Case Report

Giant cell ependymoma: Cytology of a rare entity with unusual presentation

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ABSTRACT

Giant cell ependymoma (GCE) is a slow-growing tumor that accounts for 9–13% of all ependymoma and occurs preferably at conus medullaris, cauda equina, and filum terminate. Squash cytology is a fast, simple, and reliable technique for intraoperative diagnosis. We present a case of GCE arising at the L5-S2 level and suprasellar region in a 17-year-old male who initially presented with low backache followed by headache and double vision. Intraoperative squash smears of the lumbosacral lesion were suggestive of high-grade glioma. Histomorphological and immunohistochemical profile favors the diagnosis of giant cell variant of myxopapillary ependymoma. He received craniospinal irradiation followed by a boost to the sellar-suprasellar and lumbosacral region through IGMT. After sometime, he developed papilledema and decreased vision, the suprasellar lesion was decompressed which on histopathology revealed similar features. GCE remains a diagnostic challenge on intraoperative squash smears due to its rarity. It has a good prognosis with a 5-year survival of 98.4% after total resection; however, our patient succumbed to illness due to post-operative residual lumbosacral mass and effects of the suprasellar lesion.

Key words: Cauda equina, Cytology, Ependymoma, Giant cell, Immunohistochemistry, Squash smear, Suprasellar

Ependymomas are slow-growing, rare tumors comprising 2–9% of all neuroepithelial neoplasms and 50–60% of primary intramedullary spinal cord tumors which arise from ependymal cells of the central ventricle/spinal cord wall [1,2]. Its histological types include myxopapillary, classic (subtypes: Cellular, papillary, tanycytic, and clear cell), and anaplastic [1]. Giant cell ependymoma (GCE) is an unusual variant affecting 5–89 years of age with supra/infratentorial or spinal cord involvement [3]. Intraoperative squash smear is a quick and easy diagnostic technique to identify such lesions due to characteristic cytological features such as fern-like branching papillary, perivascular pseudorosette arrangement of large pleomorphic giant cells, and pseudonuclear cytoplasmic inclusions. Globules of mucinous/myxoid material with capillaries at the center in a fibrillary background are noted [4-6].

Histopathological features of GCE include confluent, polygonal tumor cells arranged in papillary, sheet, and focal perivascular pseudorosettes patterns. These cells have eosinophilic cytoplasm, hyperchromatic nuclei with elongated fibrillary processes, however, no mitosis/microvascular proliferation/necrosis is noted. Immunohistochemical profile reveals positivity for GFAP, CD99, CD56, S100, EMA, and negativity for brachyury, synaptophysin, and pan-cytokeratin [7]. Surgical treatment primarily depends on the size of the tumor and encapsulation. GCEs arising from the spinal cord/cerebellum tended to be low grade while supratentorial ones have anaplastic features. Distant metastasis to the spinal cord and brain has been observed; could be due to treatment failure, young age, lack of initial adjuvant radiotherapy, and incomplete excision.

CASE REPORT

A 17-year-old boy presented initially with complaints of low backache, leg/joint pain in September 2017. No focal neurological deficit was noted on clinical examination. Later on, he complained of headache, vomiting, double vision, and nausea in January 2018. He underwent L4-S2 laminectomy with intradural tumor decompression in January 2018. Intraoperative

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squash smears showed increased cellularity, giant cells, perivascular pseudorosettes, and intranuclear inclusion in a fibrillary background. We offered a diagnosis of high-grade glioma (Fig. 1a and b).

Histopathology of the lesion showed polygonal, large pleomorphic giant cells having abundant, eosinophilic cytoplasm, round hyperchromatic nuclei arranged in papillary, and pseudorosettes/true rosettes patterns in the fibrillary background. Few intranuclear inclusions were noted; however, no mitoses/endothelial proliferation/necrosis were present (Fig. 1c-e). These tumor cells were immunopositive for GFAP, S100, CD99, CD56, Ki67 5–6%, and immunonegative for pan-cytokeratin, brachyury, and synaptophysin. Therefore, a diagnosis of giant cell variant of myxopapillary ependymoma or pilocytic astrocytoma (WHO Grade I) was considered. BRAF V600E mutation was not detected.

Magnetic resonance imaging (MRI) scan of the lumbosacral spine during follow-up showed a heterogeneous solid cystic neoplasm measuring 2.2 × 2.7 × 2.8 cm at L5-S1 level with thick leptomeningeal enhancement. Post-operative imaging showed an ill-defined irregular area of enhancement at the L5 level indicating residual disease. He remained asymptomatic for few months and developed decreased vision, headache, and gross papilledema.

Contrast-enhanced MRI showed an ill-defined, lobulated lesion measuring 23 × 29 × 34 mm, extending into the sella, cavernous sinus, basal cistern, third ventricle with encasement of the infundibular stalk, displacement of optic chiasma, hippocampus, and patchy leptomeningeal involvement. A well-defined, expansile, oblong mass measuring 2 × 2.7 × 7.1 cm with isointense at T1W1, heterogeneously hyperintense features on T2W1, and extension from L5 to S2 vertebra was noted. On post-contrast, nodular/sheet-like heterogeneous, intense, meningeal enhancement along the spinal cord surface, perineural sheaths of existing nerve roots extending up to L5-S2 were noted. Cerebrospinal fluid biochemical analysis of proteins (1500 mg/dl), glucose (142 mg/dl), and cytological analysis showed no microorganism/malignant cell.

Whole-body positron emission tomography-computed tomography scan revealed an ill-defined, soft density, focally calcified lesion in the suprasellar region (SUVmax; 4.1) with an ill-defined fluorodeoxyglucose avid, expansile lesion measuring 1.9 × 2.2 × 6.8 cm (SUVmax; 2.7) in the spinal cord at L5-S2 level. Histomorphological differential diagnosis of low-grade astrocytoma or giant cell myxopapillary ependymoma was considered. In view of diffuse leptomeningeal enhancement, the radiological possibility of diffuse leptomeningeal glioneuronal tumor (DLGNT) was considered.

He underwent L4-S2 laminectomy with intradural tumor decompression in January 2018 followed by 40 Gray 24# craniospinal irradiation with 14.4 Gray 8# boost to sellar/suprasellar and lumbosacral spine through radical "Intensity Modulated Radiotherapy." In view of papilledema, he underwent suprasellar mass decompression done in January 2019. Squash cytology smear showed medium to large atypical cells with small round nuclei and moderate to abundant cytoplasm (Fig. 2a and b). The histopathology section from the lesion showed predominantly necrotic tissue and blood clots. Few cells having small vesicular nuclei and foamy cytoplasm were seen. An occasional single scattered giant cell was present in the myxofibrillary background (Fig. 2c-e).

However, despite best management and supportive care, he could not recover after suprasellar mass decompression and succumb to illness.

DISCUSSION

Ependymomas constitute 8–10% and 1–3% of central nervous system tumors in children and adults, respectively [2]. Gonzalez *et al*. reported GCE of filum terminale in a 48-year-old female with atypical clinical and radiological features [2]. Approximately 60% of ependymoma arises in the posterior fossa, 30% in the supratentorial region, and the remaining 10% in the spinal canal [8]. GCE is an extremely rare variant with the preferential occurrence at conus medullaris, cauda equina, and filum terminate and exhibits non-specific clinical and radiological features [9]. Common clinical symptoms are low backache with motor-sensory deficit.

MRI depicts the extent of the tumor, its relation to central structures, nerve roots, and subarachnoid space with isointense on T1 and hyperintense on T2 features. Intraoperative cytology is a rapid, reliable, simple, technique [10,11]. Based on the high cellularity, giant cells, perivascular pseudorosettes, intranuclear inclusion, and fibrillary background on the squash

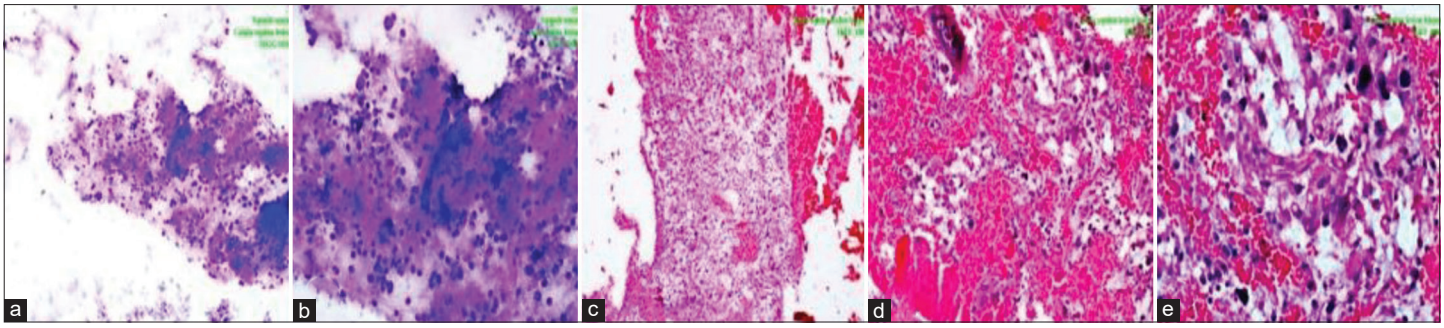

Figure 1: (a and b) Intraoperative squash smears showed increased cellularity, giant cells, perivascular pseudorosettes, intranuclear inclusion in a fibrillary background. (c-e) Histopathology of the lesion showed polygonal, large pleomorphic giant cells were having abundant, eosinophilic cytoplasm, round hyperchromatic nuclei arranged in papillary and pseudorosettes/true rosettes patterns in fibrillary background. Few intranuclear inclusions were noted; however, no mitoses/endothelial proliferation/necrosis present

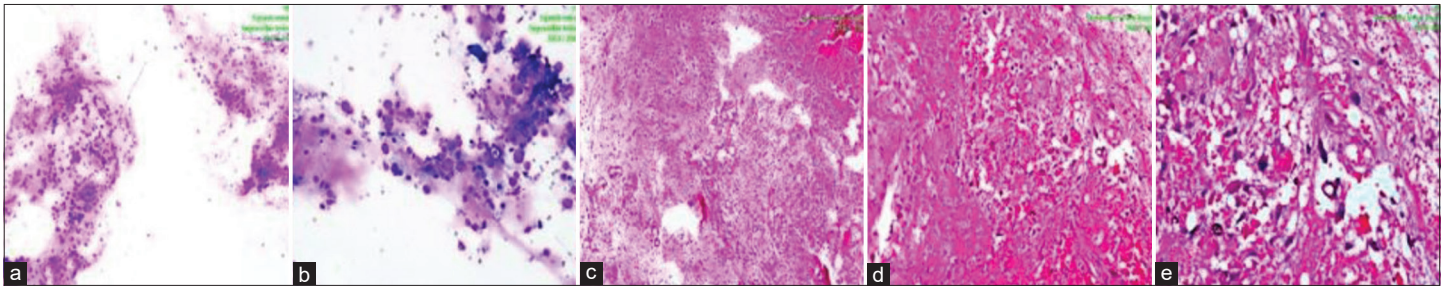

Figure 2: (a and b) Squash cytology smear showed medium to large atypical cells with small round nuclei and moderate to abundant cytoplasm. (c-e) H and E section from the lesion showed predominantly necrotic tissue and blood clots. Few cells were having small vesicular nuclei and foamy cytoplasm was seen. Occasional single scattered giant cell was present in the myxofibrillary background

smears, differential diagnosis of giant cell glioblastoma, anaplastic ependymoma, subependymal giant cell astrocytoma (SEGA), anaplastic oligodendroglioma, and pleomorphic xanthoastrocytoma (PXA) were considered [8]. We offered a diagnosis of high-grade glioma on squash cytology.

Histopathology of the lesion shows non-cohesive, polygonal, large-sized to pleomorphic giant cells (arise due to degenerative changes) arranged in papillary, trabecular, solid, nodular patterns with perivascular pseudorosettes/true rosettes in fibrillary background. These cells have abundant eosinophilic cytoplasm, large, round hyperchromatic nuclei, and few intranuclear inclusions [8]. No mitoses/endothelial proliferation/necrosis were noted [12]. Alcian blue positive myxoid material may be seen between tumor cells and blood vessels.

Differential diagnosis includes anaplastic ependymoma (marked mitosis/microvascular proliferation/necrosis with pseudopalisading pattern), giant cell glioblastoma (endothelial proliferation, pseudopalisading necrosis), and SEGA (large, plump cells resembling gemistocytic astrocytes, arranged in sweeping fascicles rich in vascular stroma with hyalinized vessels, mast cells, lymphocytes; synaptophysin, NeuN positive). PXA (pleomorphic astrocytes, eosinophilic granular bodies, lipidized cells, and no pseudorosettes), atypical teratoid/rhabdoid tumor (AT/RT; rhabdoid cells, GFAP, and INI-1 negative), chordoma (physalliferous cells, marked anisokaryosis, chondromyxoid background, pan-cytokeratin, brachyury positive, GFAP, and C99 negative) and neurofibroma (less cellular, haphazardly arranged spindle cells with wavy nuclei, NSE, CD34 positive, and GFAP negative) should also be considered as differential diagnosis. Also, extra-skeletal chondrosarcoma (cords, tiny clusters of small, epithelioid cells, S100 positive, GFAP, and CD99 negative), (DLGNT; admixed glial [monomorphic population of small cells with fine granular chromatin, and inconspicuous nucleoli], and neuronal [atypical enlarged cells with enlarged nucleoli, prominent nucleoli, and marked mitosis] phenotypes, synaptophysin, Neu-N positive, GFAP, and CD99 negative) should be considered in the differential diagnosis.

Among metastatic lesions, the differentials of paraganglioma (synaptophysin, chromogranin positive, GFAP, and CD99 negative), malignant peripheral nerve sheath tumors (NSE, CD34 positive, GFAP, and CD99 negative), malignant melanoma (HMB45, Melan-A positive, GFAP, and CD99 negative), adrenocortical carcinoma (inhibin positive and GFAP negative), anaplastic thyroid carcinoma (thyroglobulin, TTF-1 positive, GFAP, and CD99 negative), and urothelial carcinoma (pan-cytokeratin, uroplakin III, GATA3 positive, GFAP, and CD99 negative) were considered [13]. Based on histomorphological and immunohistochemical features (GFAP, S-100, EMA positivity, and low Ki67), a definitive diagnosis of giant cell variant of myxopapillary ependymoma (WHO Grade I) was concluded. Complete surgical resection yields excellent outcomes while incomplete resection is associated with a high recurrence rate and neurological deficit. In non-surgical cases, radiotherapy can be given.

CONCLUSION

We hereby discussed the characteristic features (perivascular pseudorosettes of pleomorphic giant cells with intranuclear inclusions) of GCE of cauda equina and suprasellar lesion on squash smear which mimic high-grade glioma on cytology. The diagnosis of GCE was confirmed on histopathological and immunohistochemical profiles. GCE is a slow-growing tumor with indolent clinical behavior. Preferably, complete surgical excision or radiotherapy is modalities of choice depending on patient clinical profile.

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