ABSTRACT

Subependymomas are extremely rare lesions of the spinal cord. Only 33 cases including ours have been reported in the cervical cord. These are typically benign slow growing tumors occurring eccentrically within the cord, producing minimal neurological deficits. The clinical, radiological, and histopathological aspects of this unusual lesion have been reviewed in detail. As the histogenesis of this tumor is much debated, we propose an alternate origin for the same.

Key words: Cervical subependymoma, histogenesis of subependymoma, spinal subependymoma, subependymoma, spinal tumor

Introduction

Subependymoma, first described by Scheinker in 1945, is a rare central nervous system tumor. Since its first description in the spinal cord by Boykin et al in 1954, only 47 cases have been reported. Out of these, 32 involved the cervical cord. In the spinal region, these lesions are predominantly subpial in location, with exophytic components. The location of these lesions in the spinal cord suggest a subpial glial progenitor origin rather than its proposed origin from subependymal progenitor cells.1-4

Case Report

A 37-year-old lady presented to us with complaints of neck pain and gait disturbances of 1 year duration with severe progressive weakness of her right upper limb since 3 months. She had a grade 3/5 power in her right upper limb with muscle wasting. Rest of her limbs had mild weakness with spasticity. MRI revealed a long-segment T2 hyperintense intramedullary lesion opposite to the C3 to D4 vertebral levels with mild heterogeneous enhancement on the post contrast study [Figure 1].

She underwent subtotal excision of the lesion with cervical laminoplasty. Intraoperatively, the lesion was firm, with a poor plane of demarcation from the normal cord, and was seen intermingling with posterior and anterior nerve rootlets. It was eccentric in location, involving more of the left hemicord, with exophytic components [Figure 2].

Figure 1: (a) Sagittal T2 and (b) post contrast T1-weighted MR images showing a long segment T2 hyperintense and mild heterogeneous enhancing lesions in the cervical cord, showing cord expansion.
All of the resected tissue submitted for histopathological analysis was processed and embedded in three paraffin blocks. Histopathological examination [Figure 3] revealed characteristic features of a subependymoma (WHO grade 1) with small monomorphic cells arranged in a lobular pattern against a finely fibrillary background, with occasional rosette like pattern. Features of pleomorphism, mitotic activity, endothelial cell proliferation, and necrosis were not seen. The MIB-1 proliferative index was low (<1% of tumor cells). Immunohistochemistry revealed diffuse positivity for Glial Fibrillary Acidic Protein (GFAP), whereas tumor cells failed to express epithelial membrane antigen (EMA).

She did not receive any adjuvant treatment and has been on follow up for 6 months with periodic MR imaging. She does not report any progression of symptoms.

Discussion

Subependymomas are rare central nervous system tumors accounting for 0.7% of all intracranial neoplasms and 8.3% of all ependymal tumors. They are located most frequently in the fourth ventricle (50–60% of cases) followed by the lateral ventricles (30–40%). So far, only 47 cases have been reported in the English literature in the spinal cord; of which 32 cases were located in the cervical, cervico-medullary, and cervico-thoracic locations. [Table 1]. Most are intramedullary in location, with few subarachnoid and extramedullary variants mentioned in the literature. The symptomatic subependymoma generally occur after 40 years of age and are rare in childhood.[1-3]

They have a mean age of presentation of about 44 years with a strong male preponderance [Table 2].

Histopathologically these tumors are low grade (WHO grade 1), characterized by homogenous cells with sparse cellularity showing clustering of nuclei over a fibrillary background formed by cell processes and occasional occurrence of microcysts. The tendency to form pseudorosettes and the cells being round with hyperchromatic nuclei are reminiscent of ependymomas.[1,2,5,6]

Immunohistochemical characteristics are however identical to that of astrocytic neoplasms with diffuse GFAP and S-100 protein positivity. In contrast to ependymomas, subependymomas are negative for EMA. Ultrastructurally, they demonstrate both astrocytic and ependymal characteristics. The former is evidenced by the processes containing intermediate filaments and the latter by microlumens, cilia, microvilli, and intercellular junctions.[1,2,5,6]

Histogenesis of Spinal Subependymoma

The histogenesis of these tumors has been much debated. Due to their ultrastructural similarities with ependymal cells, they were initially thought to arise from ependymal cells, with reactive astrocytic proliferation. Since immunohistochemical profile favors a glial origin, they were grouped with low-grade glial tumors. Tanyocytes were also proposed as source of origin, due to the presence of ultrastructural features of glial as well as ependymal components. However, the presence of round cells rather than spindle-shaped cells differentiates these lesions from tanyctic ependymomas. The identification of cells similar to subependymal glial precursor cells suggested alternate cell of origin.[1,2,5,6]

Subependymal zone glial precursor cell origin cannot explain the predominant peripheral and exophytic

Figure 2: Surgical finding: Typical exophytic subpial lesions, with lesion on either sides of the dorsal nerve roots.

Figure 3: Histopathology: (a) H and E staining shows lobular pattern arrangement of monomorphic nuclei in fibrillary pattern (×400). (b) MIB-1 labeling index is less than 1% of tumor cells (not shown in figure) (×400). Immunohistochemistry for (c) GFAP highlights diffusely positive tumor cells in a fibrillary background (×400) (d) Tumor cells are negative for EMA (×400)
location of these lesions in spinal cord unlike their intracranial counterparts. The current concept seems to suggest that these progenitor cells exist throughout the spinal cord white matter as well as the root entry zones. They are more localized in the outer subpial white matter than the medial zones, especially at the dorsal and ventral spinocerebellar tracts. They tend to proliferate within their template zones and do not possess trans-zonal migratory ability. The tumor origin from these cells better explains the eccentric, subpial, and exophytic locations of spinal subependymomas.

The progenitor cells origin postulated by Horner et al is an alternative to the conventional old postnatal theory [Type 1, Figure 4] where the progenitor cells migrate from the subependymal zone to the outer zones. There are two alternative postulates: one where the stem cell divides asymmetrically and the daughter cell migrates to the outer white matter where it remains as a glial progenitor cell and multiplies [Type 2, Figure 4], and the second which postulates that the stem cells exist separately in the outer zone where tracts are constantly proliferating. The progenitor cells origin postulated by Horner et al is an alternative to the conventional old postnatal theory [Type 1, Figure 4] where the progenitor cells migrate from the subependymal zone to the outer zones. There are two alternative postulates: one where the stem cell divides asymmetrically and the daughter cell migrates to the outer white matter where it remains as a glial progenitor cell and multiplies [Type 2, Figure 4], and the second which postulates that the stem cells exist separately in the outer zone where tracts are constantly proliferating.
Irrespective of their origin the subpial spinal white matter progenitor cells may be the origin of the spinal subependymoma.

The subependymomas reported are more commonly located in the cervical cord and the cervico-thoracic cord followed by the pure thoracic and lumbar segments. One rare case occurring in the filum terminale has also been reported [Table 2]. Radiologically, these lesions are located eccentrically within the cord, with iso or hypointense on T1-weighted images and mild hyperintensity on T2-weighted images. There is minimal diffuse or no enhancement on contrast.[1-8]

These lesions can usually be excised totally. Only three cases have been reported with recurrence of the tumor after initial total excision. All of them had a resurgery and were not subjected to adjuvant radiation or chemotherapy despite recurrence. The chances of recurrence after total excision are low; hence, a total excision should always be attempted [Tables 1 and 2].

However, as with our case, the size of the lesion and its extensive intermingling with the nerve roots made it sometimes necessary to settle for a subtotal excision. In such cases too, a favorable outcome has been reported without adjuvant therapy. There have been instances of postoperative radiation following subtotal excision, but it is generally not recommended. Instead a periodic follow up would be in order. Residual or recurrent tumor on follow up after gross total resection should be strongly considered for a re-excision rather than adjuvant therapy.[2-8]

References


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