

Spinal Nerve Root Extradural Melanocytoma Progressing to Malignant Melanoma: A Case Report with Review of Literature

Abstract

Melanocytomas are rare benign pigmented tumors arising from the leptomeninges with a very remote chance of progressing to malignant melanoma. They have a predilection for occurring in the posterior fossa or in the intradural extramedullary region of the cervical spine. We report the first case of malignant transformation of a nerve root (extradural) melanocytoma wherein immunotherapy has been added for its treatment. Only four such cases of malignant transformation of central nervous system melanocytoma have been reported in the literature. Definite diagnosis in such cases is based on immunohistochemistry evaluation. Surgical resection with adjuvant radiotherapy and immunotherapy is the recommended treatment.

Keywords: Immunotherapy, melanoma, meningeal melanocytoma, nerve root, spine

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Introduction

Melanocytomas comprise <0.1% of all brain tumors.^[1] The primitive neural crest cells give origin to melanocytes present in the leptomeningeal tissues. These melanocytes on acquiring melanoblastic activity give rise to the benign entity known as melanocytoma. Limas and Tio first coined this term in 1972 to describe a pigmented tumor around the foramen magnum on autopsy.^[2] The majority of spinal melanocytomas remain benign and are intradural extramedullary in location with a predilection for the cervical spine due to the increased concentration of melanocytic cells.^[3] This case stands distinct in highlighting the rare occurrence of a lumbar spinal nerve root extradural melanocytoma, emphasizing the remote possibility of its histological progression into malignant melanoma, tackled with the help of adjuvant radiotherapy (RT) and immunotherapy.

Case Report

A 36-year-old female, professional dancer, presented to us with complaints of low back pain for 6 months with acute exacerbation in the last 20 days. The pain was sharp, radiating along the anterior aspect of the thigh up to the knee, and aggravated on

walking for a few seconds or on trying to get up from sitting position. Her straight leg raising was severely restricted to 20° on the left side without any sensory or motor deficit. Magnetic resonance imaging (MRI) showed a dumbbell-shaped mass in the left L3–L4 intervertebral foramen with a large extraforaminal component and a minimal intraspinal component. The lesion was well-defined, hyperintense on T1-weighted images (T1WIs) [Figure 1a], hypointense on T2WI [Figure 1b], and showed homogeneous contrast enhancement [Figure 1c]. A provisional diagnosis of a nerve sheath tumor with bleed was made. A left paramedian Wiltse's muscle-splitting approach was taken using tubular retractors. On splitting the intertransverse ligament between the left L3 and L4 transverse process, a swollen L3 nerve root was identified. No tumor was visualized on the surface of the nerve. The epineurium of the nerve was split in the direction of the nerve fibers, and the lesion was visualized within the nerve splaying the nerve fibers. No definite attachment to the nerve fascicles was noted. It was extremely vascular and pigmented [Figure 1d]. Left L3–L4 lateral foraminotomy was performed, and the foraminal component was curetted out. There was no intradural extension or cerebrospinal fluid leak

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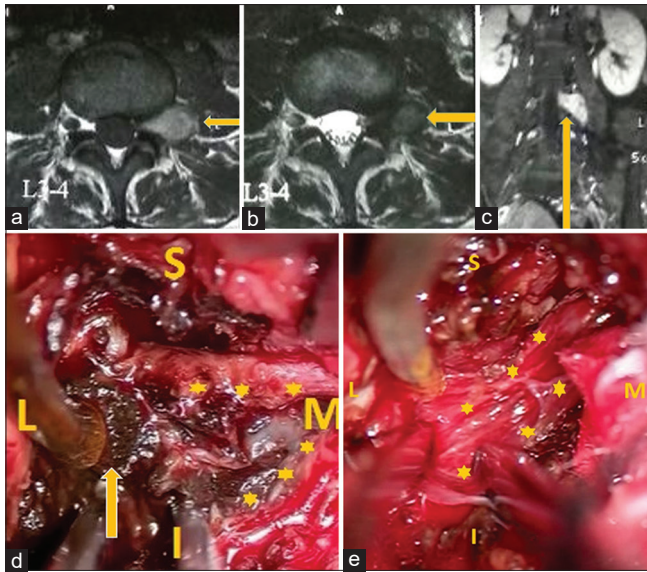


Figure 1: (a) Magnetic resonance imaging lumbar spine (T1 axial) showing a dumbbell-shaped hyperintense mass in the left L3–L4 intervertebral foramen with extraforaminal component, (b) T2 axial magnetic resonance imaging showing the hypointense lesion, (c) Postcontrast coronal magnetic resonance imaging showing homogeneous enhancement, (d) Intraoperative image of the dark brown pigmented tumor (yellow arrow) seen on incising the epineurium of the L3 nerve root (*). S = Superior, I = Inferior, M = Medial, L = Lateral. (e) Intraoperative image of the preserved nerve root (*) following complete excision of the melanocytoma. S = Superior, I = Inferior, M = Medial, L = Lateral

during the procedure. A gross resection of the lesion with preservation of nerve root [Figure 1e] was achieved.

Postoperatively, there was a marked improvement in her pain and mobility. Histopathology showed a nonencapsulated lesion with round-to-oval cell nests, eosinophilic nucleoli, and dense melanin-pigmented tumor cells [Figure 2]. Differential diagnosis of a melanocytic meningioma, intermediate-grade melanocytoma, or a melanocytic paraganglioma was considered. Immunohistochemistry was positive for S100 and homatropine methylbromide-45 (HMB-45) and negative for epithelial membrane antigen (EMA). The MIB-1 score was 3%–4%. Mitosis and pleomorphism were absent. These features were consistent with an intermediate-grade melanocytoma. Retrospectively, a detailed general examination did not reveal any cutaneous melanotic lesion. The patient was discharged without any new deficit.

On follow-up after 6 months, she had complaints of left lower-limb pain and sensory loss over the left anterior thigh. Imaging showed a recurrence at the local site [Figure 3a and b] infiltrating into the iliopsoas muscle [Figure 3c] with minimal foraminal and intraspinal extension. Positron emission tomography–computed tomography did not reveal any other systemic uptake. Oncology opinion was sought, and it was decided to do a left L3–L4 laminectomy, complete facetectomy, and a radical excision of her tumor with the affected muscle and left L3 root. She also underwent a right-sided L2–L4

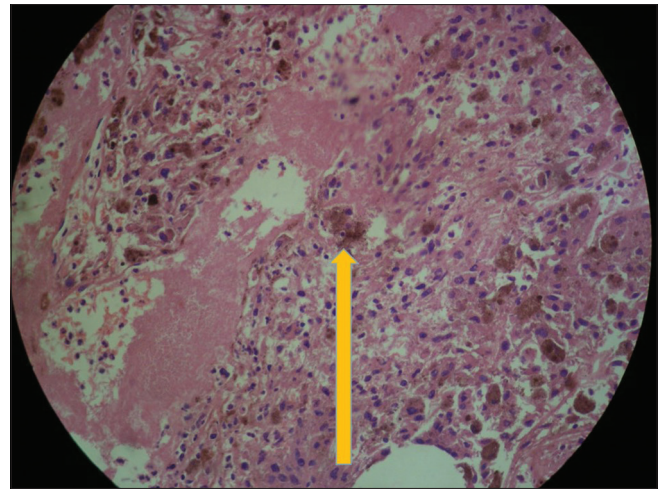


Figure 2: Histopathology image with hematoxylin and eosin stain (magnification, $\times 100$) showing round-to-oval cell nests with eosinophilic nucleoli and interspersed dense melanin-pigmented tumor cells (yellow arrow)

pedicle screw and rod fixation [Figure 3d-f]. Histopathology revealed a high-grade melanocytic tumor consistent with melanoma suggestive of histological progression. Adjuvant treatment in the form of spinal intensity-modulated radiation therapy (50 Gy in 25 fractions) and immunotherapy (240 mg nivolumab) was started. Her previous histopathology findings were revisited by a different pathologist, given the relatively short duration of recurrence, and reconfirmed to be intermediate-grade melanocytoma.

Over the next year, she developed multiple metastases in the lung, pleura, and iliopsoas muscle. The resultant pleural effusion was symptomatically managed. Lung nodule biopsy was suggestive of metastasis from the melanocytic neoplasm. Hence, ipilimumab was added (1 mg/kg), and oral targeted therapy with pazopanib (800 mg twice a day) was started. Nivolumab was temporarily put on hold. She was found to be intolerant to pazopanib, the medication was stopped after 7 days, and combination immunotherapy of nivolumab plus ipilimumab was restarted. She completed her immunotherapy cycles a few months ago (48 doses of nivolumab and 4 doses of ipilimumab). Clinically, till recently, she had a mild weakness 4+ out of 5 of the left quadriceps and subtle hypoesthesia in the anterior thigh. She was able to resume her passion for dance in a limited manner by avoiding squatting maneuvers and extreme lumbar movements. Unfortunately, she expired after 4 years of regular follow-up.

Discussion

The WHO classification of central nervous system (CNS) tumors lists melanocytic tumors as meningeal melanocytosis (Grade 0), meningeal melanocytoma (Grade I), meningeal melanoma (Grade III), and meningeal melanomatosis (Grade III).

Melanocytoma arising from within the nerve root is an extremely rare occurrence and so is its progression to

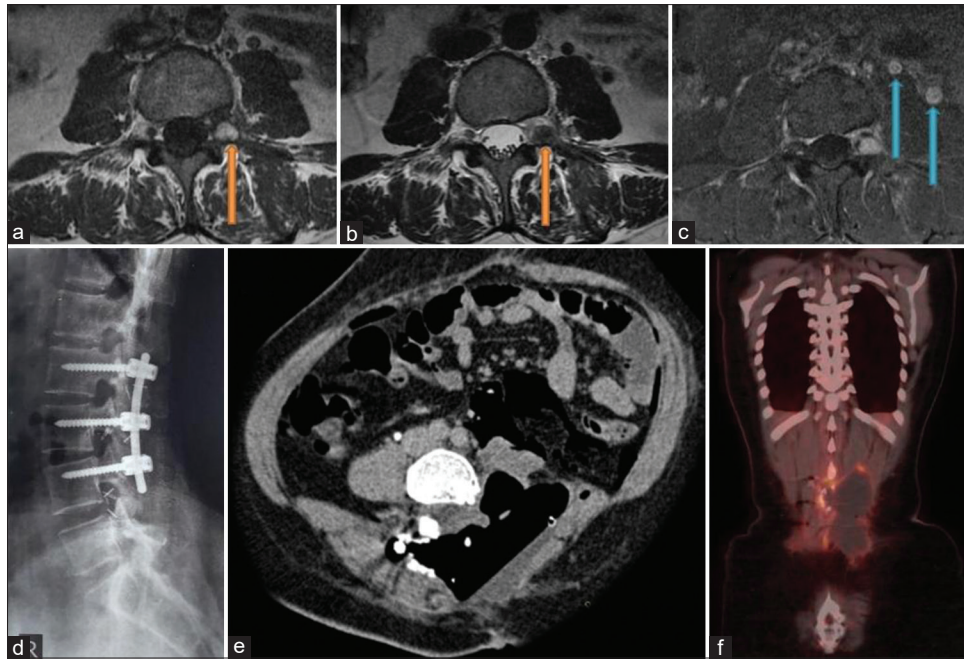


Figure 3: (a) Magnetic resonance imaging spine axial view (T1-weighted image) showing the local recurrence (orange arrow), (b) Magnetic resonance imaging spine axial view (T2-weighted image) showing the local recurrence (orange arrow), (c) Magnetic resonance imaging spine axial view (postcontrast image) showing the iliopsoas deposits (blue arrow), (d) Postoperative X-ray lateral view showing the L2–L4 pedicle screw and rod fixation, (e) Postoperative CT scan axial view showing the resected local cavity, (f) Postoperative positron emission tomography-computed tomography showing the resected local cavity

malignant melanoma with only four such cases published to date [Table 1].^[4-7] A series of 16 cases of meningeal melanocytomas followed up for close to 5 years showed no evidence of pathological progression.^[8]

Schwannoma and neurofibroma are the most common cause of a dumbbell-shaped lesion in the intervertebral foramen with associated scalloping. Other rare causes include malignant melanomas, pigmented meningiomas, and melanocytomas. Hemorrhage within a schwannoma and a malignant melanoma share similar clinical and radiological features with a benign melanocytoma. Melanocytomas are usually isointense to hyperintense on T1WI and isointense to hypointense on T2WI with homogeneous contrast enhancement, whereas spinal schwannomas are predominantly hypointense on T1WI and hyperintense on T2WI.^[9] Retrospectively, the presence of T1 hyperintense signal should have alerted us regarding the possible diagnosis of melanocytoma, however, we considered the diagnosis of a tumor with bleed due to the relatively acute onset of pain. Immunohistochemistry is diagnostic in characterizing these lesions. Melanocytomas are specifically positive for HMB-45 and S-100 and negative for EMA with a low MIB-1 index score.

The treatment goals for an intraneural melanocytoma are unknown, but complete surgical excision is generally recommended except in cases which are extremely vascular or excessively bulky. The role of adjuvant RT is still unclear. In a review of CNS melanocytomas, by Chow *et al.*,^[10] it was suggested that the long-term survival of cases, where subtotal resection was done, was not influenced by the

administration of adjuvant RT. Conversely, Rades *et al.*^[11] have suggested that the survival rate reduced significantly in patients who underwent a subtotal resection without adjuvant radiation. RT in doses of 45–55 Gy has been recommended for optimal benefit. Stereotactic radiosurgery (SRS) and dacarbazine-based chemotherapy have also been attempted in the past with limited results.^[12]

Recently, an immunotherapy combination of anti-cytotoxic T-lymphocyte-associated protein drug ipilimumab and anti-programmed cell death protein-1 drug nivolumab has been found to have better progression-free survival and overall survival in cases with metastatic melanoma.^[13] Pazopanib, a tyrosine kinase inhibitor, has been tried for advanced melanoma treatment. However, it has been found to have very poor tolerability with limited patient adherence.^[14] To the best of our knowledge, the current case is the only extradurally occurring melanocytoma to undergo malignant transformation with the previous four cases consisting of melanocytomas present in the frontal lobe, petroclival region, thoracic intramedullary spine, and lumbar intradural extramedullary location [Table 1]. This is also the first instance where immunotherapy has been employed for malignant transformation of a CNS melanocytoma. All the previous reported cases received either RT or SRS, with one case receiving chemotherapy in addition to RT and SRS [Table 1]. The survival in the literature has been extremely variable ranging from 17 months to 13 years [Table 1].

Ideal management of a spinal nerve root melanocytoma is still debatable with no single modality proven to be

Table 1: Published cases of melanocytoma showing malignant transformation (including the present case)

Author	Years	Age/sex	Location of melanocytoma	Treatment	Malignant transformation	Follow up
Uozumi <i>et al.</i> ^[4]	2002	49/male	Frontal lobe	Surgery+SRS	Local+CSF dissemination	Expired after 5 years of surgery
Rades <i>et al.</i> ^[5]	2002	23/female	Thoracic intramedullary	Surgery+RT	Local+brain metastasis	Expired after 4 years of surgery
Roser <i>et al.</i> ^[6]	2004	37/female	Petroclival	Surgery+RT+CT+SRS	Local	Expired after 13 years of surgery
Wang <i>et al.</i> ^[7]	2007	57/male	Lumbar IDEM	Surgery+RT	Local+systemic	1 year 5 months
Shaikh <i>et al.</i> (current case)	2020	36/female	L3 nerve root	Surgery+immunotherapy	Local+systemic	Expired after 4 years of surgery

SRS-Stereotactic radiosurgery; CSF-Cerebrospinal fluid; RT-Radiotherapy; CT-Chemotherapy; IDEM-Intradural extramedullary

completely effective. Close and prolonged follow-up seems prudent, given the risk of recurrence which can be as high as 50%.^[15] Patients with melanocytoma must be counseled regarding the risk of malignant progression of the disease. Radical resection of locally invasive melanocytoma may be considered in the absence of systemic disease after thorough oncology and pathology review.

Conclusion

Benign melanocytoma originating from the nerve root is a rare phenomenon. MRI features of a dumbbell-shaped lesion with T1 hyperintensity, T2 hypointensity, and homogeneous contrast enhancement should raise a suspicion of this rare entity. Definite diagnosis is based on histological and immunohistochemistry evaluation. Surgical resection followed by RT and immunotherapy should be the preferred modality of treatment in cases of malignant transformation.

Patient consent

The patient has consented to the submission of the case report for submission to the journal.

Declaration of patient consent

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

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Nil.

Conflicts of interest

There are no conflicts of interest.

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