Oncologie

Tech Science Press

DOI: 10.32604/oncologie.2022.019263

CASE REPORT

A Primary Sacral Melanoma of Unknown Origin: A Case Report

Ismail Bozkurt[1,*], Baris Yasar[1], Mehmet Baran Uslu[2] and Nazan Bozdogan[3]

[1]Department of Neurosurgery, Cankiri State Hospital, Cankiri, Turkey

[2]Department of Orthopedics, Cankiri State Hospital, Cankiri, Turkey

[3]Department of Pathology, Dr. A.Y. Ankara Oncology Training and Research Hospital, Ankara, Turkey

[*]Corresponding Author: Ismail Bozkurt. Email: ibozkurt85@gmail.com

Received: 12 September 2021 Accepted: 28 December 2021

ABSTRACT

Malignant melanoma caused by malignant transformation of melanocytes is associated with high mortality and is difficult to manage. Metastasis is not uncommon (up to 31% of all cases) and is closely associated with a poor prognosis. Although rare (4–5%), extracutaneous melanoma has been reported; however, primary malignant melanoma of the sacrum is extremely rare (only three case reports to date). Here, we present a 51-year-old patient who underwent surgical treatment for a lesion of the spinal canal and associated bony structures; extensive aggressive resection was required. She underwent partial sacrectomy and lumbo-iliac fixation (to maintain spinal stability). Pathology revealed malignant melanoma. We discuss the diagnosis, surgical intervention, and postoperative follow-up, which may assist clinicians. Although metastatic malignant melanoma is usually fatal, primary extracutaneous melanoma of the spine may respond well to surgery and adjuvant radiotherapy.

KEYWORDS

Malignant melanoma; sacrum; lumbo-iliac; extracutaneous

1 Introduction

The incidence of malignant melanoma is increasing globally, and the condition has become a public health issue [1]. The disease is an aggressive therapy-resistant malignancy of melanocytes, where 95% of all cases involve the skin. Primary (extracutaneous) ocular, mucosal, gastrointestinal, genitourinary, leptomeningeal, lymph node, and (rarely) sacral melanomas have been reported [1]. The known risk factors include a relevant family history, deep skin pigmentation, and living close to the equator [1].

The primary sites of 97% of all melanomas are known, but 3.2% have no known origin and are described as melanoma of unknown primary (MUP) [2]. Although the incidence of spinal metastasis is only 2.4%, this rate is increasing and spinal surgeons must be aware of this condition [3]. Primary spinal melanoma (PSM) of no known origin is extremely rare [3]. There are only three previous studies [3–5], which did not perform full radiological evaluations or required extensive surgical intervention. Being an extremely rare condition with limited data, here we report a 51-year-old woman with malignant sacral melanoma. The tumor had invaded the surrounding bony structures and obliterated the spinal canal. There was no obvious primary lesion. The patient underwent gross total resection and lumbo-iliac fixation. This case is unique due to its rarity and extensive invasion into the surrounding osseous structures and has been presented with detailed documentation of diagnosis, surgical approach and postoperative follow-up with the intent of aiding clinicians managing PSM.

2 Case Report

A 51-year-old otherwise healthy woman was referred to our outpatient clinic after undergoing lumbosacral magnetic resonance imaging (MRI) elsewhere because of chronic pain emanating from around the left buttock and extending down to the left lower extremity. The pain had become aggravated over the prior 3 months and did not respond to medical therapy. She also complained of urinary incontinence. Physical examination revealed a tender point over the left buttock, close to the sacrum, but no trophic change. Neurological examination revealed a diminished left Achilles tendon reflex along and a motor strength of 3/5 in ankle plantar flexion. She evidenced hypoesthesia of the lateral side of her foot, all suggesting. These findings all suggested S1 root involvement.

A plain radiograph did not yield any finding, but computed tomography (CT) revealed a destructive lesion in the sacrum and left ilium that infiltrated the spinal canal and extended to the left sacroiliac joint (Fig. 1). Contrast-enhanced T1-weighted MRI revealed a homogenously, densely enhanced lesion measuring 50 * 48 mm in diameter (Fig. 2). The radiologist suggested a chordoma or giant cell tumor. CT of the thorax and abdomen, and measurements of standard tumor markers, did not reveal any abnormality. The standard blood tests were normal. Scintigraphy was not available. Given her urgent and deteriorating symptoms, we performed surgery.

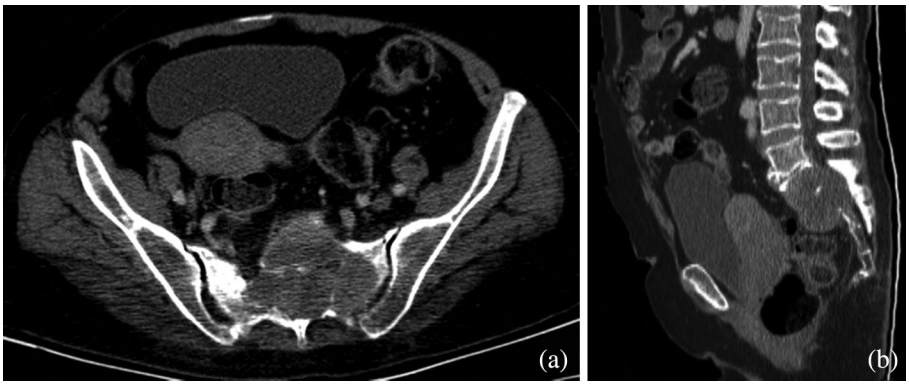

Figure 1: (a) CT demonstrating the osteolytic lesion of the sacrum invading the surrounding tissue in all aspects along with the spinal canal. (b) Sagittal reconstructed view of the CT showing the anterior and posterior invasion of the mass encompassing the S1 and S2 vertebral body

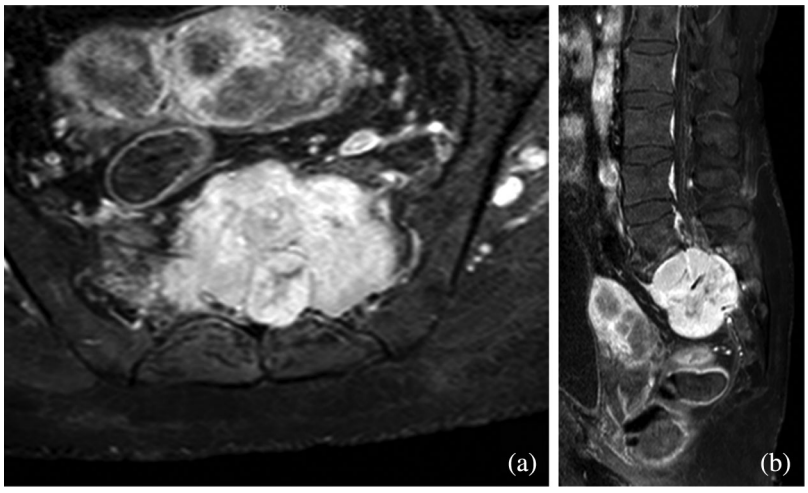

Figure 2: Contrast enhanced T1 weighted MRI. Homogenous uptake of contrast of the lesion encompassing the S1 and S2 vertebral bodies in total and obliterating the spinal canal with a predominance of the left side (a: axial, b: sagittal view)

We established intraoperative neuromonitoring (IONM) and placed the patient under general anesthesia. We created a standard midline skin incision to expose the sacrum, iliac wings, and L3-5 vertebrae. We found a large bony eminence extending from the median sacral crest to the left lateral crest and the auricular surface of the sacroiliac joint. After removal of the posterior sacrum, a large, dark colored, semi solid hypervascular lesion was detected. The lesion was removed with meticulous protection of the nervous structures (guided by IONM). Circumferential debulking of the surrounding bony structures followed and we excised the bodies of S1 and S2 vertebrae and the articular face of the left sacroiliac joint. After partial sacrectomy, transpedicular polyaxial screws were inserted bilaterally into the L3-5 vertebrae, initially connected with two rods and then connected to bilateral polyaxial screws placed in the ilium; this afforded lumbo-iliac fixation. Two more polyaxial screws were placed in the ilium and connected with a rod. This facilitated fixation of autologous fibular grafts (using a titanium cable) (Fig. 3). We performed postoperative CT (Fig. 4); the patient was mobilized (with a brace) 12 h later. She was discharged 4 days after the surgery with no additional neurological deficits.

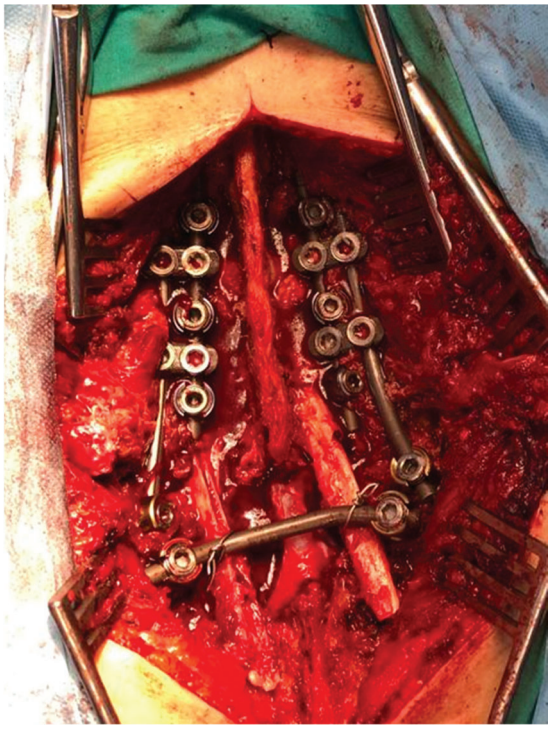

Figure 3: Intraoperative image after the removal of the mass with viable nervous structures along with the lumbo-iliac fixation and fibular autograft

On pathological examination, the tumor contained a mixoid matrix. The majority of tumor-forming cells were atypical cells containing large pleomorphic nucleoli. Tumor cells formed trabecular and papilla-like areas in focal places. 10 mitoses per 10 HPF (high power field) in the tumor were counted. Atypical mitoses were detected. Tumor cells showed an infiltration into the surrounding bone tissue. In the immunohistochemical examination, S-100 showed extensive and strong staining. There was diffuse staining with SOX-10 and MelanA and focal staining with HMB45. There was no staining with Pan CK, EMA, GFAP, actin, desmin, calponin, SMA, Fli-1 and ERG. Ki-67 index reached 35–40% in hot spots (Fig. 5). With these findings, the diagnosis of melanocytic tumor accordance with melanoma was made.

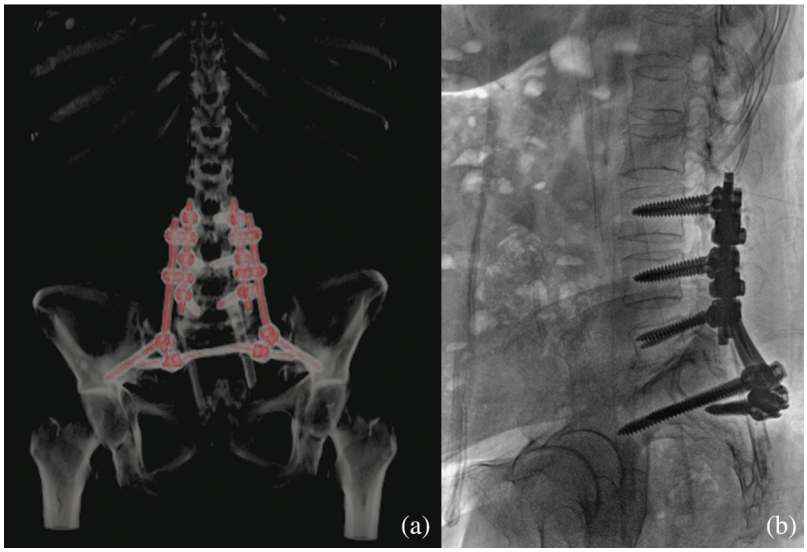

Figure 4: (a) 3D reconstruction of the postoperative CT scan showing the adequately placed polyaxial screws achieving lumbo-iliac fixation. (b) Absence of greater sciatic notch breach on the lateral plain radiograph

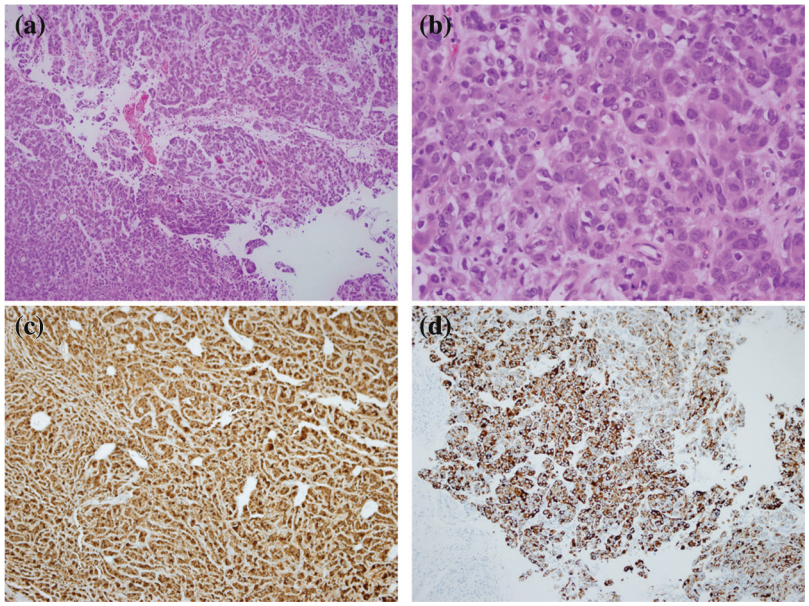

Figure 5: (a) Pathological examination of sacral melanoma with clusters of atypical spindle cells (H&E X100); (b) Prominent nucleoli in the melanoma cells (H&E X200); (c) Diffuse staining with S100 (X100); (d) Diffuse staining with MelanA (X100)

A week later, she developed severe neuropathic pain extending down to her left lower extremity. She was administered Gabapentin, which was titrated up to 800 mg/day until pain relief was achieved. She continued to use the brace for 3 weeks but was more comfortable when employing a rigid walker. After pathology revealed a malignant melanoma, she was referred to a tertiary center for oncological evaluation. There she was ordered a fluorodeoxyglucose (FDG)-positron emission tomography (PET) CT (Fig. 6) which revealed FDG uptake in the left sacrum, right foot (history of fall 4 weeks prior to surgery), left fibula

(used to harvest autologous graft), and pituitary gland (cranial and pituitary MRI did not reveal any abnormality), but not the abdomen and thorax. Thorough inspection of the skin, the oral and anal mucosa, and the eyes revealed no abnormality. She lacked any history of mole removal and denied such removal over the previous decade. We found no obvious primary melanoma lesion. She received one radiotherapy treatment of (27 Gy to the sacrum) and adjuvant chemotherapy (300 mg/day temozolomide for 5 days, repeated three times at 4-week). Three months after the surgery, MRI revealed no recurrence. The buttock pain disappeared, but the neuropathic left leg pain continued. The urinary incontinence ceased 1 week after discharge. At the 1-year follow up, no was apparent. The occasional lower limb neuropathic pain is managed with gabapentin and pregabalin. An informed consent was obtained from the patient stating her approval of publishing the findings.

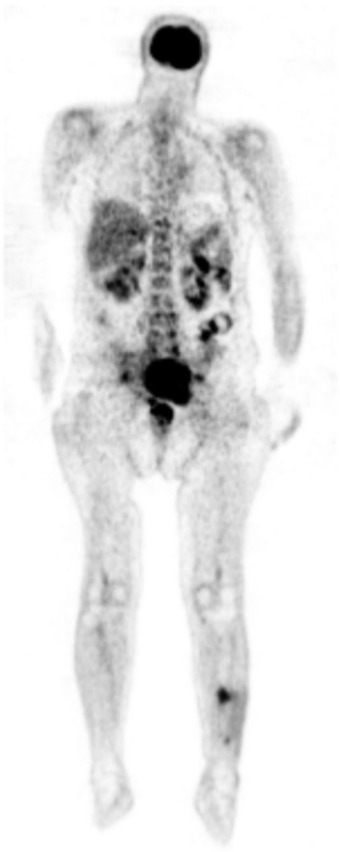

Figure 6: FDG PET scan showing a large uptake only in the sacrum and left fibula with no pathological uptake in the thorax and abdomen

3 Discussion

MUPs are rare, accounting for 3.2%–5.2% of all malignant melanomas [2,3,6]. Although metastasis to the subcutaneous tissue, skin, and or other visceral sites is not uncommon, spinal metastasis has a low prevalence (2.4%) [3]. Sacral MUP is even rarer (three reports to date) [3–5]. Two theories have been advanced to explain MUP. The first is the spontaneous regression of a primary melanoma (of the skin or a visceral organ) that has eluded clinical detection, but metastasized prior to regression [7]. The second is malignant transformation of ectopic melanocytes in a lymph node or other affected site [7,8]. Both theories are plausible and applicable to this case.

Although spinal metastasis is not common [3], management is complex. The mortality rate is high and the complications include pain, weakness, and bladder dysfunction [5]. Untreated spinal metastatic melanoma develops rapidly and the average survival time is 6–12 months [4]. Such melanomas are resistant to radiotherapy; surgical resection is indicated despite the high risk of iatrogenic neurological [9]. However, the prognosis of MUP is better than that of metastatic melanoma, with an overall 5-year survival rate of 28% [3]. Thus, the primary goal of surgical intervention is to increase survival and quality-of-life; this renders (efficient) adjuvant radiotherapy possible [10]. As is true of most spinal tumors, maximal safe resection is often associated with an arrest of further neurological impairment. As evidenced by our case, the patient benefited from the surgery by an improvement in functional condition and decreased pain. The surgical resection along with adjuvant chemo-radiotherapy has proved to be beneficial so far as well.

3.1 Diagnosis

The presenting features and symptoms of PSM are vague and typically non-specific; the complaints range from back pain to urinary incontinence [4]. This is true of all spinal malignancies; the comprised neural structures trigger a variety of findings. The primary imaging modality used in spinal malignancies is MRI [4]. Most PSMs are hyperintense on T1-weighted images and exhibit mild-to-moderate contrast enhancement (depending on the amount of melanin-containing cells) [4]. Our case evidenced intense and homogenous contrast enhancement, reflecting the amount of tumor extension and growth.

PSM was first described by Hayward et al. [11], a diagnosis requires the absence of any lesion outside the central nervous system and an appropriate histopathology. In the present case, pathology confirmed a PSM that stained diffusely for SOX-10, S100 and MelanA, suggestive of melanoma [4]. A thorough dermatological inspection revealed no history of mole removal or any other skin lesion. She also underwent thoracic, abdominal, and pelvic CT scan and FDG-PET; we found no other lesion. Additionally, a cranial and pituitary MRI was ordered and yielded no pathological findings.

CT should be used to identify pathologies that extend beyond the spinal cord into the adjacent bone. This is essential when excision of osseous structures and/or spinal fixation are/is planned. Our case evidenced extensive invasion of the S1 and S2 vertebral bodies, the posterior of the sacrum, and the sacro-iliac joint. Preoperative diagnosis of a giant cell tumor also triggers a need for maximal removal of the affected bony structures. CT facilitates planning prior to partial sacrectomy, delineation of the extent of resection, and measurements that ensure appropriate fixation.

3.2 Differential Diagnosis

A definitive PSM diagnosis requires that pathological examination of the lesion yields findings specific to melanoma [11]. However, preoperative radiology may enhance diagnosis, as different pathologies present with different findings on MRI and CT.

On MRI, the extent of contrast enhancement varies, and the differential diagnosis includes the more common giant cell tumor, as well as chordoma, meningioma, ependymoma, schwannoma, and melanocytoma [12]. Giant cell tumors are rarely found in the spine but, if present, are most common in the sacrum [13]. As was true of the PSM in our case, on CT, a giant cell tumor may exhibit osteolytic invasion of bony structures and the absence of a mineralized matrix. However, unlike PSM, a giant cell tumor exhibits heterogenous contrast enhancement on T1-weighted images [13].

A chordoma is the most common malignant sacral tumor [14]. However, chordomas tend to stray from the sacro-iliac joints, assuming a more midline pathology, and are usually found in the anterior sections of vertebral bodies [14]. Unlike PSM, chordoma usually evidences high intensity on T2-weighted images and hypointensity on T1-weighted images [14]. As malignant melanocytes may become scattered in the

leptomeninges, spinal melanocytoma is also included in the differential diagnosis [12]. The hallmark of this condition is dark pigmentation observed intraoperatively, attributable to cytoplasmic melanin [12]. However, melanocytomas are benign and expand slowly, and symptoms are detected earlier because they originate in the leptomeninges [12].

3.3 Treatment

Although no standard treatment for PSM has yet emerged, surgical decompression with maximally safe resection has been advised by most authors [5]. Surgical intervention allows immediate relief of, and prevents acute exacerbation of, symptoms and permits a definitive diagnosis that determines further treatment and follow-up [4,12].

Haberfellner et al. [4] analyzed 66 patients with PSM, of whom half underwent surgical resection only, 35% received adjuvant radiotherapy, and only 3 received both surgery and adjuvant chemoradiotherapy [5]. We scheduled both chemotherapy and radiotherapy because the mass was large and exhibited extensive local invasion; total resection is associated with a high risk of complications in such cases. We performed mass debulking to preserve the neural structures and prescribed chemoradiotherapy to control the growth of the remaining tumor cells.

3.4 Prognosis

Although there are wide estimates of overall survival, PSM is known to have better prognosis than metastatic CNS melanoma with survival rates up to 20 years [15]. Metastatic CNS melanoma has a survival rate of less than a year in most studies; surgical treatment combined with radio-chemotherapy has an average life-span of seven years [16]. This difference renders accurate diagnosis essential, to guide the appropriate treatment.

Our case is unique in that, it is only the fourth case of sacral MUP. However, the older report [3] has been presented with insufficient radiological evaluation and the second report [5] only consisted of a biopsy. Only the report by Haberfellner et al. [4] of two PSM cases is comprehensive, providing detailed analysis of the patients. The first patient was diagnosed with a thoracic intradural melanoma and the second with an intradural melanoma in the S1–S2 region. The latter patient did not exhibit any invasion of the vertebral body or the surrounding bony structures. Thus, intradural excision was sufficient. Our case is very different in that the lesion had invaded the S1–S2 vertebral bodies and the posterior bony structures. The weakened bony structures were removed by partial sacrectomy; such maximally safe resection is standard treatment [10]. The removal of the most prominent parts of the sacrum required an additional surgical approach, involving fixing the lumbar spine to the iliac wings. Additionally, the most recent report lacked PET data, which are vital when seeking a regressed melanoma or ectopic melanocytes in a lymph node, the two theories potentially explaining MUP [7,8]. The criterion proposed by Hayward et al. [11] requires the absence of any lesion outside of CNS, thus a patient without FDG-PET lacks a primary diagnostic modality. Our diagnosis was confirmed histologically; the tumor consisted of atypical cells with large pleomorphic nuclei and prominent nucleoli. The immunohistochemical findings were also diagnostic, with positivity for S-100, MelanA, HMB45, and SOX 10 suggesting melanoma. Given the high mortality rate and resistance to radiotherapy, aggressive resection with maximal preservation of neurological status is required for such cases. However, spinal instability attributable to wide resection must be considered, and appropriate fixation is required. We performed partial sacrectomy with left sacroiliac joint resection, and the upper vertebral levels became primarily dependant on the right sacroiliac joint. Thus, we performed lumbo-iliac fixation to avoid further complications related to instability.

4 Conclusion

The poor prognosis of patients with spinal metastasis from a malignant melanoma is discouraging to patients and surgeons. However, patients in reasonably good health with treatable symptoms are good candidates for resection. This maintains or improves neurological and physical functions, relieves pain, and potentially eliminates or arrests the growth of the tumor. We report an extremely rare case of PSM without a primary lesion, with a detailed account of our diagnosis, treatment, and follow-up. Surgical intervention allows a definitive pathological diagnosis, reduces the number of tumor cells (thus rendering adjuvant therapy more effective), relieves symptoms, and prevents further neurological deterioration. At the 1-year follow-up, we found that our treatment had been effective; this may encourage spinal surgeons faced with similar challenges; providing them with clues to an important challenge.

Acknowledgement: The authors thank the patient who agreed to be included in this study.

Ethics Approval and Informed Consent Statement: Informed written consent has been obtained from the patient in this case report to publish this paper. The present study involved human participant, and it was conducted considering ethical responsibilities according to the World Medical Association and the Declaration of Helsinki.

Authors' Contribution: IB: Conceptualization, methodology, writing original draft and review and editing, surgery, BY: surgery, visualization, investigation, MBU: surgery, data curation, NB: histological analysis, resources, supervision, review and editing.

Availability of Data and Materials: There is no additional data regarding to this study and all available data and materials have been shared within the case report.

Funding Statement: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of Interest: The authors declare that they have no conflicts of interest to report regarding the present study.

References

1. Markovic, S. N., Erickson, L. A., Rao, R. D., Weenig, R. H., Pockaj, B. A. et al. (2007). Malignant melanoma in the 21st century. Part 1: Epidemiology, risk factors, screening, prevention, and diagnosis. *Mayo Clinic Proceedings, 82(3),* 364–380. DOI 10.1016/S0025-6196(11)61033-1.
2. Scott, J. F., Gerstenblith, M. R. (2018). Melanoma of unknown primary. In: Scott, J. F., Gerstenblith, M. R. (Eds.), *Noncutaneous melanoma*. Brisbane: Codon Publications. https://www.ncbi.nlm.nih.gov/books/NBK506989/.
3. Kakutani, K., Doita, M., Nishida, K., Miyamoto, H., Kurosaka, M. (2008). Radiculopathy due to malignant melanoma in the sacrum with unknown primary site. *European Spine Journal, 17(Suppl 2),* S271–S274. DOI 10.1007/s00586-007-0561-1.
4. Haberfellner, E., Elbaroody, M., Alkhamees, A. F., Alaosta, A., Eaton, S. et al. (2021). Primary spinal melanoma: Case report and systematic review. *Clinical Neurology and Neurosurgery, 205(Suppl 2),* 106649. DOI 10.1016/j.clineuro.2021.106649.
5. Ku, A., Henry, A., Tunkel, R., Lachmann, E., Nagler, W. (1996). Lumbosacral radiculopathy secondary to L5 metastatic melanoma of unknown primary. *Archives of Physical Medicine and Rehabilitation, 77(3),* 307–309. DOI 10.1016/S0003-9993(96)90118-5.
6. Klausner, J. M., Gutman, M., Inbar, M., Rozin, R. R. (1983). Unknown primary melanoma. *Journal of Surgical Oncology, 24(2),* 129–131. DOI 10.1002/(ISSN)1096-9098.
7. Milton, G. W., Shaw, H. M., McCarthy, W. H. (1977). Occult primary malignant melanoma: Factors influencing survival. *British Journal of Surgery, 64(11),* 805–808. DOI 10.1002/bjs.1800641114.

8. Das, P., Kumar, N., Ahuja, A., Jain, A., Ray, R. et al. (2010). Primary malignant melanoma at unusual sites: An institutional experience with review of literature. *Melanoma Research, 20(3),* 233–239. DOI 10.1097/CMR.0b013e328334c39a.
9. Śniegocki, M., Nowacka, A., Smuczyński, W., Woźniak, K. (2018). Intramedullary spinal cord metastasis from malignant melanoma: A case report of a central nervous system secondary lesion occurred 15 years after the primary skin lesion resection. *Advances in Dermatology and Allergology, 35(3),* 325–326. DOI 10.5114/ada.2018.72760.
10. Gokaslan, Z. L., Aladag, M. A., Ellerhorst, J. A. (2000). Melanoma metastatic to the spine: A review of 133 cases. *Melanoma Research, 10(1),* 78–80. DOI 10.1097/00008390-200010010-00010.
11. Hayward, R. D. (1976). Malignant melanoma and the central nervous system. A guide for classification based on the clinical findings. *Journal of Neurology, Neurosurgery, and Psychiatry, 39(6),* 526–530. DOI 10.1136/jnnp.39.6.526.
12. Armocida, D., Pesce, A., Berra, L. V., Marzetti, F., Antonelli, M. et al. (2019). Intradural extramidullary dorsal melanocytoma in the adult: Case report and review of the literature. *Journal of Clinical Neuroscience, 62(2),* 248–253. DOI 10.1016/j.jocn.2018.12.004.
13. Kwon, J. W., Chung, H. W., Cho, E. Y., Hong, S. H., Choi, S. H. et al. (2007). MRI findings of giant cell tumors of the spine. *American Journal of Roentgenology, 189(1),* 246–250. DOI 10.2214/AJR.06.1472.
14. Farsad, K., Kattapuram, S. V., Sacknoff, R., Ono, J., Nielsen, G. P. (2009). Sacral chordoma. *RadioGraphics, 29(5),* 1525–1530. DOI 10.1148/rg.295085215.
15. Nishihara, M., Sasayama, T., Kondoh, T., Tanaka, K., Kohmura, E. et al. (2009). Long-term survival after surgical resection of primary spinal malignant melanoma. *Neurologia Medico-Chirurgica, 49(11),* 546–548. DOI 10.2176/nmc.49.546.
16. Larson T. C., Houser O. W., Onofrio B. M., Piepgras D. G. (1987). Primary spinal melanoma. *Journal of Neurosurgery, 66(1),* 47–49. DOI 10.3171/jns.1987.66.1.0047.