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Review Article

Multiple primary intramedullary ependymomas: a case report and review of the literature

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Abstract

BACKGROUND CONTEXT: Intramedullary ependymomas constitute the most frequent type of intramedullary tumor. In patients with neurofibromatosis type 2 (NF2), multiple intramedullary ependymomas are known to occur. In the non-NF2 population, however, the presence of multiple synchronous intramedullary ependymomas is exceedingly rare.

PURPOSE: In this article, the authors report the second case in the literature of multiple primary synchronous intramedullary ependymomas. To the best of the authors knowledge, this report represents the first to provide a detailed pathology of all lesions, thereby giving an added level of confidence on the primary synchronous nature of the lesions. The authors have also performed a review of the literature regarding multifocal intramedullary ependymomas.

STUDY DESIGN: A review article and case report.

CONCLUSIONS: The concomitant localization of two primary intramedullary spinal cord ependymomas in the setting of nongenetic predisposition is an uncommon phenomenon. In this article, the authors present the second report of multiple, synchronous intramedullary ependymomas. A detailed review of the literature reveals that the presence of multiple intramedullary lesions in non-NF2 patients is both rare and deserving of further study.

Keywords: Intramedullary; Ependymoma; Multifocal; Spine; Tumor

Introduction

Ependymomas are primary central nervous system (CNS) neoplasms thought to arise from ependymal cells lining the cerebral ventricles, spinal cord central canal, and cortical ependymal cell rests [1]. Ependymomas are typically solitary lesions and can be divided histologically into three grades: World Health Organization (WHO) Grade I (myxopapillary, subependymoma), WHO Grade II (cellular, papillary, clear cell, or tanycytic), and WHO Grade III (anaplastic) [1,2]. Recent genetic discoveries have identified molecular subtypes of ependymomas that depend on the anatomic location of the tumor and not on the histologic grade [3,4]. Genetic messenger RNA expression analysis using the high-throughput technology of microarrays indicates that spinal ependymomas in adults present a different molecular signature than the posterior fossa ependymomas predominantly found in children [3]. Both tumor types appear to be different from the supratentorial ependymomas that have a mixed population distribution. Spinal ependymomas, therefore, should be viewed as a distinct pathologic entity and not as the spinal variants of a cranial disease.

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Spinal cord ependymomas typically present as intradural intramedullary lesions [5,6]. Primary extramedullary ependymomas, a rare entity, are thought to derive from ectopic ependymal cells that migrated from the spinal canal during the first weeks of life, before progressively growing into a tumor [4,5]. This hypothesis was supported by the description of an intradural extramedullary ependymoma by Cooper et al. [7]. Three features of this tumor type highlighted by Cooper et al. [7] are as follows: there is a lack of gross attachment of the tumor to the spinal cord, the tumor appears encapsulated, and there is no indication of a primary neoplastic process along the craniospinal axis. A thorough review of the literature confirms the rarity of extramedullary ependymomas, as only 21 reports have been described to date in the literature [5,7–26]. Of these 21 reports, 2 describe multiple extramedullary ependymomas [5,8].

Primary intramedullary ependymomas are derived directly from the ependymal cells of the spinal canal. They are the most common intramedullary spinal cord tumors (IMSCTs) [27,28], representing 50% to 60% of spinal neuroepithelial neoplasms in adults and 2% of all central nervous system tumors [6,27]. The vast majority of these tumors are singular, but the occurrence of multiple primary synchronous intramedullary ependymomas has been reported only once in a patient without neurofibromatosis type 2 (NF2) [29].

In this study, the authors present the second case of primary synchronous intramedullary ependymomas in a non-NF2 patient. This report includes a detailed pathologic description of the lesions resected in addition to a review of the literature of an additional 39 cases (35 NF2 and 1 non-NF2 patient), including management and clinical outcomes reported.

To review the literature, the authors performed a search using the PubMed database and the search terms: spinal ependymomas, intramedullary ependymomas, extramedullary ependymomas, multifocal ependymomas, multiple intramedullary ependymomas, and multiple extramedullary ependymomas. All available English-language literatures were reviewed. One previous sporadic case and three NF2-associated reports of multiple synchronous primary intramedullary ependymomas histopathologically confirmed were identified (Table) [29–32]. The results of our search are described in the ''Discussion'' section.

Case report

History and examination

A 43-year-old previously healthy woman presented with an 18-month history of progressive upper and lower extremity paresthesias and dysesthesias associated with weakness in both hands, predominantly on the right. The patient also complained of bladder dysfunction and increasing difficulty with walking because of imbalance.

Neurologic examination revealed weakness of the hand intrinsic muscles bilaterally (Grade 4/5 Medical Research Council). Sensory examination revealed reduced sensation to pinprick and light touch in upper and lower extremities, decreased vibratory sensation in the toes, and difficulty with proprioception. Exaggerated reflexes were present in both upper and lower extremities (3+ bicipital, tricipital, and patellar reflexes). Ankle clonus was observed bilaterally. Hoffmann and Babinski signs were also present bilaterally.

Radiographic studies were obtained. Craniospinal magnetic resonance imaging revealed two distinct contrast-enhancing intramedullary spinal cord lesions (Fig. 1). The first mass was located in the subaxial cervical spinal cord at C3–C5. The lesion appeared hypointense on T1-weighted images and heterogeneous on T2-weighted images (Fig. 1, Left and Right, arrow). There was increased T2 signal compatible with peritumoral edema both above and below the lesion, extending from the craniocervical junction down to the C6 level. A small cystic component was visualized within the tumor. The second intramedullary lesion was located in the thoracic T4 level and had similar characteristics as the previously described lesion with peritumoral edema extending from the T1 through T5 levels (Fig. 1, Left and Right, arrowhead). No other lesion in the neuroaxis was identified.

Treatment

After ruling out inflammatory or demyelinating origin of the lesions, surgical excision was recommended. The patient elected to proceed with a two-staged surgical resection of the intramedullary spinal cord lesions.

First operation

The cervical lesion was addressed first. Electrophysiological monitoring (motor-evoked potentials [MEPs] and somatosensory-evoked potentials [SSEPs]) was used during the operation. The patient was placed in the prone position. Subperiosteal dissection was performed, followed by a laminectomy from C3 to C7. Dura and arachnoid membranes were opened, and the spinal cord was visualized. The tumor was roughly twice the diameter of the spinal cord. A gross total resection was achieved (Fig. 2, Left). The dura was closed in a watertight fashion. The patient tolerated the procedure well. Pathologic assessment revealed an ependymoma (WHO Grade II). Specifically, the tumor resected exhibited characteristics of a low-grade ependymoma, most consistent with a tanycytic ependymoma (Fig. 3, Top and Bottom). Cerebrospinal fluid examination yielded only a few lymphocytes with no evidence of tumor cells.

Second operation

The thoracic lesion was resected 8 months after the cervical procedure. The patient was placed in the prone position. A midline incision was made, subperiosteal dissection