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Case Report

Subdural Extramedullary Melanotic Schwannoma of the Thoracic Spinal Cord: A Case Report

Torasik Omuriliğin Subdural Ekstramedüller Melanotik Şıvanomu: Bir Olgu Raporu

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ABSTRACT

Melanotic schwannoma is a rare "Schwann" cell tumor characterized by the deposition of melanin in the cell cytoplasm. Melanotic schwannoma varies greatly in terms of morphology and clinical manifestations. Here, we describe a patient with subdural extramedullary melanotic schwannoma of the thoracic spinal cord. The 47-year-old man presented with pain in his chest and back that had lasted a year, numbness and weakness in both his lower extremities for 20 days, and urinary retention for 4 days. Magnetic resonance imaging (MRI) revealed a subdural extramedullary lesion at the level of the T2-T4 thoracic spinal cord. A total resection of the mass was performed. A diagnosis of melanotic schwannoma was made based on the histopathological examination. During the six-month follow-up period, no recurrence of the tumor was observed. A long-term follow-up will be necessary to fully evaluate this case.

KEYWORDS: Melanotic schwannoma, Extramedullary, Nerve sheath tumor

ÖZ

Melanotik şıvanom, hücre sitoplazmasında melanin birikmesiyle karakterize nadir bir "Schwann" hücresi tümörüdür. Melanotik şıvanom morfoloji ve klinik bulgular açısından büyük çeşitlilik gösterir. Burada, torasik omurilikte subdural ekstramedüller melanotik şıvanomlu bir hasta tanımlıyoruz. Kırkyedi yaşında erkek hasta, bir yıldır göğüs ve sırtında ağrı, 20 gündür her iki alt ekstremitede uyuşukluk ve kuvvetsizlik ve 4 gündür mevcut olan idrar yapamama şikayetleri ile geldi. Manyetik rezonans görüntüleme (MRG) T2-T4 torasik omurilik seviyesinde bir subdural ekstramedüller lezyon gösterdi. Kitlenin total rezeksiyonu yapıldı. Histopatolojik inceleme ile melanotik şıvanom tanısı kondu. Altı aylık takip döneminde tümör nüksü gözlenmedi. Bu olguyu tam olarak değerlendirmek için uzun süreli takip gerekecektir.

ANAHTAR SÖZCÜKLER: Melanotik şıvanom, Ekstramedüller, Sinir kılıfı tümörü

INTRODUCTION

Schwannoma is a benign, slowly-growing tumor composed of differentiated Schwann cells, which typically constitute the nerve sheath (24). Melanotic schwannoma (MS) is a variant of schwannoma characterized by the deposition of melanin in the Schwann cell cytoplasm (31). It is believed that the Schwann cells comprising this tumor themselves produce melanin, likely because Schwann cells are derived from migrated neural crest cells that have the capability of synthesizing melanin (3, 24). This melanin-producing tumor is rare, accounting for approximately 1% of primary peripheral nerve sheath tumors (24,31). The most common site of the tumor is in the nerve roots (4, 5,18,19). MS is found in extramedullary sites and in the peripheral nervous system, but is rarely seen in intramedullary sites (10, 21). MS is considered to be a benign tumor, but some tumors have been shown to be malignant with metastasis (12, 19, 22, 24, 25, 30). Since MS represents one of the most varied human tumors in terms of its morphology and clinical manifestations, its misdiagnosis is not uncommon. Clinical imaging and pathological finding can provide a correct diagnosis and indicate the appropriate treatment for patients with MS. Here, we describe the case of a 47-year-old man with MS, which was diagnosed by MRI and histopathological findings and treated with surgery.

CASE REPORT

On January 3, 2012, a 47-year-old man was admitted to our hospital presenting with a history of progressive spinal cord dysfunction. He complained of pain in his chest and back, and had been diagnosed and treated for one year previously. He complained about numbness and weakness in both his lower extremities and frequent falls while walking, which had begun 20 days before his admission. His symptoms worsened progressively over this time, with the occurrence of urinary retention four days before admission.

Examination

No obvious deposition of pigment was found in the skin and mucosa. There was no previous history of a surgical procedure for the removal of MS. On neurological examination, the

shallow sensation below the T4 level disappeared. Muscle strength was 1/5 in the left lower extremity and 3/5 in the right lower extremity. Muscle tone was normal in both lower extremities. Knee tendon reflex disappeared in the left lower extremity. No positive pathological reflexes were present bilaterally. Percussion pain was present in the thoracic spine.

Radiological Findings

Computed tomography (CT) images of the head, chest, abdomen, and pelvis were normal. A magnetic resonance imaging (MRI) scan of the thoracic spine revealed a multinodular extramedullary lesion with shorter T1 and short T2 signals. The lesion exhibited low signal intensity on fat-suppressed images. MRI images showed a mass lesion of 4.5 × 1.5 cm in size extending from T2 to T4. The enhanced MRI revealed that the mass exhibited less homogeneous enhancement with nodular changes in some regions and meningeal thickening and enhancement. The T2-T4 spinal cord exhibited obvious suppression, and abnormal patchy signals with equal T1 and long T2 were observed. The lesion showed high signal intensity on fat-suppressed images (Figure 1A-D). The preoperative diagnosis was a subdural extramedullary tumor (possible melanotic schwannoma) of the T2-T4 thoracic spinal cord.

Cerebrospinal Fluid (CSF) Examination

Lumbar puncture revealed a CSF pressure of 150 mmH_2O. The white blood cell count was 3×10^6/L, and the protein level was 3.3 g/L. Glucose levels and chloride content were normal. No tumor cells were identified in the CSF. Immunoreactivity for tumor markers, such as CEA, CA125, CA19-9, and CYFRA21-1, was negative.

Operation

Under general anesthesia, T2-T4 laminectomies were performed. After the dura mater was exposed, the black bulging dura was seen at the T2-T4 level. No spinal cord pulsation was observed. After the dura mater was opened, the black and thickened arachnoid and pia mater was seen. The tumor, 2.5 cm × 1.5 cm × 4.5 cm in size, was black, oval-shaped, and hard, with well-demarcated borders. The tumor was located ventrally to the spinal cord, and had compressed the spinal cord to arch posteriorly toward the right side (Figure 2). The spinal cord had become thin due to the tumor's compression. The tumor had an intact capsule, which adhered to the dura and the spinal cord, and was well supplied with blood vessels. The T3 spinal nerve root was also invaded by the tumor. Total *en bloc* removal of the tumor was achieved by dissection of the tumor's blood vessels and adhesions using an operating microscope. The pulsation of the spinal cord was recovered.

Histopathological Examination

Under a light microscope, a large number of tumor cells were

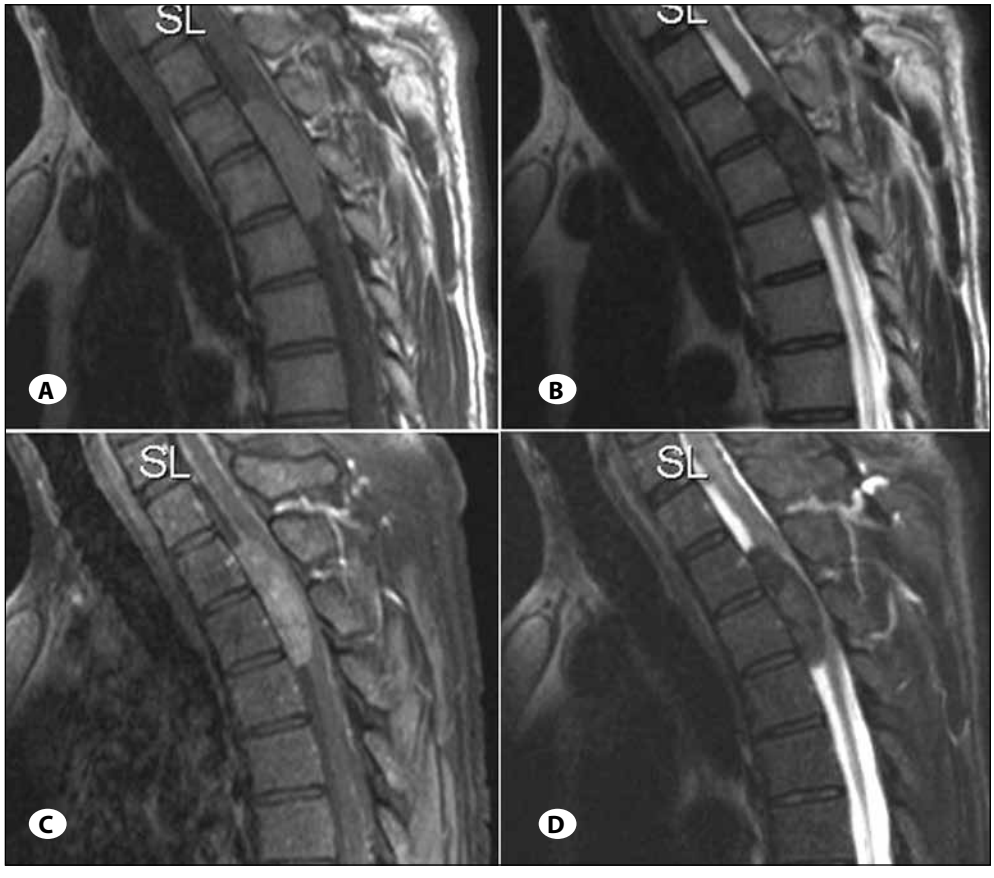

Figure 1: Sagittal magnetic resonance imaging (MRI) showing an extramedullary tumor of the T2-T4 thoracic spinal cord. **A)** T1-weighted MRI showing that the tumor exhibited slightly higher intensity. **B)** T2-weighted MRI showing that the tumor exhibited low signal intensity. The tumor was 4.5 × 1.5 cm in size and had a wide base attached to the dura mater. The spinal cord was migrated due to the tumor's compression. **C,D)** Enhanced MRI showing that the lesion exhibited less homogeneous enhancement with nodular changes in some regions and meningeal thickening and enhancement.

seen (Figure 3, 4). The tumor was composed of polygonal epithelioid cells and spindle-shaped cells. The abundant cytoplasm contained melanin granules, and hemorrhage was observed in the tumor. Immunocytochemistry for HMB45 (Figure 5), Ki-67 (1% of cells were positive), p53 (weak positive, 30% of cells were positive), Vimentin, and S-100 was positive, and immunoreactivity for PR, EMA, CD34, and GFAP was negative. The pathological diagnosis was melanotic schwannoma.

Postoperative Course

At one day following the operation, sensory disturbances were obviously decreased. After one week postoperatively, the patient had 2/5 muscle strength in the left lower extremity and 4/5 muscle strength in the right lower extremity. The deep and shallow sensation in both lower extremities was normal. Urinary retention was remarkably improved. The patient's stitches were removed at 12 days following the operation, at which time the surgical wound was primarily healed. The follow-up MRI showed that the tumor was completely removed (Figure 6). The patient was discharged with a

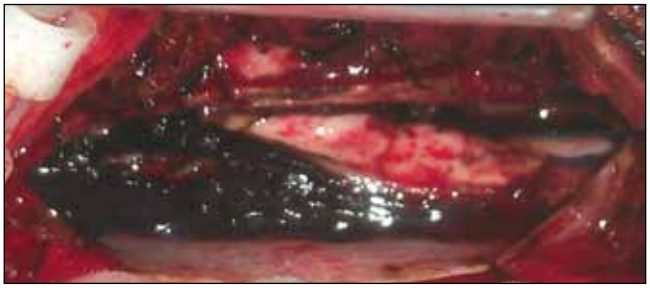

Figure 2: A dark-pigmented tumor was observed during the operation. The spinal cord was compressed to arch posteriorly toward the right side.

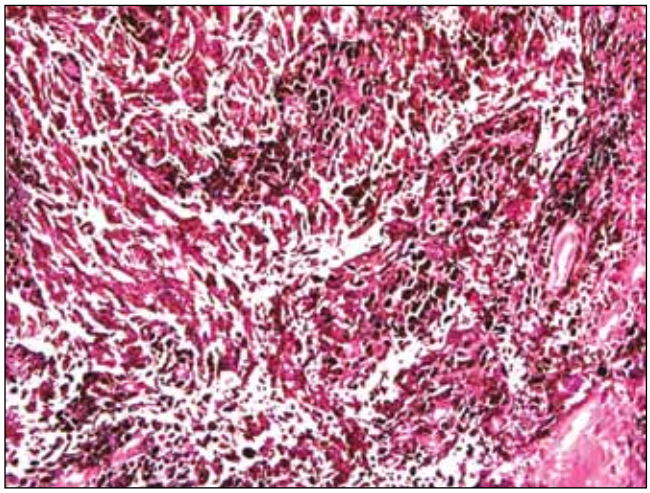

Figure 3: Photomicrograph showing a tumor composed of polygonal epithelioid and spindle-shaped cells with uniform sizes. The tumor cells were arranged in a nest-like pattern, with little interstitial tissues. The deposition of melanin granules was observed in the cell cytoplasm. Hematoxylin-Eosin (HE) x100).

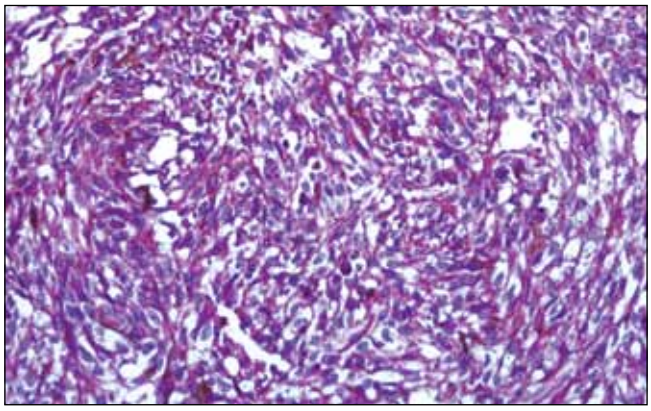

Figure 4: Photomicrograph showing tumor cells arranged in short bundles or interlacing fascicles consistent with the features of an Antoni area.

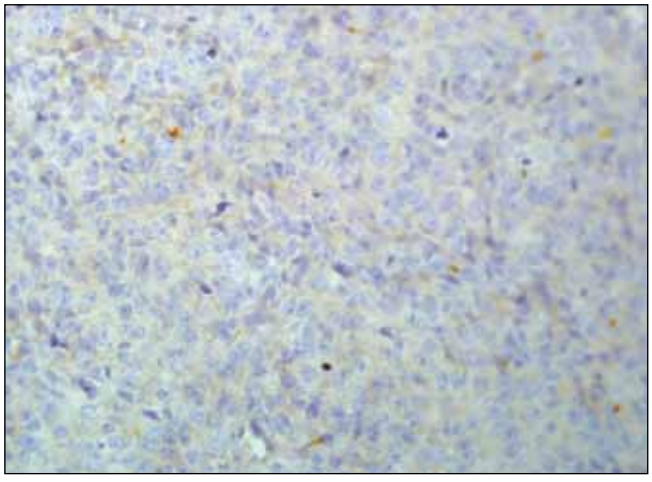

Figure 5: Immunocytochemistry showing that tumor cells were immunoreactive for HMB45.

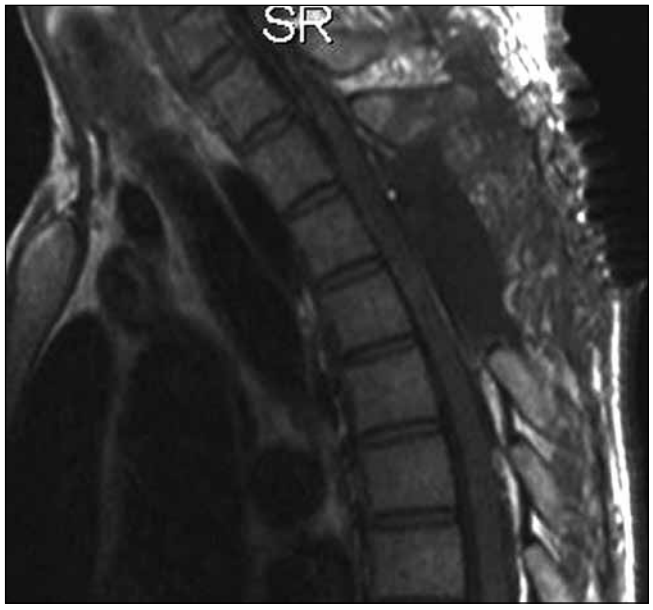

Figure 6: The postoperative gadolinium enhanced MRI demonstrating the absence of the tumor.

recommendation for functional exercises. During the follow-up period of 6 months, no tumor recurrence was found. The patient was able to work and study normally.

DISCUSSION

Primary central nervous system (CNS) melanoma is defined by World Health Organization (WHO) as a group of diffuse or localized, benign or malignant tumors derived from the pia mater, including melanotic schwannoma, melanocytic nevus, and primary malignant melanoma (17). The diagnosis of primary CNS melanoma is based on three criteria, including exclusion of melanoma in skin and eye, no history of melanoma excision, and no visceral melanoma metastasis (23). Primary central nervous system (CNS) melanoma is rare, accounting for approximately 1% of all melanoma cases (23). The preoperative diagnosis of primary CNS melanoma is difficult, and is associated with a high misdiagnosis rate. A correct diagnosis depends upon both pathological findings and treatment results (23).

MS is a tumor derived from progenitor neural crest cells that can differentiate into both Schwann cells and melanocytes. Most MS tumors are benign, but some exhibit malignant transformation. MS is often present in young patients. The most frequent sites of melanotic schwannoma are nerve roots and sympathetic chains (2, 4, 5, 16, 18, 19, 24, 31). It has been reported that melanotic schwannoma sporadically occurs in the orbit, oral cavity, skin, and pancreas (1, 7, 9, 14). The most frequent sites of MS include subdural extramedullary locations, or intradural locations at the level of the cervical, lower thoracic, and thoracolumbar spinal cord. The tumor can invade and damage the intervertebral foramen through the nerve root cuff. Because the tumor originates in the vicinity of the spinal nerve roots, these structures are often compressed by the tumor, leading to the spinal nerve root and lower back pain that is often the first clinical manifestation of patients with MS, and which can be easily misdiagnosed as signs of an intervertebral disc disorder. With the growth of the tumor, spinal cord compression can lead to clinical signs of sensory, locomotor, urinary, and fecal dysfunction, depending upon the site of compression. Signs of meningeal irritation may also occur due to tumor metabolic products and apoplexy. In the current case, our patient exhibited classical symptoms and signs of spinal nerve pain and progressive spinal compression, without signs of meningeal irritation. The physical examination did not identify obvious deposition of pigment in the skin and mucosa. In addition, the patient had no previous history of a surgical procedure for the removal of melanotic schwannoma, and had normal CT images of the head, chest, abdomen, and pelvis. All these findings are consistent with the diagnosis of primary MS in the vertebral canal.

MS tumors exhibit hyperintensity on T1-weighted (T1WI) and hypointensity on T2-weighted (T2WI) MRIs due to the paramagnetic effect of melanin (11, 26). MRI findings can vary depending on the contents and distribution of melanin in the MS. Only MS comprised of more than 10% melanin-containing cells exhibited hyperintensity on T1WI MRI and hypointensity on T2WI MRI (11, 13). Hypointensity on T2WI is a characteristic feature of melanoma, but only occurs in approximately 25% of all melanomas (13). The appearance of a hematoma and the uneven distribution of melanin in the tumor can lead to inhomogeneous signals in the lesion, which can exhibit mild, moderate, and strong enhancement (11, 13). Based on MRI patterns, Isiklar et al. (1995) categorized MS into melanotic, mixed, amelanotic, and hematoma types (11). The melanotic MRI imaging pattern accounts for 70% of the MS (11). Tumor apoplexy is an important factor that affects MRI findings of MS (6, 28). Because deoxy-hemoglobin, methemoglobin, and the iron-containing heme released following hemorrhage of tumor exhibit different paramagnetic effects, the tumor may display different patterns on MRI images at different stages of hemorrhage. Therefore, the percentage of melanin-containing cells in the tumor and the presence of hematoma contribute to the complexity accompanying MRI of MS.

It is important to differentiate MS from meningioma, schwannoma, epidural hematoma, lipoma, and dermoid cysts based on the imaging findings. MS is often located in the intradural extramedullary sites at the level of the thoracolumbar spinal cord, similar to meningioma and schwannoma. MS can invade the intervertebral foramen through the nerve root cuff, and grow to form a dumbbell-shaped tumor, leading to enlargement of the intravertebral foramen and the destruction of the bone. This dumbbell morphology is a common imaging feature of schwannoma. These similarities of location and dumbbell-like morphology make it difficult to distinguish MS from schwannoma using imaging alone. In addition, MS can have a wide base attached to the dura mater, and grow along the dura to form a "grape-like" tumor. In this case, MS can exhibit "dural tail" sign (thickening of the dura adjacent to the tumor in contrast enhanced MRI), which is a typical feature of meningioma. However, these tumors may be differentiated by MRI features. For example, MS exhibits hypointensity on T1WI MRI, slight hyperintensity on T2WI MRI, inhomogeneous signals in tumors with cystic changes, and inhomogeneous enhancement on enhanced MRI. In contrast, meningioma exhibits isointensity on T1WI MRI, isointensity or slight hyperintensity on T2WI MRI, homogeneous enhancement on enhanced MRI, and hypointensity in tumors with calcification (20, 27). These different imaging features can be useful to distinguish MS from meningioma. In addition, subacute and chronic epidural hematoma exhibits hyperintensity on MRI with short T1 and long T2 signals, and the MRI signals may show dynamic changes with the development of the hematoma. Lipoma and dermoid cysts exhibit short T1 and slightly long T2 signal on MRI, and reduced T1 hyperintensity on fat-suppressed images. In contrast, MS exhibits shorter T1 and short T2 signals on MRI, and hypointensity on fat-suppressed images. These imaging features are helpful in distinguishing MS from epidural hematoma, lipoma, and dermoid cysts.

Total *en bloc* resection of the tumor is the first choice treatment for MS, and is necessary to prevent both tumor recurrence

and malignant transformation. Because the blood supply to the tumor is very rich, care should be taken to dissect the blood vessels of the tumor as well as the adhesions between the tumor and the dura mater, pia mater, and spine cord. The partial resection of the tumor should be avoided prior to blocking the blood supply to the tumor. If tight adhesions occur between the tumor and the spinal cord, the forcible dissection of the adhesions should be avoided. In this case, a residual capsule of the tumor should be left to prevent the catastrophic consequences of spinal cord injury caused by forcible dissection and postoperative radiotherapy should be given to patients with partially resected tumors. In the current case, as total *en bloc* resection of the tumor was performed, postoperative radiotherapy was not given. At one day after the operation, the patient exhibited reduced sensory disturbances. At one week postoperatively, the patient had 2/5 muscle strength in the left lower extremity and 4/5 muscle strength in the right lower extremity. The deep and shallow sensation in both lower extremities was normal. Urinary retention was remarkably improved. We concluded that the results of the operation were satisfactory.

Following surgery, the correct diagnosis of MS relies upon the pathological findings. Under the light microscope, MS is composed of epithelioid Schwann cells and pigmented spindle-shaped cells arranged in short bundles, interlacing fascicles, or in a wheel-like pattern. The nuclei of these cells are round or oval with distinct nucleoli. Mitoses are rare. A typical MS exhibits palisades-like nuclei and verocay body-like structures accompanied with cystic changes, hemorrhagic necrosis, psammoma bodies, calcification, and areas of mature fat (31). Ultrastructurally, MS exhibits characteristic features of Schwann cells such as a continuous basement membrane and long-spacing collagen fibers. Immunohistochemically, MS is characterized by immunoreactivity for HMB45 and Menlan A (makers for melanocytes), as well as SOX10 and MBP (makers for schwannoma) (31). Most MS tumors exhibit low mitotic and proliferation indexes, with low MIB-1 positive rates. The presence of increased mitoses associated with nuclear atypia and zonal necrosis indicates the malignant transformation of the MS (29). In the current case, we found that the MS was composed of polygonal epithelioid cells and spindle-shaped cells containing melanin granules in the cytoplasm. Immunoreactivity for HMB45 was positive. These histopathological findings are important in order to differentiate MS from metastatic or primary malignant melanoma, pigmented neurofibroma, intraspinal hematoma, and meningeal melanocytoma.

The prognosis of MS is unpredictable, since MS can locally invade and metastasize without the presence of malignant histological features (8, 29). It has been reported that MS recurs following resection in 15%-24% of patients, and metastasis occurs in 9.1% -26.3% of patients with MS (15, 29, 31). This recurrence has been found only in partially removed tumors (15). In the current case, no recurrence or metastasis was found during the follow-up period of 6 months. A long-term follow-up will be needed for this patient.

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