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Case Report

Case report of a huge primary malignant melanoma of the spine

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Abstract: Primary spinal melanoma (PSM) is very rare and the diagnosis of PSM is difficult because of its unusual location and variations in its appearance on MRI output. A 42-year-old female patient was admitted to our hospital with her chief complaint being back pain, especially at night, over an 8 month period. The physical examination of the patient showed hypoesthesia in the lateral area of her left lower leg and myodynamia of the right hip flexor muscles and knee extensor muscles weakened to Grade 4. Lumbar CT scan and MRI confirmed the bone destruction of the L5 vertebrae and posterior elements. A biopsy pathological examination supported a melanoma-rich tumour. A surgery of posterior partial tumour resection, spinal canal decompression, and instrumentation with a pedicle screw system was performed. The tumour was black, invasive to the L5 vertebra and posterior elements, surrounding the anterior part of the L5 vertebra, and involving muscles, tissues, and dura. HE staining showed a melanoma-rich tumour with significant fibrous, and granulation, tissue present. Immunohistochemical staining results showed S-100 (+), HMB45 (+), A103 (+). Systemic examinations excluded the possibility of a metastatic tumour. The patient was finally diagnosed as primary spinal malignant melanoma. After surgery the patient was sent to the oncology department for further treatment which included chemotherapy and radiotherapy. No deterioration of neurological function was detected with a follow-up after three months. In conclusion, the diagnosis of malignant melanoma is based on the discovery of melanin granules in the tumour cells upon histological examination, and a positive test for HMB-45, melanoma-specific antigen (Melan-A), and S-100 upon immunohistochemical examination. Systemic examinations including full-body skin examinations, head-MRI, chest and abdomen CT scan, abdominal and pelvic ultrasound examination, and PET/CT were also recommended to exclude the possibility of a metastatic tumour.

Keywords: Primary malignant melanoma, spine, vertebrae, diagnosis

Introduction

Since Hirschberg first reported a case of primary spinal melanoma (PSM) in 1906, approximately 30 cases of PSM have been reported to date [1]. PSM can occur throughout the cranial and spinal regions, however, it occurs most frequently in the middle or lower thoracic spine [2]. PSM was observed more frequently in Caucasians and PSM in Asians is rare. Most PSMs were reported to be intraspinal without irritation of the vertebrae and peri-vertebral space: the diagnosis of PSM is difficult because of its unusual location and the possible variations in its appearance on magnetic resonance imaging (MRI) output. In some cases, even where post-operative histopathological and immunohistochemical examinations were performed, the diagnosis can still be difficult as was the case with this patient. Considering the paucity of knowledge of this area we present this special case of huge primary malignant melanoma involved in the L5 vertebrae and peri-vertebral space with unusual radiographic features in a non-Caucasian patient to share our experience.

Case report

The patient provided informed consent for the publication of her clinical, pathological, and radiological data. This case report was approved by the Medical Ethics Committee of West China Hospital, Sichuan University.

A 42-year-old female patient was admitted to our hospital with her primary complaint being back pain, especially at night, over an eight

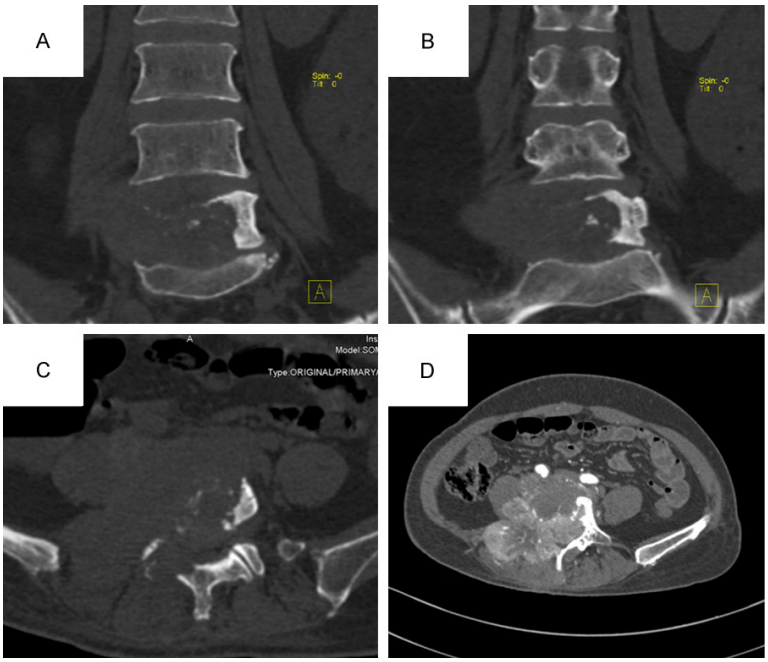

Figure 1. The pre-operative lumbar computed tomography (CT) scan three-dimensional reconstruction images of this patient. The pre-operative lumbar computed tomography (CT) scan three-dimensional reconstruction images (A, B: Coronal view reconstruction images; C, D: Axial view images) showed the bone destruction of the L5 vertebrae and soft tissue image around L5: this supported the diagnosis of malignancy.

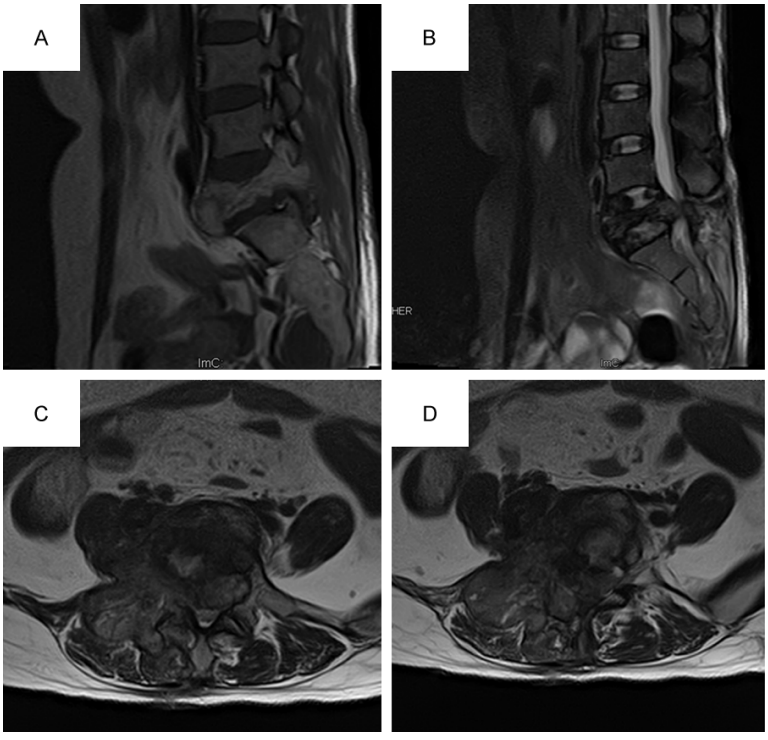

Figure 2. The pre-operative lumbar magnetic resonance imaging (MRI) of this patient. The pre-operative lumbar magnetic resonance imaging (A, B: Sagittal view; C, D: Axial view) showed the bone destruction of L5 vertebrae and posterior elements, the vague boundary supported the diagnosis of malignancy.

month period. Physical examination of the patient showed hypoesthesia in the lateral area of her left lower leg, normal sensation in the saddle area, myodynamia of the right hip flexor muscles, and knee extensor muscles weakened to Grade 4 (the myodynamia of other muscles was of Grade 5), limitation of lumber movement, Abdominal reflex (+), Hoffmann sign (-), Babinski sign (-), and Ankle clonus sign (-). Laboratory findings were as follows: Alpha foetal protein (AFP) 2.66 ng/ml, Cancer embryo antigen (CEA) 0.59 ng/ml, CA15-3 12.34 U/ml, CA19-9 7.00 U/ml, CA-125 11.46 U/ml, CA72-4 10.32 U/ml, CYFRA21-1 1.29 ng/ml, NSE 12.75 ng/ml, ALP 130 IU/L, N-MID 8.1 ng/ml, CRP 55.00 mg/L, ESR 73.0 mm/h, RBC 3.82 × 10^{12}/L, HGB 116 g/L, PLT 255 × 10^{9}/L, WBC 6.84 × 10^{9}/L, ALB 38.7 g/L, and β-HBA 0.31 mmol/L. Lumbar anterior-posterior, lateral, extension and flexion X-rays showed bone destruction of L5 and limitation of lumber movement. A lumbar computed tomography (CT) scan confirmed the bone destruction of L5 vertebrae and soft tissue around L5 (**Figure 1**). Lumbar MRI confirmed the bone destruction of the L5 vertebrae and posterior elements (**Figure 2**). Positron Emission Tomography/Computed Tomography (PET/CT) showed a tumour lesion at L5 and no other tumour-like findings elsewhere. Biopsy pathological examination supported the diagnosis of a melanoma-rich tumour (**Figure 3**). Chest X-ray, abdominal ultrasonography, and other examinations showed no significant abnormality. Considering the lack of a past history of tumours, no evidence of other tumours

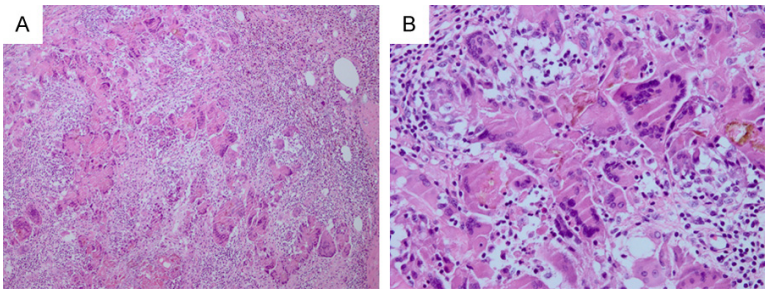

Figure 3. Biopsy pathological examination images. Biopsy pathological examination (A: Hematoxylin-eosin staining (100 × magnification) image; B: Hematoxylin-eosin staining (400 × magnification) image) showed many melanoma-rich cells with a significant amount of fibrous and granulation tissue present.

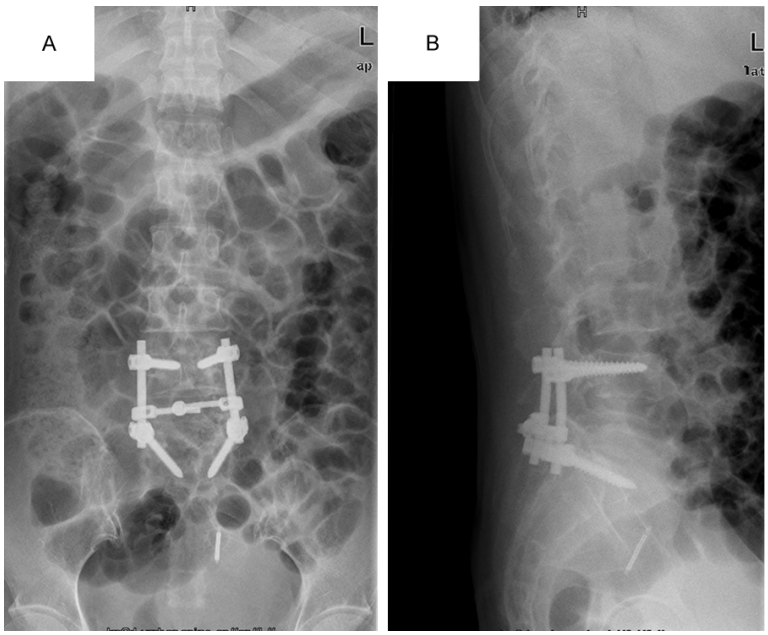

Figure 4. Post-operative lumbar anterior-posterior and lateral X-ray images. Post-operative lumbar anterior-posterior and lateral X-ray images (A: Anteroposterior view; B: Lateral view) showed the accurate positioning of the pedicle screws and rods without irritation of the spinal canal.

from the findings of systemic examinations, the patient was diagnosed as having a primary lumbar tumour.

A surgery plan of posterior approach tumour resection, spinal canal decompression, and instrumentation with a pedicle screw system was reached after discussion among several spinal surgeons in our department and effective communication with the patient and her family. The tumour was black, invasive of the L5 vertebra and posterior elements, and it surrounded the anterior part of the L5 vertebra, and involved muscles, tissues, and dura. The patient suffered a massive haemorrhage upon completion of spinal canal decompression and their blood pressure decreased to 50/80 mmHg thereupon. Considering the difficulty of complete resection and the massive haemorrhage, the surgery was changed to partial tumour resection, spinal canal decompression, and instrumentation with a pedicle screw system (**Figure 4**). The tumour was surgically resected and then the tumour was sent for pathological examination. Pathological hematoxylin-eosin (HE) staining and immunohistochemical staining were performed to determine the nature of the tumour. HE staining showed a melanoma-rich tumour with a large amount of fibrous and granulation tissue present (**Figure 5**). Immunohistochemical staining results were as follows: S-100 (+), HMB45 (+), A103 (+), PCK (-), EMA (-), CR (-), CK8 (sporadic +), PAX-8 (-), RCC (-), TFE-3 (-), CD 10 (-), CgA (-), Inhibin-α (-), SMA (-), TFEB (-), Ki-67 positive rate 5% (**Figure 6**).

As it was difficult to make a definite diagnosis, pathologists, radiologists, oncologists, and spinal surgeons in our hospital took a part in a group consultation. At first, difficulties in diagnosis were centred around the differential diagnosis between three kinds of tumour: 1) malignant melanoma; 2) TFE-3/TFEB Wilms tumour; 3) malignant PEcoma. The results of immunohistochemical examination tended to favour the diagnosis of malignant melanoma but pathologists still recommended that we focus on a renal examination to exclude certain rare renal tumours. At the same time pathologists also recommended systemic examinations to confirm a primary malignant melanoma or a metastatic malignant melanoma. According to their suggestions, systemic examinations, including full-body skin examinations, head-MRI, a chest and abdomen

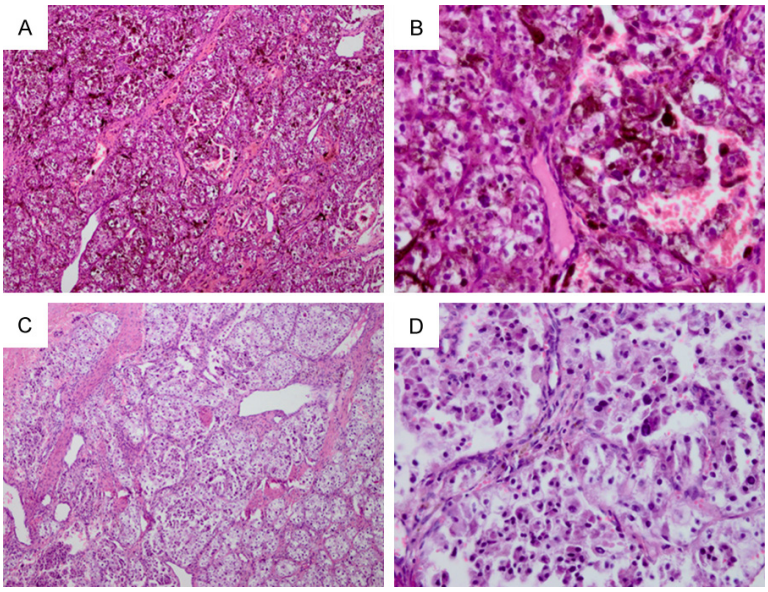

Figure 5. Post-operative pathological hematoxylin-eosin (HE) staining and HE depigmentation staining images of this patient. A: Post-operative pathological hematoxylin-eosin (HE) staining (100 × magnification); B: Post-operative pathological HE staining (400 × magnification); C: HE depigmentation staining (100 × magnification); D: HE depigmentation staining (400 × magnification); HE staining and HE depigmentation staining showed melanin granules in the tumour cells.

CT scan, and abdominal and pelvic ultrasound examination, were performed.

Considering no evidence of other tumours from the findings of repeated systemic examinations (including PET/CT), the patient was finally diagnosed as having a primary malignant melanoma. Surgery involving partial tumour resection, spinal canal decompression, and instrumentation with a pedicle screw system was performed and the patient was sent to the oncology department for further treatment including chemotherapy and radiotherapy. No deterioration in neurological function was detected with a follow-up assessment after three months.

Discussion

Malignant melanoma has been reported to be an aggressive malignancy associated with a high mortality rate which often occurs in the skin [3, 4]. According to a report from the National Cancer Research Centre, the incidence of cutaneous malignant melanoma in the Caucasian American population increased from 7.5 per 100,000 in 1973 to 22.5 per 100,000 in 2011, and cutaneous malignant melanoma accounts for 75% of all skin cancer related mortalities in the United States [5, 6]; however malignant melanoma can also occur in other parts such as lung, liver, vagina, oesophagus, and spine (although these incidences were rare) [2, 7-15]. Considering the paucity of knowledge of this area, we present this special case of a huge primary malignant melanoma involved in the L5 vertebrae and peri-vertebral space with emphasis on the difficult diagnosis. At the same time, previously reported primary spinal malignant melanoma cases were also reviewed in the literature (**Table 1**) [16-21]. Pathological HE staining and HE depigmentation staining were the examination techniques which often showed the presence of melanin granules: immunohistochemical examination plays a crucial role in the diagnosis of malignant melanoma especially in differential diagnoses from other carcinomas such as Wilms tumour and malignant PEcoma. Upon immunohistochemical analysis, malignant melanoma was positive for HMB-45 and S-100: this was important with regard to accurate diagnosis. The diagnosis of malignant melanoma is based on the discovery of melanin granules in the tumour cells upon histological examination, with a positive result for HMB-45, melanoma-specific antigen (Melan-A), and S-100 in immunohistochemical examinations [22, 23]. If it is difficult to reach a differential diagnosis through pathological examination, clinical and radiological examinations can be helpful. Clinical and radiological examinations were also important in determining the nature of any primary, or metastatic, malignant melanoma. Systemic examinations including full-body skin examinations, head-MRI, chest and abdomen CT scan, abdominal and pelvic ultrasound examination, and PET/CT were recommended before making a definite diagnosis.

Primary spinal malignant melanoma is exceptionally rare and most cases are reported as being intraspinal. Diagnosis is difficult because of the unusual tumour location and the variations in its appearance on MRI output: in some

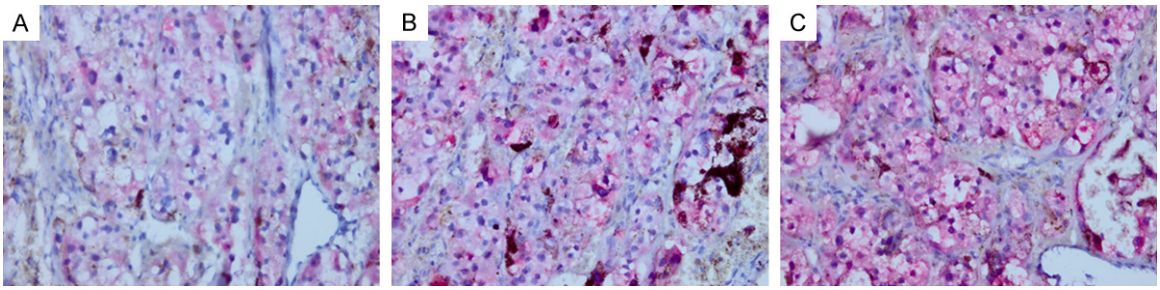

Figure 6. Immunohistochemical examinations of HMB-45, A103 and S-100. Immunohistochemical examinations showed positive results for A103 (A), HMB-45 (B), and S-100 (C), the diagnosis of malignant melanoma was reached as positive for HMB-45, A103, and S-100 based on immunohistochemical examinations.

Table 1. Summary of the reported cases of primary spinal malignant melanoma

Author	Year	Age	Gender	Location	Symptom	Diagnosis	Treatment method	Follow-up time
Kobayashi	2012	78	Female	T11 level	Paraparesis and disturbance of bowel movements	Pathological examination	Surgery, Radiation	3 years
Lee	2010	71	Female	C6-7 level	Left upper extremity tingling sensation	Pathological examination	Partial resection	Unclear
Kwon	2004	45	Female	C7 level	Neck pain	Histopathological investigation	Surgery	Unclear
Ryu	2010	55	Male	T4 level	Hypesthesia	Pathology report/ PET-CT	Surgery	Unclear
Kanatas	2007	76	Female	C6/7 level	Neck pain, paraesthesia, and weakness in her right arm	Pathological examination	Surgery, Radiation	6 months
Nishihara	2009	49	Male	T6 level	Headache	History + MRI	Radiation, interferon beta	38 months
This study	2016	42	Female	L5 level	Back pain	Pathology report/ PET-CT	Surgery, Radiation	12 months

cases, even where post-operative histopathological and immunohistochemical examinations were performed, the diagnosis remains difficult, as was the case with this patient. The diagnosis of malignant melanoma is based on the discovery of melanin granules in the tumour cells upon histological examination, with a positive result for HMB-45, Melan-A, and S-100 found after immunohistochemical examination. Systemic examinations including full-body skin examinations, head-MRI, chest and abdomen CT scan, abdominal and pelvic ultrasound examination, and PET/CT were recommended to determine the nature of the primary, or metastatic, malignant melanoma.

Disclosure of conflict of interest

None.

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References

[1] Lee CH, Moon KY, Chung CK, Kim HJ, Chang KH, Park SH and Jahng TA. Primary intradural extramedullary melanoma of the cervical spinal cord: case report. Spine (Phila Pa 1976) 2010; 35: E303-307.

[2] Li YP, Zhang HZ, She L, Wang XD, Dong L, Xu E and Wang XD. Primary extramedullary spinal melanoma mimicking spinal meningioma: a case report and literature review. Oncol Lett 2014; 8: 339-344.

[3] Miller AJ and Mihm MC Jr. Melanoma. N Engl J Med 2006; 355: 51-65.

[4] Ren JW, Li ZJ and Tu C. MiR-135 post-transcriptionally regulates FOXO1 expression and promotes cell proliferation in human malignant melanoma cells. Int J Clin Exp Pathol 2015; 8: 6356-6366.

[5] Xin Y, Huang Q, Zhang P, Yang M, Hou XY, Tang JQ, Zhang LZ and Jiang G. Meta-analysis of the safety and efficacy of interferon combined with dacarbazine versus dacarbazine alone in cutaneous malignant melanoma. Medicine (Baltimore) 2016; 95: e3406.

[6] Siegel R, Ma J, Zou Z and Jemal A. Cancer statistics, 2014. CA Cancer J Clin 2014; 64: 9-29.
[7] Du F, Yang M, Fang J and Jing C. Primary hepatic malignant melanoma: a case report. Int J Clin Exp Pathol 2015; 8: 2199-2201.
[8] Liu H, Yan Y and Jiang CM. Primary malignant melanoma of the esophagus with unusual endoscopic findings: a case report and literature review. Medicine (Baltimore) 2016; 95: e3479.
[9] Liu GH, Liu J, Dong H and Tang XJ. Primary malignant melanoma of the lung: a case report. Int J Clin Exp Med 2014; 7: 1757-1759.
[10] Chen L, Xiong Y, Wang H, Liang L, Shang H and Yan X. Malignant melanoma of the vagina: a case report and review of the literature. Oncol Lett 2014; 8: 1585-1588.
[11] Cetinalp NE, Yildirim AE, Divanlioglu D and Belen D. An uncommon intramedullary tumor: primary spinal cord melanoma. Asian Spine J 2014; 8: 512-515.
[12] Jeong DH, Lee CK, You NK, Kim SH and Cho KH. Primary spinal cord melanoma in thoracic spine with leptomeningeal dissemination and presenting hydrocephalus. Brain Tumor Res Treat 2013; 1: 116-120.
[13] Clifford JH, McClintock HG and Lubchenco AE. Primary spinal cord malignant melanoma-case report. J Neurosurg 1968; 29: 410-3.
[14] King AB, Chambers JW and Garey J. Primary malignant melanoma of the spinal cord. AMA Arch Neurol Psychiatry 1952; 68: 266-275.
[15] Vuori EE and Hormia M. Primary malignant melanoma of the spinal canal. Duodecim 1972; 88: 652-657.
[16] Kobayashi N, Kuwashima A and Abe T. A case of primary intramedullary malignant melanoma. Neurosurgery Quarterly 2012; 22: 50-52.
[17] Lee NK, Lee BH, Hwang YJ, Sohn MJ, Chang S, Kim YH, Cha SJ and Cho HJ. Findings from CT, MRI, and PET/CT of a primary malignant melanoma arising in a spinal nerve root. Eur Spine J 2010; 19 Suppl 2: S174-178.
[18] Ryu DS, Park YM, Hyun KK, Isa and Soo KK. Primary intradural extramedullary malignant melanoma in the thoracic spine: case report and literature review. Korean Journal of Spine 2010; 7: 184-187.
[19] Kwon SC, Rhim SC, Lee DH, Roh SW and Kang SK. Primary malignant melanoma of the cervical spinal nerve root. Yonsei Med J 2004; 45: 345-348.
[20] Kanatas AN, Bullock MD, Pal D, Chakrabarty A and Chumas P. Intradural extramedullary primary malignant melanoma radiographically mimicking a neurofibroma. Br J Neurosurg 2007; 21: 39-40.
[21] Nishihara M, Sasayama T, Kondoh T, Tanaka K, Kohmura E and Kudo H. Long-term survival after surgical resection of primary spinal malignant melanoma-case report. Neurol Med Chir (Tokyo) 2009; 49: 546-548.
[22] Krathen M. Malignant melanoma: advances in diagnosis, prognosis, and treatment. Semin Cutan Med Surg 2012; 31: 45-49.
[23] Pflugfelder A, Kochs C, Blum A, Capellaro M, Czeschik C, Dettenborn T, Dill D, Dippel E, Eigentler T, Feyer P, Follmann M, Frerich B, Ganten MK, Gartner J, Gutzmer R, Hassel J, Hauschild A, Hohenberger P, Hubner J, Kaatz M, Kleeberg UR, Kolbl O, Kortmann RD, Krause-Bergmann A, Kurschat P, Leiter U, Link H, Loquai C, Loser C, Mackensen A, Meier F, Mohr P, Mohrle M, Nashan D, Reske S, Rose C, Sander C, Satzger I, Schiller M, Schlemmer HP, Strittmatter G, Sunderkotter C, Swoboda L, Trefzer U, Voltz R, Vordermark D, Weichenthal M, Werner A, Wesselmann S, Weyergraf AJ, Wick W, Garbe C, Schadendorf D; German Dermatological Society; DermatologicCooperative Oncology Group. Malignant melanoma S3-guideline “diagnosis, therapy and follow-up of melanoma”. J Dtsch Dermatol Ges 2013; 11 Suppl 6: 1-116, 1-126.