



A Rare Case of Adult Medulloblastoma Associated with Multiple Sclerosis: Case Report and Literature Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Medulloblastomas are the most common primary malignant brain tumors in childhood. They are responsible for around 20–40% of all brain tumors in children. They rarely occur in adulthood, but here they only make up less than 1% of all brain tumors. The standard therapy consists of an operation in combination with radiation and chemotherapy, which are individually determined for the patient. In this article, we discuss a case of 47 years old female patient diagnosed with primary progressive multiple sclerosis since 1 year. After 3 months of the diagnosis, she deteriorated and became unable to walk. MRI showed a large patchy enhancing midline cerebellar mass with evolving hydrocephalus. Tumor expressed positive reaction with synaptophysin immunohistochemical stain rendering medulloblastoma diagnosis.

Keywords: *Medulloblastoma; multiple sclerosis; adult brain tumor.*

1. INTRODUCTION

Medulloblastoma has been described as a high-grade embryonal tumor (grade IV) according to the World Health Organization (WHO) classification of central nervous system Tumors. It is the most common intracranial malignant tumor of childhood [1]. However, in adults, medulloblastoma accounts for less than 1 % of adult intracranial tumors, with an incidence rate of about 0.5 per million [2]. The majority of affected adults 63 % are aged 20–40 years, occurrence in individuals aged >50 years is exceedingly rare [3]. Clinical features of medulloblastoma include a short history of increased intracranial pressure, headaches, and ataxia [1]. WHO classifies medulloblastoma into molecular as well as morphological variants, all are with clinical utility. In making a diagnosis of medulloblastoma, it is most important to rule out other entities that arise in the posterior fossa with the same morphology, such as high-grade small cell gliomas, embryonal tumors with multilayered rosettes, and atypical teratoid/rhabdoid tumor [1]. We present a case of an adult with medulloblastoma, who is being treated for multiple sclerosis (MS). Clinical presentations, pathological features and treatment outcomes in addition to a review of the literature are also discussed. The patient signed an informed consent before using the case data in this report.

2. CASE PRESENTATION

A 47-year-old female, known case of multiple sclerosis, was evaluated in February 2017 with a one-year history of gait disturbance. Her initial neurological examination showed bilateral lower limbs weakness with bilateral cerebellar signs and brisk deep tendon reflexes. It is important to mention that the patient has three children with multiple sclerosis (Familial multiple sclerosis).

Axial Magnetic Resonance Imaging (MRI) FLAIR image showing periventricular confluent T2/FLAIR hyperintensities likely representing CSF permeation. Multiple nodular hyperintensities could represent MS or tumor lesion (Fig. 1). She was started on weekly oral Vitamin D, monthly Vitamin B12 injection, and Ocrevus (Ocrelizumab). Three months later, she got a severe headache, more unsteadiness, and was unable to stand. She was dysarthric and ataxic. Post-contrast T1 weighted axial image (LHS) MRI of the brain showed a large heterogeneous solid lesion with nodular enhancing areas as well as diffusion restriction (Fig. 2a and 2b). Sagittal MRI T2W image

showed a T2 hyperintense mass in the posterior fossa with obstructive hydrocephalous (Fig. 3).

Due to the clinical and radiological progression of the posterior fossa lesions, the patient underwent suboccipital posterior fossa decompression with open biopsy of the cerebellar lesions followed by ventriculoperitoneal shunt insertion. She recovered nicely from the procedure and samples were sent for analysis.

3. HISTOPATHOLOGY RESULTS

H&E-stained sections from formalin-fixed posterior fossa mass showed multiple fragments of tumor tissue with adjacent unremarkable brain parenchyma (Fig. 4a). The tumor consisted of small round blue cells arranged in a syncytial pattern. The tumor cells exhibited marked pleomorphic hyperchromatic nuclei associated with a high mitotic rate (Fig. 4b). Immunohistochemical study revealed diffuse positivity for synaptophysin (Fig. 5), focal positivity for GFAP and S100, and negative reaction for pan-CK and P53 confirming medulloblastoma WHO grade IV diagnosis.

3.1 Follow Up

Planned for palliative radiation therapy 25Gy/5Fx but received only one fraction and couldn't tolerate the remaining treatment and canceled her further treatment. Two years later a brain & spine MRI was done that shows stable brain and spinal demyelinating plaques, showing no enhancement.

4. LITERATURE REVIEW

The medulloblastoma is an embryonic tumor of the cerebellum, which means that it emerges from immature, undifferentiated cells of the central nervous system (CNS) and grows very quickly. Medulloblastomas are extremely malignant [4]. In the meantime, the genetic analysis of the tumors has identified 4 molecular subtypes of medulloblastoma, which differ in their molecular genetic features and also have different prognoses.

A medulloblastoma mostly arises from the upper cerebellar sail. Medulloblastomas are typically found in the posterior fossa in the area of the 4th ventricle. A spread of the tumor cells via the brain CSF to other brain regions or the spinal cord area is possible [5]. Most commonly, medulloblastoma locally infiltrates the cerebellum and brain stem as well as to the spinal column as sugar coating infiltrations. Spreading into the cerebrum is more common in adults.



Fig. 1. Axial FLAIR image showing periventricular confluent T2/FLAIR hyperintensities likely representing CSF permeation. Multiple nodular hyperintensities could represent MS or tumor load

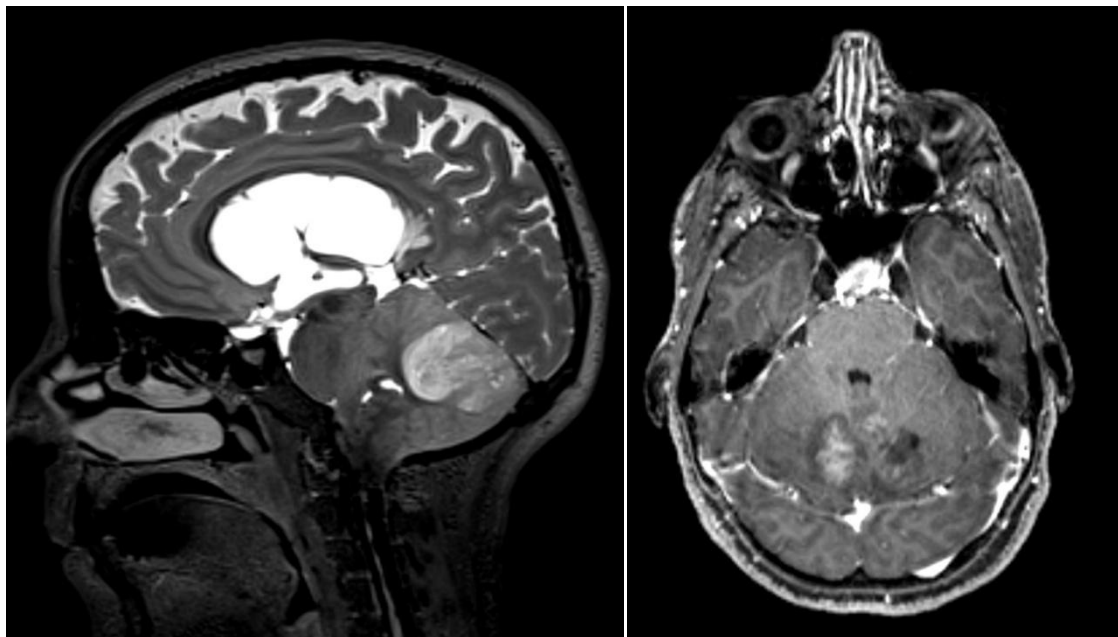


Fig. 2a. and Fig. 2b. Post contrast T1 weighted axial image (LHS) MRI of brain showed a large heterogenous solid lesion with nodular enhancing areas as well as diffusion restriction

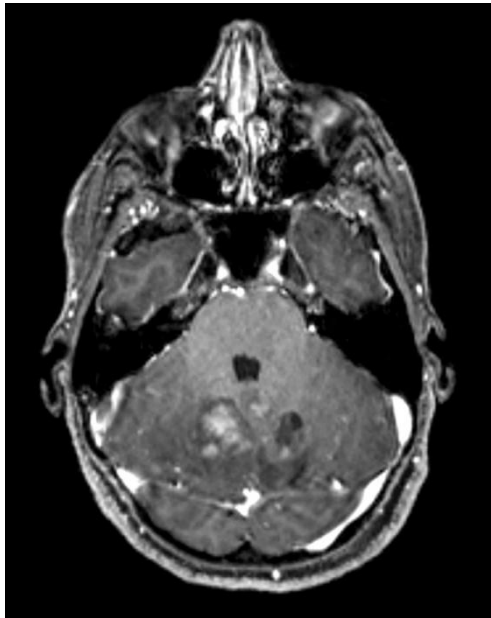


Fig. 3. Sagittal T2W image showing a T2 hyperintense mass in the posterior fossa with obstructive supratentorial hydrocephalus

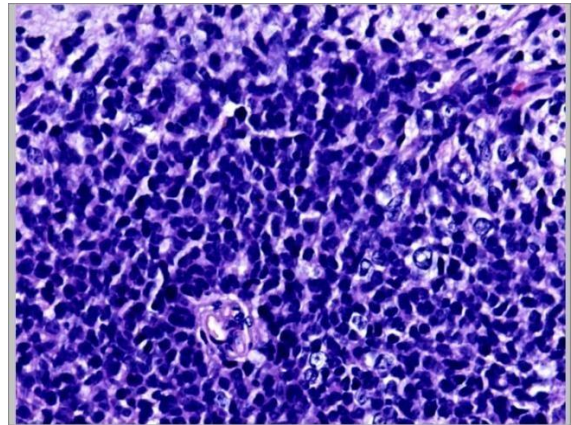
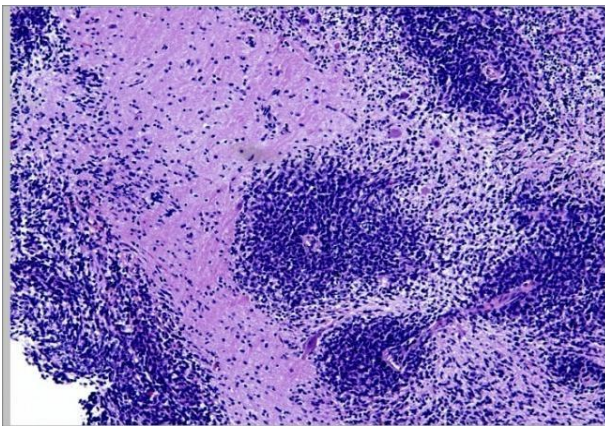


Fig. 4a. H&E stained section (10X), multiple fragments of tumor tissue with adjacent unremarkable brain parenchyma

Fig. 4b. H&E stained section (40X), mitotically active tumor with hyperchromatic and marked pleomorphic nuclei

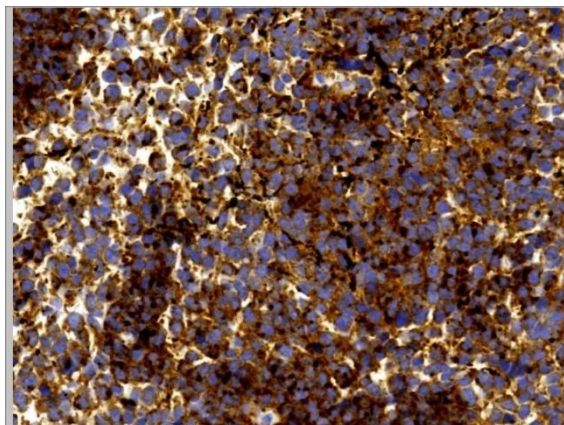


Fig. 5. Synaptophysin positive tumor cells



Fig. 6. MRI scan image

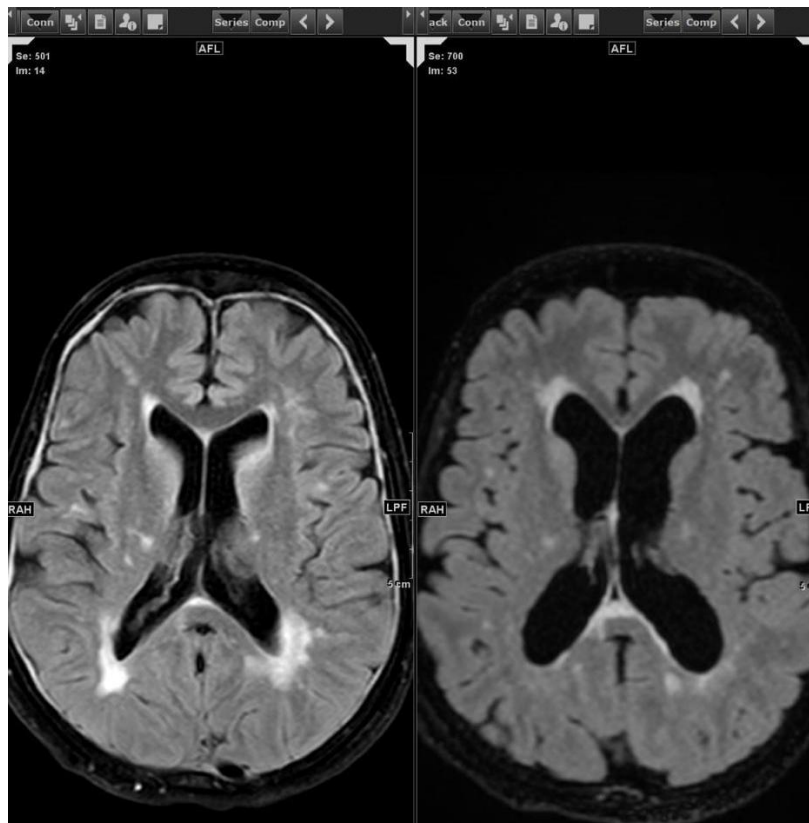


Fig. 7. MRI scan image of skull

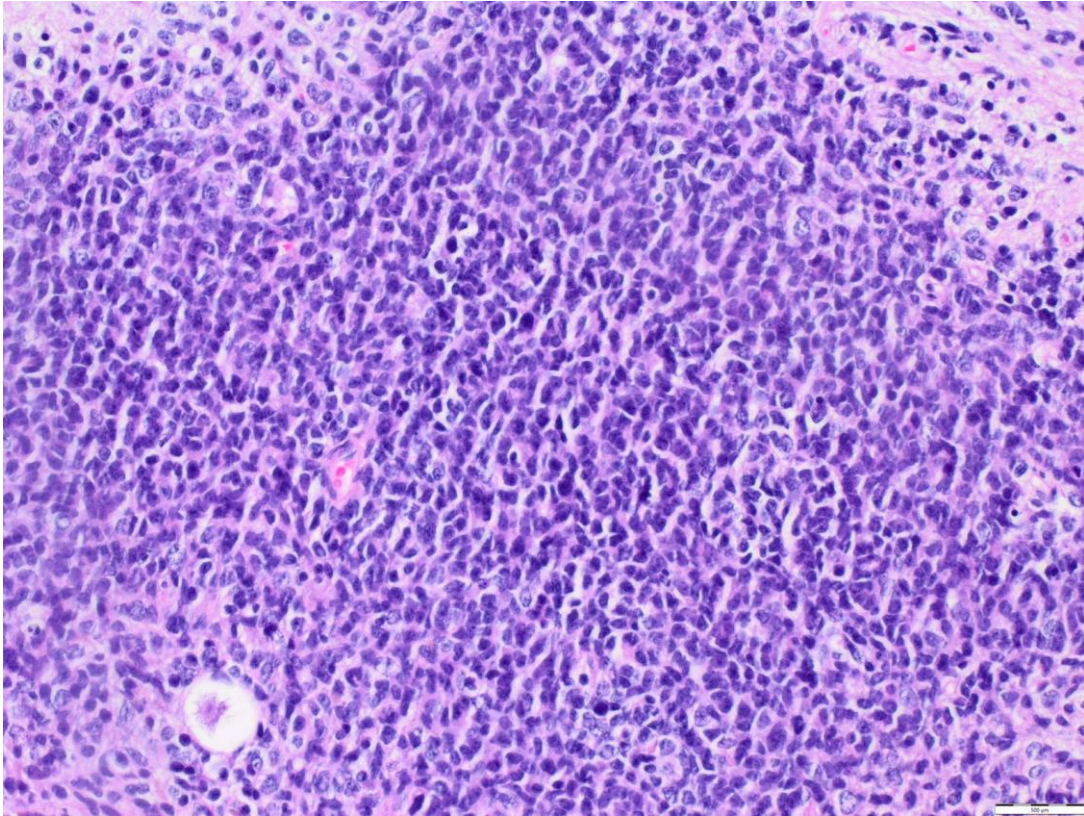


Fig. 8. Histopathology

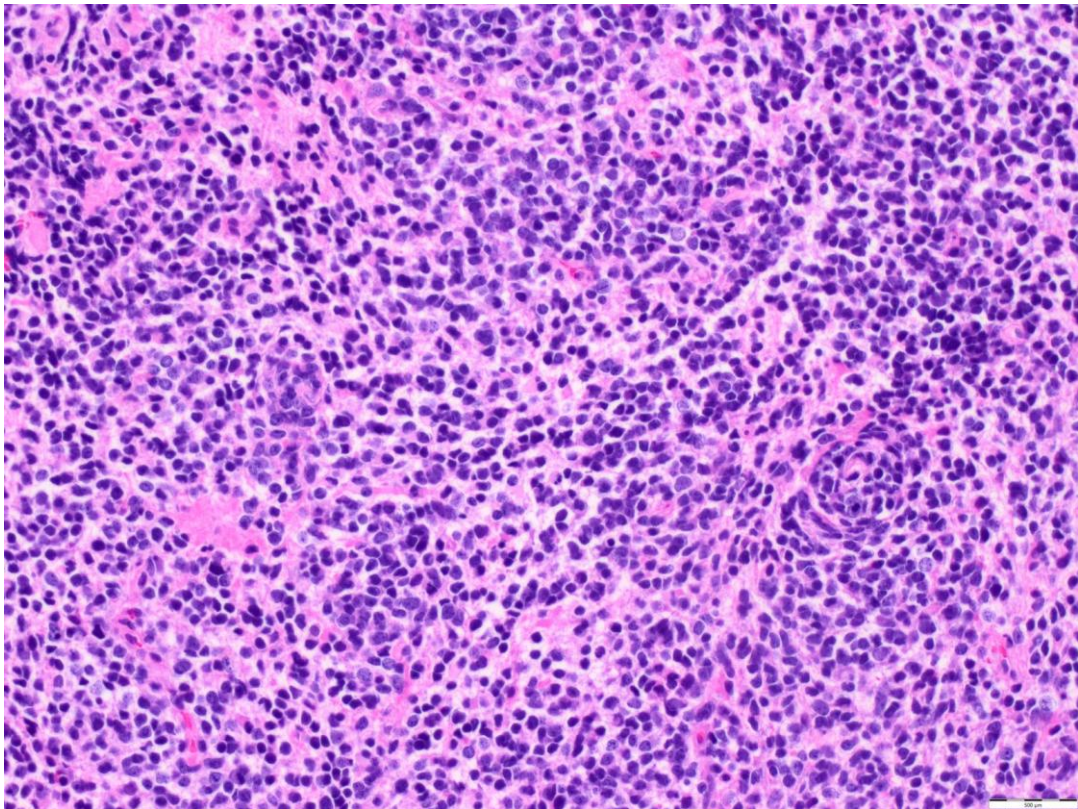


Fig. 9. Histopathological slide

Due to the rapid and aggressive growth of medulloblastomas, adjacent, vital structures can be displaced and damaged. In addition, depending on its exact localization, the tumor can cause a life-threatening drainage disorder of the cerebral fluid.

The main clinical manifestations of medulloblastoma are increased intracranial pressure and cerebellar ataxia. If the brain stem cell nucleus is damaged, the patient will experience gait disturbance, diplopia, and anesthesia. If the tumor involves the fourth ventricle, it may cause obstructive hydrocephalus. The clinical symptoms of this patient are not serious and are related to the tumor site.

The age of onset for medulloblastoma varies with the subtype of the tumor. There is a bimodal age distribution: on the one hand for small children, on the other hand for adults over 16 years of age. 10–50% of medulloblastomas have already spread at the time of diagnosis. The most common are so-called drip metastases [6] other case reports mentioned that some cases presented at age of more than 65 years. These spread along the subarachnoid space or the spinal axis. Metastases outside the nervous system are much less common. These occur in around 5% of patients.

On a computed tomography (CT) scan, the medulloblastoma typically looks light and absorbs contrast medium. Calcium deposits in the tumor can often be seen [7]. However, the gold standard for imaging is Magnetic Resonance Imaging (MRI), which should also include the spine in addition to the skull in order to exclude possible metastases in the entire central nervous system.

In addition to the imaging, a lumbar puncture is performed to examine the CSF, as tumor cells can occasionally be detected here [8]. However, a definitive diagnosis is only possible after the histological assessment of the surgically removed tumor tissue. The fine tissue composition has a direct influence on the therapy and also on the prognosis of the patient.

The therapy of choice is microsurgical resection of the tumor. The planning of the operation and the subsequent treatment takes place in close cooperation with an interdisciplinary team consisting of neurosurgeons, neuroradiologists, neuropathologists, oncologists and radiation

oncologists [9]. Due to the relatively rapid and aggressive growth of these tumors, today's treatment consists of a combination of surgical removal of the tumor as completely as possible, with maximum protection of the healthy surrounding brain tissue, with subsequent radio and / or chemotherapy.

The origin, pathological subtype, clinical treatment and prognosis of adult medulloblastoma are different from those of children; in adults, the 5-year survival rate after surgery is ~64.9-81.0%, and the 10-year survival rate after surgery is ~52.0-62.0%. The median survival time is 8.1–17.7 years [8].

Some studies have reported that elderly patients with medulloblastoma may have a better prognosis [9]. As the general population ages, there may be more similar cases reported in the future.

The therapy is based on individual criteria such as the subtype of the tumor, the patient's age, the general state of health of the patient as well as the possible extent of the surgical rehabilitation, the metastasis and, last but not least, the patient's tolerance of the therapeutic measures [10].

With the help of this aggressive therapy, up to 80% of medulloblastoma patients can be cured. The chances of success vary, however, depending on the subtype of the tumor. In children under 3 years of age, radiotherapy has severe side effects (neuropsychological deficits, endocrinopathies), so that such young patients only receive postoperative chemotherapy [11]. The primary goal of surgical treatment is a safe, minimally invasive and yet maximally radical removal of the tumor with restoration of unrestricted CSF drainage. If your own CSF flow cannot be restored, a ventriculoperitoneal shunt may be required [12]. Then the CSF is drained through a catheter under the skin into the abdomen.

5. DISCUSSION

Medulloblastomas are malignant brain tumors arising from primitive neuroepithelial cells in the cerebellum. They are the most common malignant brain tumor of childhood with a peak incidence between 5 and 9 years and a much smaller peak of 20- 24 years of age [13,14]. Ana. Da Silva has reported a 37-year-old MS female on Glatiramer acetate (GA), Five years later had

classic medulloblastoma. Following surgery, the patient was treated with craniospinal radiation therapy and multiagent chemotherapy [15]. Another 38-year-old MS woman has been reported by Abhimanyu Ghose. 4 to 5 months she developed post-diagnosis, dysmetria, bilateral nystagmus on lateral gaze. MRI showed a large left cerebellar tumor with Chiari 1 malformation and mild hydrocephalus. Positron emission tomography (PET)/CT showed FDG-avid masses involving the left lower lobe of the lung, left hilum, mediastinum, and bilateral supraclavicular lymph nodes. Excisional biopsy of a left supraclavicular lymph node showed metastatic medulloblastoma positive for GFAP, NSE, and synaptophysin [16]. A third case has been reported by Enshan Feng, who was a 72-year-old woman who had progressive dizziness and nystagmus for over 1 year. It was proved to have medulloblastoma, nodular type. The patient was treated with radiotherapy of the posterior cranial fossa [17].

6. CONCLUSION

The co-existence of adult medulloblastoma and multiple sclerosis has been described, many doubts regarding their possible causal association persist. Since MS is caused by putative CNS autoimmune mechanisms whereas brain neoplasms may be dependent on a subclinical immunosuppressive state, these pathologies can coexist only in particular situations. The patients affected by both diseases, which are located at the opposite ends of immunosurveillance, could allow to find the key to their pathogenesis.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s). The mentioned patient signed an informed consent for using her information in this case report.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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