CASE REPORT

A headache presenting in the emergency room, a clinical manifestation of an unfortunate diagnosis (grade III left frontal anaplastic ependymoma with 1p deletion)

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SUMMARY

An 18-year-old girl presented with a headache and behavioural changes. She was found to have a frontal mass. Neuroimaging revealed an intra-axial mass, located at the left frontal cortical/subcortical region approximately 6×7, 5×7, 5 cm (TxApXL), having a heterogeneous density with cysts and calcification. She had total gross excision of the neoplasm. Histopathological examination revealed an anaplastic ependymoma. Fluorescence in situ hybridisation, a molecular cytogenetic test, reported deletion of 1p without deletion of 19q. The patient had a good postoperative improvement.

6×7, 5×7, 5 cm with cystic and calcified areas corroborated by MRI (figures 1–3). The patient was admitted to neurosurgery.

DIFFERENTIAL DIAGNOSIS

- Oligodendroglioma
- Papiloma

TREATMENT

Neurosurgeons performed a complete excision of the mass without complications (figures 4 and 5). The pathology showed neoplastic cells with little nuclear atypia arranged differently in different parts of the tumour. In some areas, there was a predominant presence of numerous cells with clear cytoplasm and nuclei located in the centre of the cells (figure 6). In other areas, there was a tendency

BACKGROUND

Ependymomas are a rare group of tumours arising from ependymal cells of the ventricular system (central nervous system).¹ Ependymomas are uncommon nervous system tumours constituting less than 10% of all intracranial neoplasms.^{2–8} Purely extraventricular ependymomas with no connection to ventricular lining are extremely rare. This is a case of an ependymoma in the cortical/subcortical extraventricular region with a 1p deletion.

It is very important for an emergency room (ER) doctor to determine which patients, presenting with headaches, are high risk and take a decision.

CASE PRESENTATION

A previously healthy 18-year-old girl presented to the ER with a 15-day sudden frontal headache. Previously assessed twice and prescribed acetaminophen and naproxen without any improvement. Within 48 h of consultation, her headache became worse and was now experiencing disorientation and behavioural changes consistent with abulia. Physical examination revealed conceptual apraxia, abulia, no focal neurological signs, cranial nerves preserved, no neck stiffness, no papilloedema, sensation and reflexes were normal, and no history of seizures.

INVESTIGATIONS

Emergency management

Blood chemistry, complete blood count, coagulation and haematocrit were normal. CT scan revealed an intra-axial mass, located at the left frontal cortical/subcortical region approximately

Figure 1 A cortical/subcortical intra-axial mass measuring 6×7, 5×7, 5 cm, found in the left frontal region, demonstrating intralesional heterogeneous density with cystic and calcified areas. There is also a small amount of perilesional oedema causing the mass effect on the left lateral ventricle and midline shift of approximately 5 mm. Suggesting a malignant process.

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Figure 2 A heterogeneous cortical/subcortical lesion with intralesional hypointense foci, as calcium deposits observed in the T2 sequence. After administering gadolinium, a polycystic component was discovered with a more solid area superior to the lesion.

of the cells to be placed in a perivascular formation (perivascular pseudorosettes). Others had true-type forming rosettes with ependymal calcifications in proximity (see figure 7). In the immunohistochemical study, the tumour expresses glial fibrillary acidic protein, synaptophysin (weak expression) and epithelial membrane antigen (with a characteristic pattern of fine granular intracytoplasmic expression). It was negative for chromogranin. The proliferative index (Ki-67) was 30%. Fluorescent in situ hybridisation (FISH), a molecular cytogenetic test, reported deletion of 1p without deleting 19q. A WHO grade III frontal left ependymoma with 1p deletion was the diagnosis given. We can see that the tumour makes contact with the left frontal horn of the lateral ventricle's wall and displaces the ventricle, but does not invade it. During tumour resection surgeons stated that there was no ventricular invasion (figure 8).

Figure 3 A practically complete resection of the left/frontal intraparenchymatous tumour consisting of solid and cystic components.

Figure 4 Complete tumour resection.

OUTCOME AND FOLLOW-UP

Ten days after surgical resection the patient was discharged with neurological improvement and an appointment to review pathology results and evaluate the need for radiotherapy. During the hospitalisation steroids were administered to prevent complications of oedema.

DISCUSSION

The most common infratentorial sites affected are the fourth ventricle (the extension to the subarachnoid medulla) and the upper cervical cord.⁹

Supratentorial ependymomas have better prognosis than the infratentorial.¹⁰ This may be related because supratentorial ependymomas have complete resection performed more often.¹⁰

Ependymoma is a tumour that anatomically would be an uncommon find in the frontal cortical/subcortical region. This case reported 1p deletion without a 19q deletion. These deletions are more frequent in patients with oligodendroglioma, although, tumours can be reported in other anatomical locations. Evidence has shown origin sites in the spinal cord and supratentorial posterior fossa.¹¹ The clinical divergence was observed in cells that look of 'fried egg' that characterise the oligodendroglioma (although not pathognomonic). However, by looking at the ependymal rosettes (which is a pathognomonic finding) a final diagnosis is reached. Neither the weak expression of synaptophysin primitive neuroectodermal tumour nor the isolated 1p deletion (which would support oligodendroglial lineage tumour) in the FISH technique contradict the diagnosis of ependymoma because both events can occur in these tumours (although this is rare). However, the extensive necrosis

Figure 5 A 4.6 cm resected tumour with irregular borders and heterogeneous yellow necrotic areas.

Figure 6 Cells with a fried egg appearance (large nucleus) suggest oligodendroglioma. This characteristic can appear in different neoplasias.

and, above all, the high-proliferative index with Ki-67 (in this case 30%) gave this neoplasm greater biological aggressiveness. Clinical manifestations depend on the location of the tumour. When the tumours are supratentorial, focal neurological deficits or seizures are common presentations. However, our patient presented with aphasia.⁹ The initial treatment consisted of the complete excision of the lesion. The outcome depends on the extent of the surgical resection.¹² Many consider that incomplete resections require a follow-up surgery after chemotherapy to see if clearance has been achieved.⁹ To reduce the possibility of recurrence, radiotherapy is the standard postoperative treatment for tumours in the posterior fossa and supratentorial region. However, some disagree with radiotherapy as treatment in patients with a completely resected tumour.^{9 13 14}

Chemotherapy is used mainly in patients with incomplete resection of the tumour. Major studies have been conducted in children using more effective agents such as etoposide, carboplatin and cisplatin.⁹ A cooperative group study has demonstrated, with 32 patients, a 40% complete response to preradiation chemotherapy, while 14% demonstrated progressive tumour growth.¹⁵ There was 5-year overall survival rate of 71% for all patients.⁹ Chromosomal changes—deletion of CDKN2A and gain of chromosome 1 are associated with shorter overall and progression-free survival. In contrast, loss of chromosome 6 or gains of chromosomes 9, 15 or 18 were associated with

Figure 7 The arrows indicate the pathognomonic ependymal rosettes.

Figure 8 In the image of RM with gadolinium we can see that the tumour makes contact with the left frontal horn of the lateral ventricle's wall and displaces the ventricle, but does not invade it.

significantly better overall and progression-free survival.¹⁶ The group of Tong *et al*¹⁷ found multiple genomic imbalances in ependymomas resected in 20 adults and 8 children, including loss of chromosomes 1p, 6, 16, 17, 19q, 20q and 22q, as well as gain of chromosomes 4q, 5q, 7q, 9q and 12q on comparative genomic hybridisation. The aim of this study was to map in more detail the commonly affected regions in ependymomas.¹⁷ For example, the treatment of anaplastic oligodendroglioma and anaplastic oligoastrocytoma is influenced by the 1p/19q status, as allelic codeletion of chromosomes 1p and 19q predicts increased sensitivity to chemotherapy and prolonged survival.¹⁸ Literature has not shown an association between 1p deletion without 19q and a prognosis.^{19–23}

Headaches represent 5% of ER visits. A well-documented history and physical examination are the most important factors in determining the aetiology. It is very important for an ER doctor to determine which patients presenting with headaches are high risk. Criteria for determining high-risk patients are as follows: sudden onset and intense headache, no medical history of similar events, coinfections, behavioural changes, strain-associated headaches, first episode if over 50 years old, immunocompromised, neurological sequelae, altered mental status, complex partial seizures, meningism and papilledema.²⁴

This rare case serves as a good example of the importance for ER doctors to recognise which patients fit the high-risk criteria for headaches.

Learning points

- ▶ This rare case serves as a good example of the importance for emergency room doctors to recognise which patients fit the high-risk criteria for headaches.
- ▶ Although a 'fried egg' appearance on histological examination is suggestive of oligodendroglioma it is not pathognomonic. Observing, in this patient, the ependymal rosettes (which is a pathognomonic finding) a final diagnosis of ependymoma can be reached.
- ▶ It is very important for emergency room doctors to determine which patients presenting with headaches are high risk (for example in this patient).

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