidity, horizontal nystagmus, generalized hypotony, hypotrophy and hyper-reflexia, decrease in muscle strength in all four limbs, Babinski’s sign and left VI cranial nerve palsy. At this time, a hydrocephalus was diagnosed and the patient underwent a ventricle-peritoneal shunt. The CT-scan examination showed a rounded hypodense ill-defined lesion at the pineal region with extension to the right thalamus. After contrast administration the mass showed heterogeneous enhancement (Fig 1 and 2). The MRI revealed a lesion at the pineal region with malignant characteristics infiltrating discretely the right thalamic region. On account of the size of the mass and its extension to thalamus, the patient underwent a right parieto-occipital craniotomy with a transtentorial approach (Ausman technique) in order to excise the lesion. The surgery revealed a yellow swelling and bleeding mass, which was partially (60%) excised.

Histopathological study of the resected tissue revealed a lesion composed of highly anaplastic glial cells, with mitotic activity, microvascular proliferation and areas of necrosis, defining the diagnosis of GBM (Fig 3 and 4).

The after surgery period elapsed normally in spite of a right hemiparesis, which was not present when the patient went home. At this time radiotherapy was recommended but the patient refused the treatment and died two months afterwards.

DISCUSSION

The pineal region is defined as the space delimited superiorly by the splenium of the corpus callosum and choroid plexus of the third ventricle, anteriorly by the third ventricle, antero-inferiorly by the lamina quadrigemina, inferiorly by the anterior face of the cerebellum culmen and laterally by the thalami and medial faces of the cerebral hemispheres. The tumors of the pineal region are uncommon, ranging from 0.5 to 2% of all intracranial neoplasms in several review papers. The origin of the tumors of this region can be the pineal gland itself, the posterior portion of the third ventricle and the quadrigemina cistern. The symptoms are generally related to the compression of the adjacent structures and not related to the histopathology of the tumor. The most frequent symptoms are hydrocephalus (compression of the Sylvius aqueduct) and dysfunctions of the eyes movement. CT-scan and MRI make the diagnosis of the presence of the pineal region tumor. These tumors are usually variable in shape, often irregular, with thick walls (more than 2 mm), larger than 20 mm, frequently compressing neighbor structures and infiltrative. The MRI is essential to analyze the tumor characteristics and its relation to neural and vascular structures. The association of the MRI (or CT image) and the clinical data may suggest a possible diagnosis. For instance, a young man with a homogeneous, round tumor probably has a germ cell tumor. The hypodense pineal mass with heterogeneous contrast enhancement and invasion of the adjacent space is characteristic of GBM.
Fig 2 (A) and (B). Axial CT scan after contrast injection revealing heterogeneous enhancement of the mass and demonstrating the invasion of the right thalamus (arrow).

Fig 3. Histological section showing a tumor composed of anaplastic glial cells with mitosis and extensive area of necrosis (N) (HEx40).

thalamus presented in our case denotes a malignant lesion and has to be differentiated from any other malignant lesion of the pineal region. The main aspects for this differentiation are discussed below. However, the final diagnosis should only be given with the histopathologic examination. The majority of the pineal region tumors appears to be of germ cell origin and include germinomas, teratomas, and less commonly, embryonal carcinoma and choriocarcinoma. In fact, the pineal region is the most common site of intracranial germinomas and teratomas. These tumors usually develop in the first two decades of life and predominate in males\textsuperscript{1,4,11}. The germinomas would appear hyperdense on CT-scan, with a strong contrast enhancement. MRI would show a lesion isodense to the gray matter. The teratomas do not have
Fig 4. Histological section showing in detail a vessel with proliferation, common in glioblastoma multiforme (HEx100).

Table 1. Clinical and imaging findings of 10 cases diagnosed as glioblastoma multiforme of the pineal region.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Clinical presentation</th>
<th>CT scan findings</th>
<th>Treatment</th>
<th>Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho et al.5</td>
<td>male</td>
<td>63</td>
<td>↑I CP and changing behavior</td>
<td>Hyperdense pineal mass with ring contrast enhancement and hydrocephalus</td>
<td>Surgery and RTX</td>
<td>6</td>
</tr>
<tr>
<td>de Girolami et al.6</td>
<td>female</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>RTX and CTX</td>
<td>18</td>
</tr>
<tr>
<td>Frank et al.7</td>
<td>male</td>
<td>36</td>
<td>↑I CP, Parinaud’s syndrome, hearing loss and tremors</td>
<td>Third ventricle mass and hydrocephalus</td>
<td>RTX</td>
<td>4</td>
</tr>
<tr>
<td>Kalynaraman 8</td>
<td>female</td>
<td>52</td>
<td>↑I CP and oculomotor nerve disturbance</td>
<td>-</td>
<td>RTX</td>
<td>4</td>
</tr>
<tr>
<td>Norbut et al.9</td>
<td>female</td>
<td>68</td>
<td>Ataxic gait, dementia, blurred vision and upward gaze palsy</td>
<td>Calcified midline mass and hydrocephalus</td>
<td>Surgery and RTX</td>
<td>4</td>
</tr>
<tr>
<td>Pople et al.10</td>
<td>male</td>
<td>50</td>
<td>-</td>
<td>Hydrocephalus</td>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td>Vaquero et al.11</td>
<td>female</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bradfield et al.14</td>
<td>-</td>
<td>-</td>
<td>↑I CP and vertical gaze palsy</td>
<td>-</td>
<td>Surgery and RTX</td>
<td>-</td>
</tr>
<tr>
<td>Bradfield et al.14</td>
<td>-</td>
<td>-</td>
<td>↑I CP</td>
<td>-</td>
<td>RTX</td>
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<tr>
<td>Bradfield et al.14</td>
<td>-</td>
<td>-</td>
<td>↑I CP</td>
<td>-</td>
<td>RTX</td>
<td>-</td>
</tr>
<tr>
<td>Gasparetto et al.</td>
<td>female</td>
<td>29</td>
<td>↑I CP, fever, seizures</td>
<td>Hypodense pineal mass with heterogeneous contrast enhancement</td>
<td>Surgery</td>
<td>2</td>
</tr>
</tbody>
</table>

↑I CP, symptoms of increased intracranial pressure; RTX, radiotherapy; CTX, chemotherapy.
a specific image characteristic usually appearing as mixed density/intensity lesions.

The neoplasms originating from the pineal parenchymal cells occur with considerably less frequency. This tumors include pineocytoma, which is composed of relatively mature pineal cells, and the pineoblastoma, a more immature, poorly differentiated neoplasm. These tumors tend to occur in a slightly older age group and occur evenly in males and females. The pineocytomas are radiologically indistinguishable from the benign pineal cysts. The pineoblastomas appear as big non-encapsulated masses with a strong or heterogeneous contrast enhancement and frequently invade the adjacent parenchyma.

Additional tumors arising from the glial components of the pineal gland include ganglioneuroma, ganglioglioma, chemodectoma, meningeoma, and gliomas, more frequently low-grade astrocytomas. The gliomas originate either from the glial tissue of the pineal gland (astrocytes are a normal component of the pineal gland) or from the glial cells of the vicinity of this gland, such as the posterior portion of the third ventricle or the lamina quadrigemina. The low-grade astrocytomas would appear on CT-scan as iso or hypodense lesions with heterogeneous moderate contrast enhancement. MRI would show an iso or hypointense lesion on T1-weighted image and hyperintense on T2-weighted images. Edema, hemorrhage and contrast enhancement are common features. Nonneoplastic processes that may also simulate a pineal tumor at this location include epidermoid, dermoid and glial cysts.

Although GBM (WHO’s astrocytoma grade IV) is the most frequent brain tumor, it is exceedingly rare at the pineal region with only few reported cases. Because these tumors are usually included within series of pineal region tumors it is difficult to study the clinical and imaging features of these cases (Table 1). However, in 7 cases the age and sex of the patients were recorded. The age ranged between 6 and 68 years (mean age: 50 years). The predominant symptoms were related to hydrocephalus and ophthalmologic symptoms (specially Parinaud’s syndrome). The CT scan examination often showed hydrocephalus. The lesion on CT has different patterns such as a calcified mass in the midline, a mass lesion in the posterior third ventricle, or a rounded hyperdense mass at the pineal region with ring enhancement after contrast administration. One of the reported cases had a diffuse leptomeningeal involvement, with spinal subarachnoid metastases. In all cases which survival time has been reported the prognosis had been poor.

The presented case, along with the others previously reported, suggest that the GBM, in spite of its rarity at this location, should be considered in the differential diagnosis of aggressive lesions at the pineal region.

REFERENCES