Uncorrect diagnosis of tubercolar spondylodiscitis in aggressive and bone destructive metastasis of melanoma: A case report and literature review

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Abstract

Differential diagnosis of destructive osteolytic spinal lesions can be a diagnostic challenge. In this study, we described a rare case of spinal metastases from primary desmoplastic melanoma which had incorrectly been diagnosed and treated as tuberculous spondylodiscitis. An 82-year-old male patient with ongoing low back pain and a history of lumbar localized Pott's performed a lumbar spine MRI that showed osteolytic lesion with first hypothesis of spondylodiscitis L2-L3. The patient was hospitalized and cause of worsening of the lumbar pain underwent a following series of non-diagnostic CT-guided and open lumbar biopsy at L2-L3 with unsuccessful antibiotic-antitubercular therapy. A new MRI revealed a worsening of previous lesions, extension of the osteolytic lesion at the level of L1-L2 and L3-L4 with neurological impairment. The diagnosis of metastatic melanoma was obtained with surgical decompression and open posterior biopsy procedure. The case described is pathognomonic of the difficulty in detecting the correct diagnosis in front of similar clinical and radiological manifestations. The presence of a previous Pott's disease in the same involved vertebral site was of crucial importance in deflecting the correct diagnostic classification of the pathology, which was possible to ascertain only following an extensive biopsy sampling in the last surgery performed.

Introduction

Differential diagnosis of osteolytic spinal lesions can be challenging. Numerous conditions can indeed display similar symptoms and their diagnosis is not always straightforward. In this manuscript, we describe a rare case of spinal metastasis from a desmoplastic melanoma which had previously been erroneously diagnosed and treated as a tuberculous spondylodiscitis.

Case Report

An 82 years-old man was admitted to our hospital because of ongoing low back pain not responsive to pharmacological therapy. Symptoms, which started 7 months before admission, consisted of low back pain, fatigue and weight loss of around 15 kg in the absence of fever, neurological deficits and night sweats. The patient had a history of Pott's disease of the lumbar spine which had been treated medically 50 years before and prostatic adenocarcinoma which was surgically excised 5 years earlier. Up until the most recent hospital admission the patient was considered free from both conditions. Two months before the current admission, the patient had been admitted in another hospital complaining of epigastralgia irradiated to the lumbar spine. During the hospitalization the patient underwent several investigations including full blood count, EGDS and colonoscopy which were all normal, as well as a lumbar spine MRI which showed a lytic lesion centered around the L2-L3 disc space (Figure 1). In consideration of the patient medical history, a reactivation of Pott's disease was suspected. Nevertheless, further studies including sputum examination for mycobacteria, hemoculture and sierological testing for HIV, HBV and HCV and PCR test for atypical mycobacteria were negative. A CT-guided lumbar biopsy was thus performed but the final histological exam was non diagnostic, characterized by a fibrous tissue with lymphocytic infiltration and bone spicules with no signs of neoplasia. The patient was therefore treated with broad spectrum antibiotics (Piperacillin/Tazobactam for two weeks followed by Rifampicin and Levofloxacin for additional six weeks) and was discharged afterwards with a rigid lumbar brace for pain comfort and mobilization. Because of severe worsening of the lumbar pain and an increase in the inflammatory markers (ESR and PCR) the patient was admitted to our hospital. A new contrast-enhanced lumbosacral MRI was obtained which revealed a worsening of the destructive lesion at L2-L3 with a destruction of the posterior wall of L2 and involvement of the anterior epidural space and the left nerve root canal in addition to the extension of the osteolytic lesion at the level of L3-L4 and to both of the ileopsoas muscles (Figure 2). After a wash-out period of the antibiotic therapy, a repeat CT-guided bone biopsy was performed at L2-L3 level but it was once again non diagnostic. Broad spectrum antibiotic therapy was thus continued with Ertapenem and Teicoplanin for four weeks leading to a decrease in the inflammatory markers. Nevertheless, due to further worsening of the low back pain, an open vertebral biopsy of L2-L3 disc space was performed through standard posterior approach. The histological examination highlighted the presence of a chronic gigantocellular inflammatory granulomatous process, with no cellular atypia. At this stage,

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Key words: Spinal metastases; Malignant Melanoma; Osteolytic spinal lesion; Tubercolar spondylodiscitis;

Contributions: VC and LAN contributed equally to this work, generated the figures and wrote the manuscript; LP, CP, EG contributed to the writing of the manuscript; EP and GM reviewed and approved the manuscript.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none.

Availability of data and materials: Address correspondence and reprint requests to Enrico Pola.

Ethics approval and consent to participate: Not applicable.

Informed consent: Not applicable.

Received for publication: 11 April 2020.
Accepted for publication: 17 June 2020.

Orthopedic Reviews 2020; 12(s1):8674
doi:10.4081/or.2020.8674

because of the non-conclusive diagnosis, standard antitubercular therapy with Isoniazide, Rifampicin, Ethambutol and Pyrazinamide was started and showed some positive effect of patient's low back pain. After eight weeks of anti-tuberculosis therapy, repeat CT and lumbosacral MRI (Figure 3) scans were performed because of the onset of bilateral muscular weakness in L2 and L3. Imaging studies showed the extension of the disease also to the L1 vertebral body. Therefore, a surgical procedure of decompression, curettage and posterior biopsy at the L2-L4 level was performed. Histological examinations excluded an ongoing tuberculosis process and documented the presence of findings compatible with metastatic melanoma. The definitive diagnosis was subsequently obtained through immunohistochemistry: anti-melanoma antibodies HMB-45, S-100 protein which were strongly positive. Life expectancy of the patient was calculated in less than 6 months due to the involvement of more than 3 spinal levels and the presence of extraperitoneal involvement. After careful discussion of the available options with the patient, decision was made not to pursue any further surgical therapy. The patient received adjuvant radiotherapy and immunotherapy and died four months afterwards due to liver metastases and the development of acute liver failure.

Discussion

Skeletal metastases affecting the spine represent the most frequent tumor of the bone; in fact, it is believed that over 10% of patients with cancer develop a symptomatic vertebral metastasis regardless of the origin of the primary tumor.[1,2] Metastases of the spine have a prevalence of 30-70% in cancer patients and are associated in 5-10% of cases with acute spinal cord compression (ESCC) causing: impaired mobility, neurological deficits and decreased quality of life.[3,4] The peak incidence of metastasis of the spine is in the age group between 40 and 65 years.[5] Vertebral metastases need multidisciplinary treatment, and radiotherapy, chemotherapy and surgery must be integrated in order to obtain the best possible local control of the lesion.[6,7] Malignant melanoma metastases account for 1-3% of all malignant neoplasms.[1,8] Malignant melanoma originates from cancerous proliferation of melanocytes and it's more frequent in Caucasians.[9] The two main route of diffusion are hematogenous and lymphatic spread, with a selective tropism for noble organs with terminal vascularization: (i.e. liver,

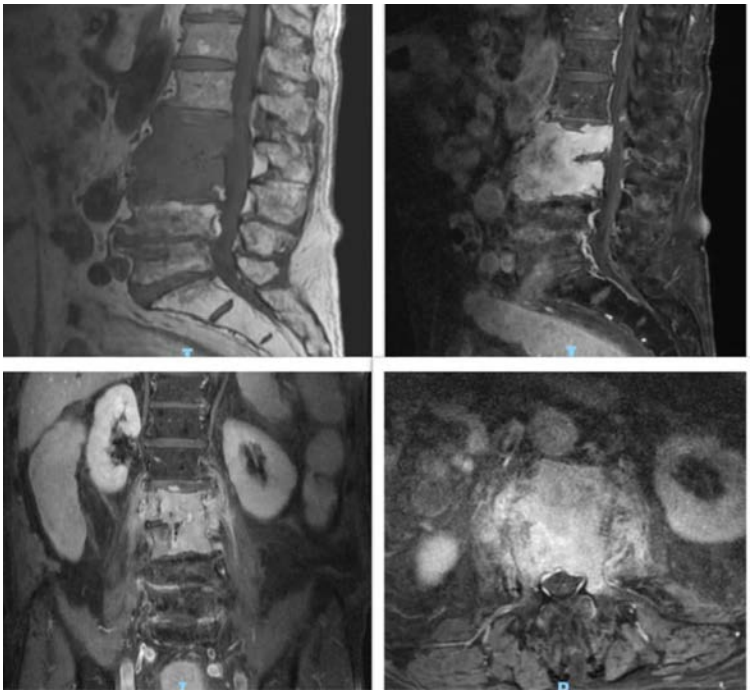

Figure 1. MRI scan of the lumbar spine performed at a different hospital when the diagnosis of osteolytic lesion at L2-L3 level was first established. After the MRI, a CT-guided biopsy was performed which was non diagnostic.

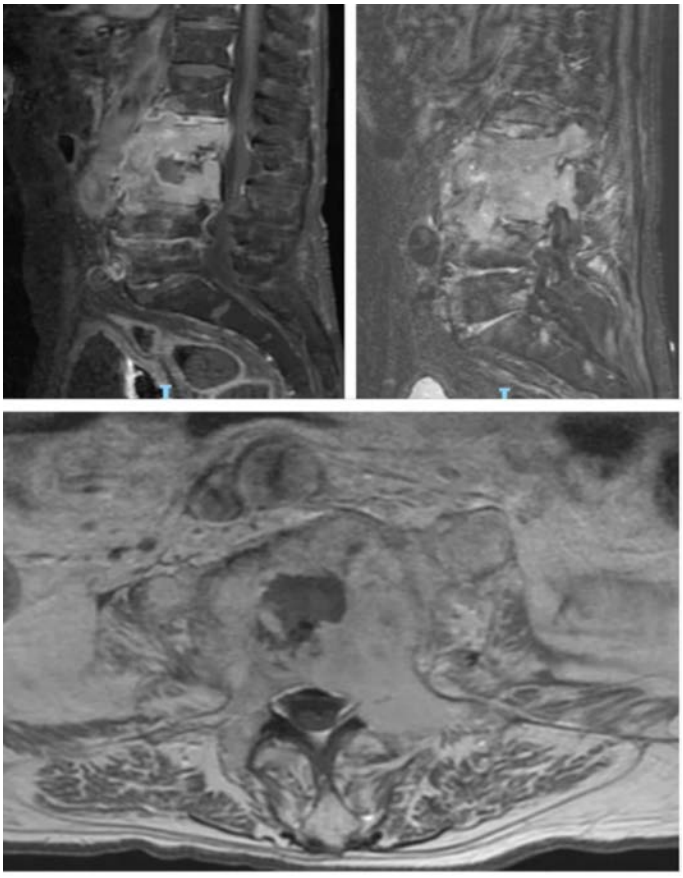

Figure 2. First MRI scan of the lumbar spine performed after admission at our hospital. The MRI scan confirms the presence of an osteolytic lesion at L2-L3 level with extension to the posterior elements and pre-vertebral tissues. A repeat CT guided biopsy was performed but again was not conclusive.

brain, bone). Melanoma metastasizes to the following organs: epidermis, subcutaneous tissues and lymph nodes (50-75%), liver (54-77%), brain (36-54%), bone (23-49%), gastrointestinal system (26-58%), cardiac tissue (40-45%), adrenal (36-54%), kidney (35-48%), spleen (30%) and others.[10,11] Nevertheless, bone locations of metastatic melanoma appear clinically in an advanced stage of the disease and typically spread to the appendicular skeleton, spinal column, ribs and pelvis.[12,13] Diagnosis can suspected with imaging modalities: like CT, MRI and FDG-PET/CT but it is confirmed through a biopsy of the lesion.[14] The therapy is based on radio-chemotherapy and immunotherapy combined or surgical treatment associated with medical therapy. Available surgical techniques for treatment of spinal metastases comprise two approaches: 1) decompression and stabilization, 2) intralesional excision or debulking followed by reconstructive procedures; in either case an anterior, posterior or combined approach can be used.[1,15-17] In this type of spinal metastasis, the prognosis is poor with an average survival of four months (range from 1 week up to 43 months).[18]

Spinal column appears to be the most frequently involved site by melanoma metastases. A partial explanation of this phenomenon can be found in some studies that have documented an impaired lymphatic drainage in primitive melanomas of the skin of the back of the trunk.[19] Through the use of lymphoscintigraphy, the authors have discovered that lymphatic drainage proceeds directly through the vertebral body up to the paravertebral lymph nodes. Gokaslan *et al* authored a review of 133 cases analyzed over 11 years recording their clinical presentation, various patterns in diagnostic imaging and the prognosis. According to these data CT imaging can give up to 15% of false negatives. The median overall survival was 4 months and palliation was the primary objective of treatment. Sellin *et al* described a retrospective study with 64 cases of patient affected by spinal metastatic malignant melanoma that underwent surgery. These authors reported that the median survival time was 5,7 months. Furthermore they demonstrated that condition is progressive and a total spine disease burden involving more than 3 vertebral levels, at the time of spine surgery, was associated with a significantly worse survival. Spigel *et al* completed a review of 114 cases analyzed over 21 years recording their clinical and radiographic characteristics, demographics, risk factors and prognostic data. These authors reported that risk factors included primary lesions that were ulcerated, deeper than 0.76 mm, categorized as level II on the Clark scale, or located on the trunk or mucosal surfaces. The median survival time for all patients was only 86 days, but this was reduced in patients with more than one metastatic site in addition to the spine. As for surgical spinal management they agreed that there was no absolute contraindication in patients with multiple regions involvement, and that surgical therapy should indeed be directed towards the symptomatic regions only, such as a posterior decompression laminectomy in case of neurologic compromise secondary to spinal metastasis from melanoma. Goodwin *et al* performed a systematic review of clinical outcomes for patients diagnosed with spinal metastases from skin cancer including those with metastatic melanoma. The authors determined that the median overall survival for the patients with melanoma spinal metastasis was about 4 months, the overall percentage of known continued disease progression after spine metastasis diagnosis was 40,1%, the rate of known recurrence of the primary skin cancer lesion was 3,5% and the rate of known spine metastasis recurrence despite treatment for all skin malignancies was 2,8%. Furthermore, these authors debated that the following factors were associated with a significant decrease in survival in patients with a primary skin cancer spinal metastasis: age greater than 65 years, sacral spinal involvement, presence of a neurological deficit and nonambulatory status. It has been shown that metastasis from malignant spinal melanomas show an extremely aggressive biological behavior and present with a predominant lytic pattern and the occasional discovery a vertebral collapse can hence be suspicious and worthy of further study.[20] Metastatic bone lesions can have different presentation patterns: more frequently they are osteolytic-destructive, less often they can be blastic or present only with the collapse of the vertebral body.[21] The involvement of paravertebral soft tissues, the epidural space and spinal cord compression are rare events, which can further complicate differential diagnosis with conditions such as spondylodiscitis. In our case, the patient had a previous history of lumbar Pott's disease

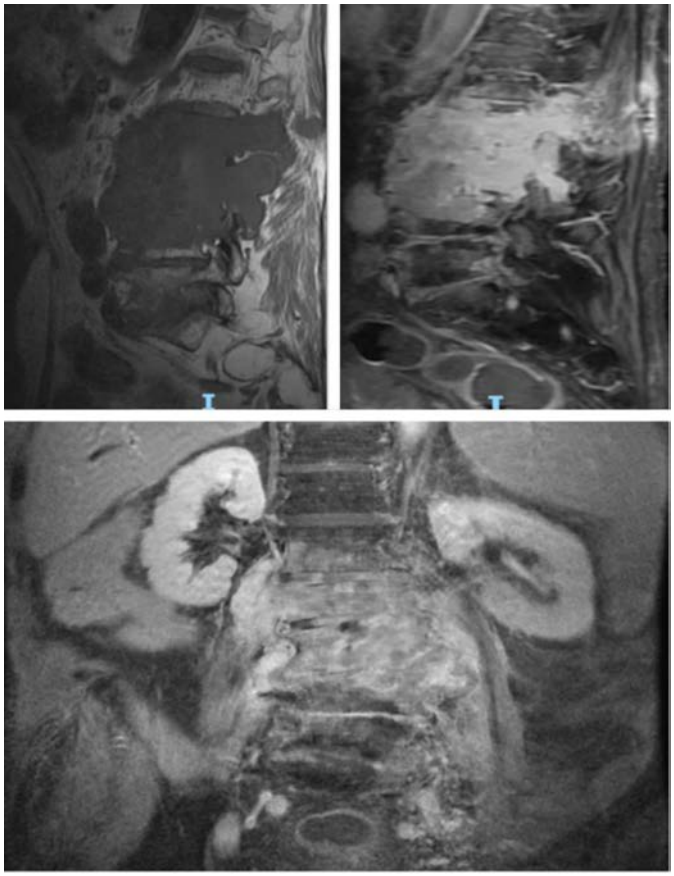

Figure 3. Repeat MRI scan of the lumbar spine after 8 weeks of anti-tuberculous therapy. Patient had worsening pain and bilateral proximal weakness in the lower limbs. There is also further spread to the posterior elements and ileo-psoas muscles. The patient underwent an extended open biopsy which confirmed the final diagnosis of metastatic desmoids melanoma.

and a past prostate adenocarcinoma previously treated, for these reasons the diagnosis of metastatic melanoma was delayed and was taken into consideration from the beginning.

Conclusions

Vertebral metastases from melanoma are an infrequent event and represent a complex diagnostic problem. The case described in this report is pathognomonic of the difficulty encountered also by a multidisciplinary team in formulating the correct diagnosis. The presence of a previous Pott's disease in the same vertebral site involved was of crucial importance in delaying the correct diagnosis of the pathology, which was only possible after an extensive open biopsy.

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