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CASE REPORT

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A Novel Case of Primary Conus Medullaris Epithelioid Glioblastoma with Gliosarcomatous Differentiation

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Abstract

Intramedullary location is seldom seen in spinal cord neoplasms. Ependymomas and astrocytomas comprise the vast majority of these intramedullary lesions. Primary spinal origin is rarely seen in gliosarcomas. No epithelioid glioblastomas have been reported in the spine. We describe the case of an 18-year-old male who presented with symptoms suggestive of a spinal mass lesion. Magnetic resonance imaging revealed a homogeneous intradural-intramedullary lesion involving the conus medullaris. Biopsy of the lesion showed a unique morphology comprising gliosarcoma and epithelioid glioblastoma differentiation, supported by relevant immunohistochemistry. The prognosis of such an entity is expected to be poor. However, the presence of mutant BRAF V600E, as seen in the current case, and the availability of targeted therapy against it are expected to improve the prognosis.

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Full Text

Spinal cord neoplasms are usually extradural or intradural and extramedullary in location. Spinal intramedullary neoplasms are the rarest. The majority of these intramedullary neoplasms comprise ependymomas and astrocytomas. Gliosarcomas are rare neuraxial tumors with a dismal prognosis. They are generally cerebral in location. Only rare cases of spinal gliosarcomas are on record. Glioblastomas are also predominantly cerebral in location and only rarely show epithelioid histology. Epithelioid glioblastomas have not as yet been reported in the spinal cord. We report an intramedullary tumor in the conus medullaris in a young male which showed overlapping gliosarcoma and epithelioid glioblastoma-like morphology, supported by molecular analysis. The utility of molecular analysis in the diagnosis and prognostic prediction of this entity are discussed.

Case History

An 18-year-old boy presented with low back pain back for 3 months followed by progressive weakness of both the lower limbs for 2 months with involvement of bladder and bowel. He was unable to walk for the past 10 days. On examination, the bulk and tone of both the lower limbs were decreased, and manual muscle testing revealed a power of 2/5 at both hips and knees and 1/5 at both ankles. Bilaterally, knee jerks were diminished, while ankle jerks were absent; both plantars

were non-elicitable. All sensory modalities below the L2 dermatome were diminished. There were no neurocutaneous markers. Magnetic resonance imaging (MRI) of the spine showed a homogeneous intradural-intramedullary lesion (6.0 cm × 1.2 cm, D11–D12 vertebral levels) involving the conus. [Figure 1] Radiologically, the possibility of a neoplastic etiology (ependymoma, astrocytoma) was kept.{Figure 1}

Preoperatively, a well-defined, vascular, reddish-gray intradural mass, extensively adhered to roots at the conus, was observed. A complete microsurgical excision of the lesion was performed. On histology, a tumor-infiltrating spinal cord white matter and large peripheral nerve roots were seen, showing intermixed fascicles and organoid cell nests. The fascicles showed cells with ovoid to spindled nuclei with hyperchromasia, moderate pleomorphism, and frequent mitosis. The nests showed cells with epithelioid morphology, showing moderate pleomorphism, rounded peripherally placed nuclei, prominent nucleoli, and frequent mitosis. Foci of hemorrhage and necrosis along with endothelial proliferation were noted. Both components were focally positive for GFAP and diffusely positive for Vimentin and S-100. IDH 1 R132H was nonreactive, p53 wild type, ATRX showed retained nuclear expression and H3K27M was nonmutant on immunohistochemistry. TLE-1, CD34, smooth muscle actin, myogenin, pan-cytokeratin, and epithelial membrane antigen were negative. INI-1 did not reveal loss of staining. Ki-67 proliferation index was 30% in hot spots in both components [Figure 2]. CSF analysis was done postoperatively and did not reveal CSF metastasis. The patient was initiated on radiotherapy but deteriorated and succumbed to the disease 6 months after diagnosis. Targeted therapy could not be offered due to financial constraints. {Figure 2}

Discussion

The biphasic morphology brought to mind several differentials. Synovial sarcoma was excluded by negative IHC for epithelial markers and TLE-1. A close histologic differential was a primary epithelioid malignant peripheral nerve sheath tumor (MPNST) of the nerve roots infiltrating the conus medullaris. However, numerous GFAP-positive cells, intramedullary location with dural extension, and no association with neurofibromatosis 1 helped exclude MPNST.[1],[2] Negative HMB45 helped exclude melanoma. Among glial tumors with epithelioid morphology, gemistocytic astrocytomas are IDH and p53 mutant, whereas gliosarcomas with epithelial metaplasia show cytokeratin immunoreactivity, which was not observed in our case. BRAF V600E IHC revealed diffuse cytoplasmic positivity in the epithelioid and spindled cells. A diagnosis of epithelioid glioblastoma with gliosarcomatous change was rendered.

Primary spinal gliosarcomas are extremely rare. A systematic review of primary spinal glioblastomas and gliosarcomas reported up to March 2015 revealed only two spinal gliosarcomas among 157 such tumors.[3] Rare cases of spinal metastases from primary cerebral gliosarcomas are on record, but no evidence of an intracranial lesion was present in our patient.[4]

Epithelioid glioblastomas show a predilection for children and have not been encountered in the spinal cord.[1] An exceptional case with similar gliosarcomatous and epithelioid glioblastoma-like areas has recently been reported in the temporal-parietal lobe in an 80-year-old woman.[5] The analogy in this case and ours is a mutant BRAF V600E mutation which is found in many epithelioid glioblastomas.

The prognosis of gliosarcomas parallels that of glioblastomas, while that of epithelioid glioblastomas is worse.[1] Whereas the prognosis of an entity comprising both these components can be expected to be grave, the availability of targeted therapy against BRAF V600E can be expected to improve it. Our case brings to light a new entity and emphasizes the importance of diligent radiologic and histologic workup in substantiating its diagnosis. Similar immune profile of both epithelioid and gliosarcomatous areas, despite different cellular morphologies, highlights the possibility of divergent lines of differentiation of a single entity rather than a collision tumor.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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Figure 1: MRI of the spine shows an intramedullary lesion (corresponding to D11–D12 vertebral levels) hypo- t intense on T1-weighted (arrowhead, a) and iso- to hyper-intense on T2-weighted sequences (arrowhead, b Heterogeneous enhancement of the lesion, along with enhancement of the overlying meninges, can be appreciа the T1-gadolinium-contrast sequence (arrowhead, c). There is no evidence of syrinx formation proximal to the

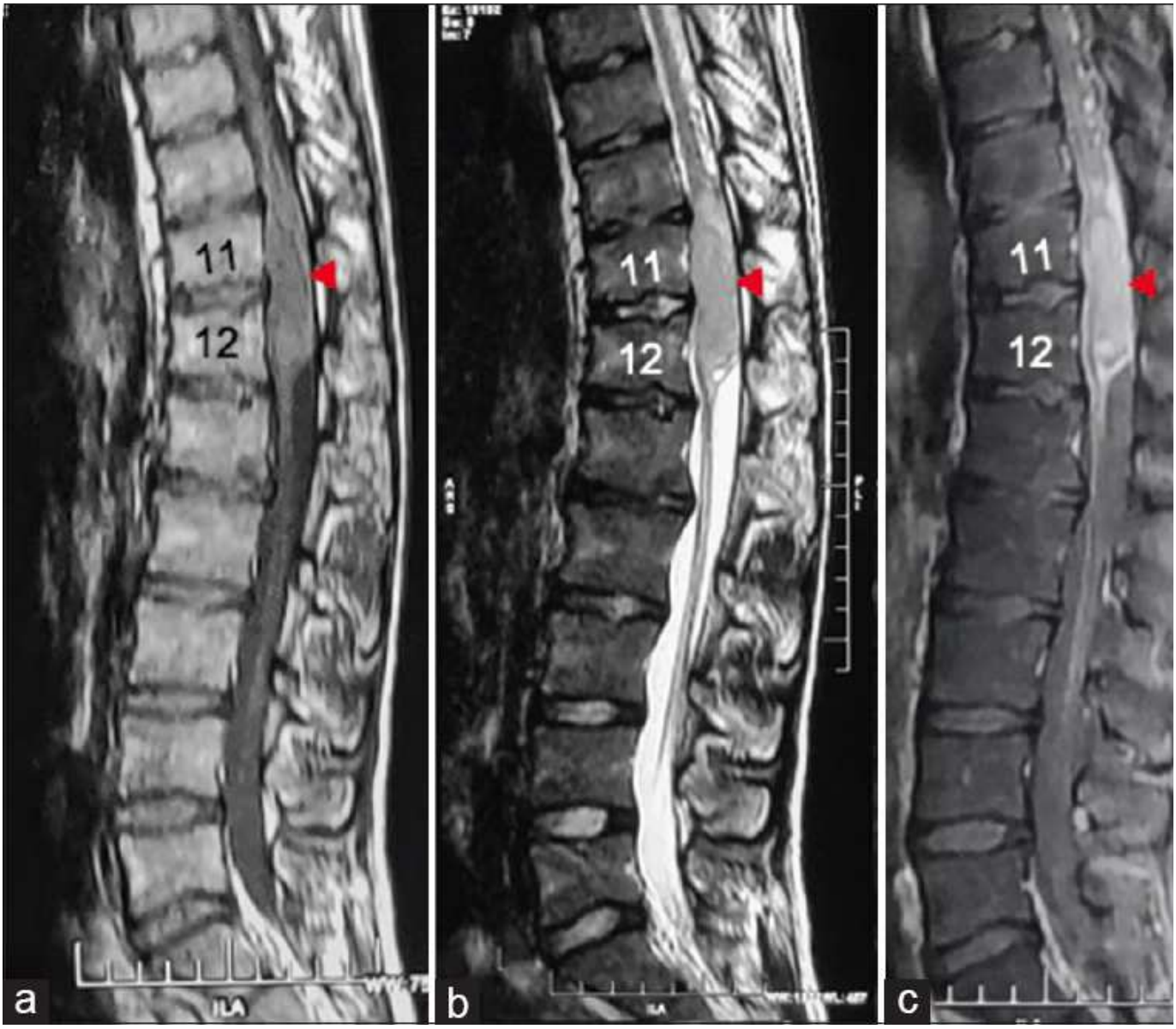

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Figure 2: Tumor showing fascicles (arrow) and organoid nests (asterisk) of cells (a). Nest of moderately pleomo of cells with spindled pleomorphic nuclei (c). Both spindled (arrow) and epithelioid (asterisk) cells are positi R132H (g); positive for BRAF V600E (h) and show high Ki 67 proliferation i