Intraoperative squash cytology and histology of giant cell ependymoma: A diagnostic dilemma

ABSTRACT

Giant cell ependymomas (GCE) are extremely rare tumors, with 24 cases described in the literature. Squash cytology is a rapid, reliable, simple technique for intraoperative consultation in neurosurgical practice. We describe a rare case of GCE arising at level of L4-L5 in a 66-year-old woman and discuss the cytologic/histologic features. Intraoperative smears were highly cellular with a prominent fibrillary background and exhibited papillary structures and sheets composed of highly atypical and bizarre cells. Some of the cells showed nuclear pseudoinclusions and rarely formed pseudorosette-like arrays. Intraoperative diagnosis was high grade glial tumor. On paraffin sections, besides extensive polymorphism, there were no microvascular proliferation, necrosis, and mitosis and the final diagnosis was WHO grade II GCE. GCE may be a diagnostic challenge on intraoperative smears, frozen, and paraffin sections. It must be kept in mind in the differential diagnosis of giant cell exhibiting benign and malignant tumors of brain.

Key words: Cytology; ependymoma; giant cells; squash smear

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Introduction

Ependymomas are rare slow growing tumors originating from the wall of the ventricles or from the spinal canal. World Health Organisation (WHO) recognized four histopathologic subtypes, namely, cellular, papillary, clear cell, and tanyctic. Apart from this classification, giant cell ependymoma (GCE) is described by the WHO as a rare histologic variant. To date, 24 cases of giant cell ependymoma have been reported but cytopathologic features have been discussed only in two reports. We describe a rare case of GCE arising at the level of the L4-L5 vertebral bodies in a 66-year-old woman.

Case Report

A 66-year-old woman was admitted to our hospital with lumbago, bilateral leg pain, and lower extremity weakness lasting for several years. The physical examination was unremarkable except claudicatio intermittens. Magnetic resonance imaging revealed an intramedullary tumor expanding the spinal cord at the level of L4-L5 vertebra bodies. The lesion was 50 × 18 mm in size and slightly T2-hypointense. Surgical resection was performed through a L4-S1 laminectomy. The mass was separated from the nerve roots and biopsies were sent to the pathology department for intraoperative diagnosis.

A small biopsy was squashed, smeared, fixed in alcohol, and stained with hematoxylin and eosin. Smears were highly cellular and had a prominent fibrillary background. Cohesive papillary structures with fibrovascular cores and sheets with irregular borders were observed [Figure 1a]. These structures and sheets were composed of highly atypical, pleomorphic, multi/mononuclear cells, with hyperchromatic nuclei, coarse chromatin, and a large eosinophilic cytoplasm. Some of the atypical cells were highly bizarre like a monster cell. Small and medium-sized mildly atypical cells were accompanied the large cells. Some of the cells formed rosette-like arrays [Figure 1b], and some cell clusters exhibited eosinophilic globule-like material [Figure 1c]. Our intraoperative diagnosis was of a high grade glial tumor.

Histopathologic examination revealed a highly cellular tumor in a hyalinized and hemorrhagic stroma. The tumor composed predominantly of sheets of giant cells, with irregular hyperchromatic and usually monstrous nuclei, dispersed between medium-small sized cells. Eosinophilic intranuclear inclusions and perivascular pseudorosette formations were observed [Figure 1d]. Microvascular proliferation and necrosis were not seen. Mitotic figures were 0–1/10 high-power field.

Periodic acid Schiff positive extracellular hyaline round bodies were present.

Immunohistochemically, tumor cells were positive for glial fibrillary acidic protein, vimentin, synaptophysin, CD99, and bcl-2 and focal positive for S-100 and neuron specific enolase (NSE). Epithelial membrane antigen was immunoreactive focally either as paranuclear dots or similar to cytoplasmic bands. A few cells showed mild p53 positivity. Ki-67 proliferation index was 5%. Final diagnosis was WHO grade II GCE.

Three months after the surgery, the patient is well with neither local recurrence nor metastatic spread.

Discussion

Ependymomas constitute 8–10% and 1–3% of central nervous system tumors in children and adults, respectively. GCE are extremely rare tumors, with 24 cases described so far in the literature. Zec et al. first described two cases of GCE of the filum terminale in 1996. Of the 24 cases, 18 occurred in adults. The median age of the patients was 33 (5–89 years) and male-to-female ratio was 1/1. Of the 24 tumors, 11 were arising from spinal cord (6 cervical, 3 thoracic, 2 filum terminale), 9 supratentorial region, and 4 cerebellum. All the cases arising from spinal cord and cerebellum were grade II. Anaplastic features were all examined in supratentorial cases. The present case is of a 66-year-old woman with a L4-L5 spinal cord tumor. Besides extensive cell polymorphism,
there were no other features suggestive of anaplasia such as necrosis, microvascular proliferation, and high mitotic activity. In addition, the tumor exhibited some features which were indicative of slow growth such as extensive stromal hyalinization and low Ki67 proliferation index, and hence, the tumor was diagnosed as WHO grade II.

Squash cytology is a rapid, reliable, simple technique for intraoperative consultation in neurosurgical practice with high overall accuracy. Ependymomas can also be diagnosed and graded by squash smear. Although a rare variant of ependymoma, GCE may be a diagnostic challenge both on the intraoperative squash smears and frozen and paraffin sections. Giant cells can be found both in low grade neoplasia such as pleomorphic xanthoastrocytoma (PXA), subependymal giant cell astrocytoma (SEGA), and high grade neoplasms such as giant cell glioblastoma, anaplastic oligodendroglioma, and anaplastic ependymoma. PXA are mainly superficial tumors with meningeal involvement and show large xanthomatous and lipidized cells and intercellular reticulin network as diagnostic hallmarks. SEGA is frequently associated with tuberous sclerosis and located in lateral ventricle. Both of these tumors show cellular pleomorphism and giant cells but pseudorosette formation is not a feature of them. The presence of perivascular pseudorosettes are diagnostic hallmark for the diagnosis of ependymoma. It is usually easy to find these structures on histologic sections, however, they cannot be easily found on intraoperative smears and frozen sections. In the present case, pseudorosettes were extremely rare in squash smears so a definitive diagnosis of ependymoma could not be performed intraoperatively. Intranuclear inclusions are another key histologic feature to establish a diagnosis of GCE. Intranuclear inclusion-like bodies or pseudoinclusions are probably results of intranuclear cytoplasmic invaginations. The present case also exhibited these inclusions both in smears and paraffin sections.

Giant cell glioblastoma is another entity in the differential diagnosis. The smears of this entity show malignant astrocytic tumor cells on a necrotic background. These tumors exhibit prominent microvascular proliferation. In the squash smears and paraffin sections of the present study, we did not observe any microvessel proliferation or necrosis. However, the presence of anaplastic appearing giant cells resulted in the intraoperative diagnosis of high grade glial tumor.

**Conclusion**

GCE must be kept in mind for the differential diagnosis of giant cell exhibiting benign and malignant tumors of the brain both in squash smears and histologic sections. Because of the extreme rarity of GCE, reports of cases with cytologic, histopathologic, and clinical features have great value.

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**Conflicts of interest**
There are no conflicts of interest.

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