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CASE REPORT

Giant cell ependymoma of the cervical spinal cord: case report and review of the literature

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Abstract Ependymomas account for 2–6% of all central nervous system neoplasms. They develop from the ependymal cells that line the ventricular cavities of the brain and the central canal of the spinal cord, as well as from ependymal clusters in the filum terminale. Giant cell ependymoma (GCE) is a rare subtype, with few cases reported, mostly in the brain. We describe the case of a cervical spinal cord ependymoma with pleomorphic giant cells and focal calcifications occurring in a 25-year-old woman. Magnetic resonance imaging revealed a large multicystic and partially enhancing intramedullary tumour extending from C2 to C5. Intraoperative analysis of frozen section tissue fragments suggested a malignant tumour; however, an obvious cleavage plane was present around most of the mass, and a macroscopically complete tumour removal could be achieved. Subsequently, paraffin sections and immunohistochemical investigations revealed unequivocal evidence of a GCE with focal calcifications. This case, the second giant-cell ependymoma to be described in the spinal cord and the first with focal calcifications, highlights the features of GCE and the discrepancy between the worrisome histological appearance, the surgical findings and the clinical relatively good prognosis.

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Introduction

Ependymomas are uncommon central nervous system (CNS) neuroepithelial tumours arising from the ependymal cells lining the ventricular cavities of the brain and the central canal of the spinal cord, as well as from ependymal clusters in the filum terminale. They account for about 2–6% of CNS tumours [13, 18], and for 60–70% of spinal cord tumours [5]. Ependymomas with several morphological features and different biological behaviour have been described [5].

Giant cell ependymoma (GCE) is a rare subtype, first described in 1996 [19], characterized histologically by the presence of pleomorphic giant cells and clinically by a favourable prognosis. Differential diagnosis of GCE includes anaplastic oligodendroglioma, subependymal giant cell astrocytoma, pleomorphic xanthoastrocytoma and giant cell glioblastoma [1]. So far, only eight cases of GCEs have been reported.

We describe the second case of spinal cord GCE, and the first with intratumoural focal calcifications.

Case report

A 25-year-old woman presented with a 7-month history of progressive upper extremities movement difficulty; particularly, the right upper limb abduction and flexion–extension movements of both forearms appeared to be impaired. The patient also complained of muscular tension and subjective weakness of lower limbs. Over the next

months her clinical picture included impaired gait, because of difficulties in flexing the right leg, and raised frequency of micturition. Yet, during the last weeks before admission she reported onset of hypoesthesia in the last two fingers of both hands. Neurological examination revealed weakness of the right upper limb abduction (4−/5 BMRC—British Medical Research Council) and of the left one (3/5); weakness of biceps (4/5), of the right (4+/5) and left (4/5) triceps as well as of the right hallux dorsiflexion (4−/5). Sensory examination showed pinprick and light touch reduced sensation from C4 downwards. Medium and lower abdominal reflexes were absent, the superior being present only on the left side. Hoffmann and Babinski signs were present bilaterally (right > left). Sustained, and occasionally spontaneous, patellar clonus was present in the lower limbs. Obvious signs of lower extremities spasticity and ataxic gait were also evident.

Routine haematological investigation was normal. A plain cervical spine X-ray showed a slight reduction of the C3–C4 and C4–C5 disc spaces height.

A sagittal, T1-weighted, gadolinium-enhanced, magnetic resonance imaging (MRI) scan revealed a large, multicystic, and partially enhancing, cervical intramedullary tumour extending from C2 to C5, along with satellite "syringomyelic cavity" extending from C1 down to Th1 (Fig. 1a). Such "syringomyelic cavity" and cysts were clearly shown on T2-weighted, sagittal images (Fig. 1b). The patient underwent a C2–C5 laminotomy. After performing the myelotomy, a firm and rubbery mass, purple in colour with mixed grey and yellow patches, was identified. Small cystic areas were present within the tumour. Upon dissection off the neural tissue, the mass appeared to be well-circumscribed and with an obvious interface (cleavage plane) with normal tissue; macroscopically its features were compatible with a poorly infiltrating neoplasm. Despite such surgical findings, frozen section analysis of the initial few small tissue fragments was not conclusive for a less aggressive, "low-grade" neoplasm, but rather for a high-grade, malignant tumour. In fact, there were non-cohesive giant cells with single or multiple hyperchromatic nuclei, evident nucleoli and plump eosinophilic cytoplasm. However, as features of an infiltrating tumour were only present in a small area, rostrally on the left side, and an obvious cleavage with the medullary tissue could be identified around all the remaining mass, a gross total resection of the tumour was performed using standard microsurgical technique. After closing the arachnoid and suturing the dura mater, the laminar plateau was repositioned and secured with miniplates.

In the early postoperative course a neurological worsening with deltoid, biceps and triceps weakness was evident bilaterally. No changes in strength were recorded either in the hands or in the lower limbs, and no changes were observed in sensation, muscle tone and gait. However, she was started on rehabilitation therapy and over time gradually improved neurologically.

At 18-month follow-up strength is normal and superficial sensation is mildly reduced in the upper limbs; gait is normal. Sagittal, T1-weighted, gadolinium-enhanced, MRI confirmed the complete tumour removal and absence of recurrences (Fig. 1c).

Pathological examination

The surgical specimen consisted of a nodular mass of soft red-to-grey tissue fragments measuring up to 4.5 cm in greatest dimension. The paraffin sections, stained with haematoxylin and eosin (H&E), revealed a moderately cellular tumour with a biphasic pattern. One pattern was characterized by a monomorphous proliferation of neoplastic cells with perivascular pseudorosettes (Fig. 2). A few ependymal canals lined by small columnar cells and

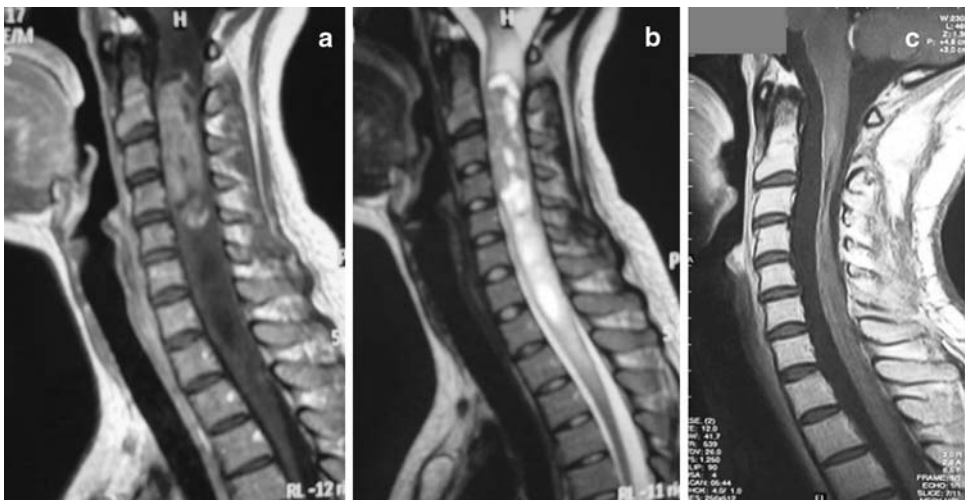

Fig. 1 **a** Sagittal, T1-weighted, gadolinium enhanced, magnetic resonance imaging (*MRI*) showing a large multicystic and partially enhancing cervical intramedullary tumour extending from C2 to C5. A syringomyelic cavity is present from C1 to Th1. **b** Sagittal, T2-weighted MRI demonstrating intratumoural cysts and the satellite syringomyelic. **c** One-year, sagittal, T1-weighted, gadolinium-enhanced MRI showing the complete tumour removal, and absence of recurrence

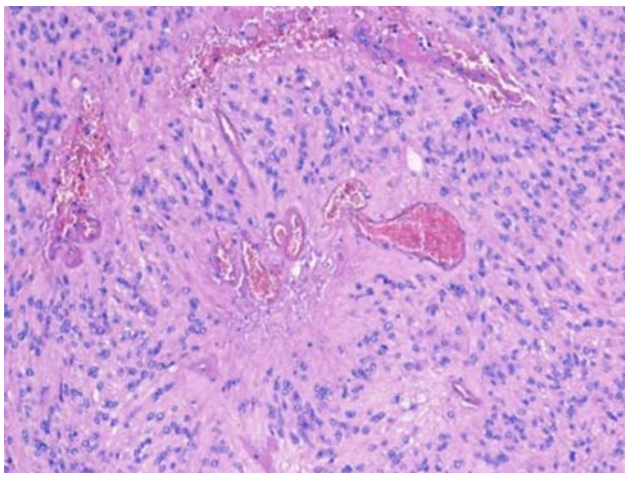

Fig. 2 Monomorphous proliferation of neoplastic cells with perivascular pseudorosettes (H&E ×10)

eosinophilic inclusions were also observed. The second pattern, observed only in one-third of the tumour area, was characterized by non-cohesive giant cells, with rhabdoid-like features, near foci of calcifications. These cells were round or oval with eccentrically single or multiple hyperchromatic nuclei, evident nucleoli and plump eosinophilic cytoplasm (Fig. 3). Mitoses or necrosis were not observed in the areas with perivascular pseudorosettes and pleomorphic giant cells. Immunohistochemically, both the giant cells and the cells forming perivascular pseudorosettes strongly expressed GFAP (Fig. 4), S-100 protein and vimentin in the cytoplasm. EMA was positive only in few neoplastic cells and stained the cell surfaces of true rosettes. CD99 was immunoreactive in diffuse strong membranous and cytoplasmic dot-like pattern. The Ki-67 labelling index was about 2% in the areas with perivascular pseudorosettes and negative in the giant cell areas.

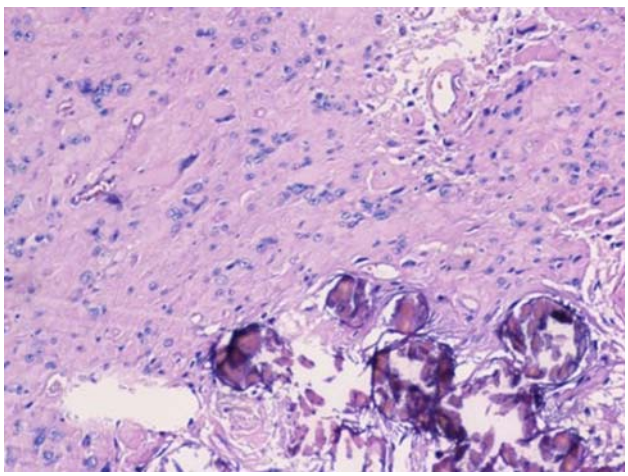

Fig. 3 Non-cohesive giant cells, with rhabdoid-like features, near foci of calcifications (H&E ×10)

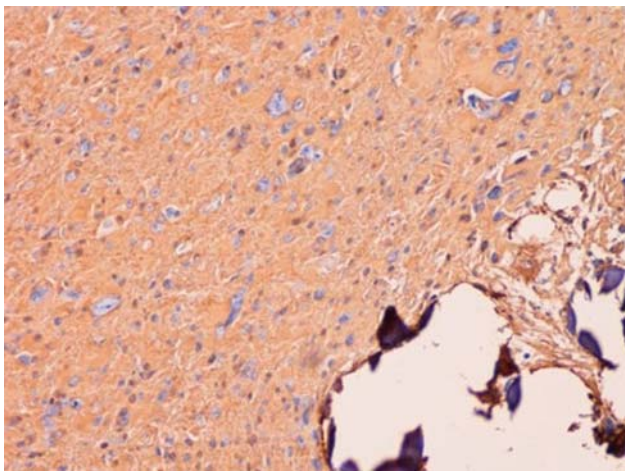

Fig. 4 GFAP immunostaining in the giant cell areas (×10)

Considering the morphological aspect and immunohistochemical features, a diagnosis of GCE of the cervical spinal cord was made.

Discussion

According to the World Health Organization (WHO) classification, the term ependymoma comprises a histologically heterogeneous group of tumours that include cellular, papillary, clear cell and tanycytic subtypes. Ependymoma with lipomatous differentiation [17], ependymoma with extensive tumour cell vacuolization [8], melanotic ependymoma [16], signet-ring cell ependymoma [20] and GCE are rare variants.

Zec et al. [19] first described two cases of giant-cell ependymoma of the filum terminale in 1996. They suggested that the absence of perivascular pseudorosettes in GCE might reflect the failure of the neoplastic cells in this tumour to elaborate perivascular processes.

To date eight cases of GCE have been documented in the literature [1, 3, 6, 7, 10, 14, 15, 19]; only one of these was located in the spinal cord [7]. Our case is the second example of a cervical spinal cord GCE, and the first with focal calcifications.

Recognizing ependymoma in frozen sections can be difficult, particularly in cases without the characteristic epithelial features and perivascular pseudorosettes. On frozen sections ependymoma often appear distinctly astrocytic because the freezing process exacerbates the fibrillarity and gemistocyte-like appearing of the neoplastic cells.

In the present case the tumour appeared to have a definite cleavage plane for almost its entire extension, a minor area of apparently infiltrating lesion being localized rostrally on the left side. Intra-operatively, in view of both the

surgical anatomical features of the mass and the relatively ease of its dissection off the spinal cord, the neoplasm appeared less-infiltrating and less-aggressive. Therefore, given such gross appearance and surgical features, although frozen section analysis suggested a high grade, malignant tumour, the decision to continue debulking the mass until total macroscopic removal was taken. Subsequently, only paraffin sections and immunohistochemical investigations revealed unequivocal evidence of an ependymal tumour with pleomorphic giant cells and focal calcifications.

The histological grading of ependymomas has been a matter of debate, and the wide range in the incidence of anaplastic ependymoma (7–89%) highlights the difficulty in agreeing on a histological grading system [12]. One of the reasons for such conflicting results are the histopathological criteria currently used to classify an ependymoma as benign or malignant. These are often subjective and not clearly defined. Our case did not satisfy the criteria established by the WHO for anaplastic ependymoma because no significant mitotic activity, microvascular proliferation and pseudopalisading necrosis were present.

Differential diagnosis of GCE includes anaplastic oligodendroglioma, subependymal giant cell astrocytoma, pleomorphic xanthoastrocytoma and giant cell glioblastoma [1]. GCE has a good prognosis [19] because, as well as in subependymal giant cell astrocytoma [4] and pleomorphic xanthoastrocytoma [11], the presence of pleomorphic giant cells has no correlation with an aggressive behaviour. These histopathological features correlate with the clinical outcome in the present case: at 18-month follow-up progressive neurological improvement has been registered and no signs of tumour recurrence are shown on MRI scan, despite no adjuvant therapy, i.e. radiotherapy, has been administered. The latter should be reserved for tumour recurrences or in cases of partially resected lesions showing evidence of progression over time. We agree with Zec et al. [19] who attribute cellular pleomorphism to degenerative changes; in fact, in our case, giant cells were strictly observed in association with focal calcifications. And these did not worsen the prognosis, as also reported by Ho et al. [9]. Ki-67 is an adjunctive prognostic indicator for ependymoma [2], and the low Ki-67 labelling index in our case has been associated with no disease progression.

The present case highlights the limits of frozen section examination, particularly if a sufficient amount of tissue is not available. It also shows that areas with increased cellularity, increasing variations in nuclear size, in shape, coarseness or dispersion of chromatin, and nucleolar prominence can easily suggest the wrong diagnosis of a malignant, higher-grade neoplasm. Despite possible worrisome histological features, GCE is associated with a relatively good prognosis. It is, hence, important to perform a radical tumour resection in order either to cure the patient or to avoid any further treatment, usually deemed unnecessary for a less aggressive tumour.

Conflict of interest statement None of the authors has any potential conflict of interest.

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