Letter to the Editor

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Pain control of hypertrophic pulmonary osteoarthropathy related with lung cancer: A clinical case report

Sara Alves, MD*, Filipa Pereira, MD, Ana Afonso, MD, Carolina Sales, MD, Inês Guerreiro, MD, Cristina Oliveira, MD, Maria Cassiano, MD, Júlio Oliveira, MD, Ana Rodrigues, MD, Inès Pousa, MD, Isabel Azevedo, MD, Marta Soares, MD

Introduction

Hypertrophic osteoarthropathy (HOA) manifests clinically as clubbing of the digits, periostisis of the long tubular bones, painful swelling, and arthralgias of the distal upper and lower extremities[1–3]; 95% of cases is classified into secondary form. The term "hypertrophic pulmonary osteoarthropathy" (HPO) was defined by Marie in 1890, when was reported a case of pulmonary tuberculosis with HOA. In almost 90% of cases, HPO is associated with intrathoracic neoplasm and 80% of these are lung cancers.[4,5] Most of the patients with HPO are men[5] and reports have described heavy smoking history in more than 60% of the patients.

HPO is diagnosed based on symptoms (pain, erythema, and edema in the extremities) and radiographic findings. Bone scintigraphy is a useful to detect HPO[5] and shows diffusely increased uptake throughout most of the skeleton.

Symptoms can respond to treatment of the underlying condition[5–7] but are often resistant to conventional analgesic medications.

Intravenous zoledronic acid 4 mg[6] and pamidronate in doses of 30 to 90 mg[8] have been described to be efficient in obtaining pain relief in cases of disabling secondary—including paraneoplastic—HOA.

Clinical case

We describe a 75-year-old man former heavily smoker. In September 2017 initiated dyspnea and cough. At emergency department of his local hospital was performed an X-ray: hypotransparency in the upper right lobe of the lung.

Computed tomography scan showed "a nodular lesion in the upper right lobe." Biopsy revealed a nonsmall cell lung cancer. He was admitted at our institution, and he presented strong pain in both legs and malleolar edema. It was started weak opioid. It was performed a scintigraphy: "diffuse hypercaption of the radiopharmaceutical along the cortical of the long bones, suggesting osteoarthropathy hypertrophic" (Fig. 1).

The disease was staged as a cT2bN3M0, IIIB. It was decided to do chemotherapy and radical radiotherapy after reevaluation.

He started carboplatin (AUC 5)/paclitaxel (175 mg/m^2) on April 2018. After 2 weeks, he was admitted on hospital with pain exacerbation (mostly located on lower limbs, but also arthralgias and edema in both hands). It was initiated naproxen, and after associate a strong opioid (morphine 5 mg subcutaneous every 4 hours), with pain control. After 1 week at home, he received second cycle of chemotherapy.

After 3 weeks, he was admitted again with another pain exacerbation and it was escalated the opioid doses and added corticosteroid.

Although the medication adjustment, the patient was needing several day morphine extra doses, so he received a single dose of pamidronate 90 mg. After 1 week, the opioid was changed to tapentadol 200 mg b.i.d., and patient was sent home with pain control.

He had pain resolution on upper limbs, pain on lower limbs was controlled, and after 2 weeks, patient only needed 2 extra doses of morphine 20 mg per day.

Disease progression after the 2 cycles of treatment with carboplatin and paclitaxel. Treatment was changed to monotherapy with oral vinorelbine (dose reduction). It was done also a saphenous nerve bloc with steroids, with a pain relief during 2 days. After 3 cycles of treatment, patient presented clinical benefit (almost disappearance of feet swelling and lower limbs pain). He was tolerating very well the treatment and he was motivated to continue. Bone scintigraphy showed less captation of the radiopharmaceutical (Fig. 2).

Discussion

HOA may be primary or secondary.[4,5] Lung cancer accounts for over 80% of the secondary cases. According to different series,[4,5] 0.2% to 17% of lung cancer patients develop HPO.

The pathophysiology of HOA remains a subject of debate. Given the diversity of underlying disease and its symmetric manifestations, it is likely that some type of circulating mediator triggers the changes seen in HOA.[9] One protein implicated in the pathogenesis of HOA is platelet-derived growth factor (PDGF). It

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Medical Oncology Department, Instituto Português de Oncologia do Porto Francisco Gentil (IPO-PORTO), Porto, Portugal

** Corresponding author. Medical Oncology Department, Instituto Português de Oncologia do Porto Francisco Gentil (IPO-PORTO), Rua Dr. António Bernardino de Almeida, 4200-072 Porto, Portugal. E-mail address: saramotaalves@gmail.com (Sara Alves).*

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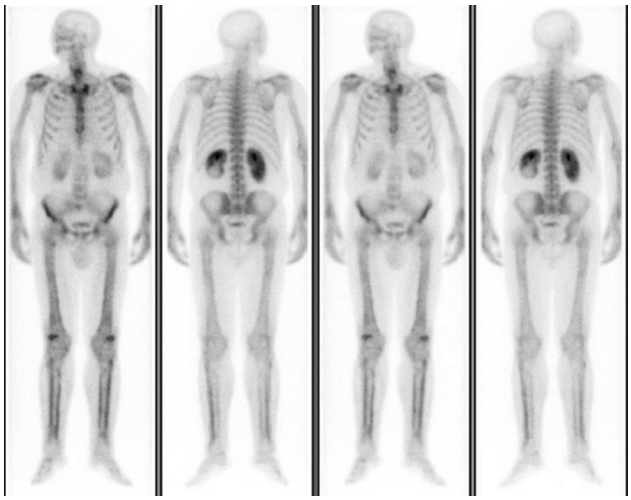

Figure 1. Bone scintigraphy showing diffuse hypercaptation of the radiopharmaceutical along the cortical of the long bones.

plays an important role in normal embryogenesis, wound healing, angiogenesis, and response to inflammation. Silveri et al demonstrated that PDGF levels were higher in patients with HOA versus control patients.[10] In the case of lung cancer, direct tumor production of PDGF has been demonstrated.[11]

In our case, we first diagnosed the lung cancer, and after that, patient developed lower limbs pain, but later upper extremities were also mentioned. Bone scintigraphy helped to exclude bone blastic metastasis and diagnosed the HOA.

Classically, HOA is diagnosed based on symptoms/radiographic findings. Periostisis in HOA specially associated with malignancies, occurs more often in lower extremities, but the upper limbs may be also involved. Bone radiography reveals periosteal membrane thickening and periosteal new bone formation. Bone scintigraphy is another imaging procedure by showing bracelet like or diffusely increased uptake throughout most of the skeleton.[5]

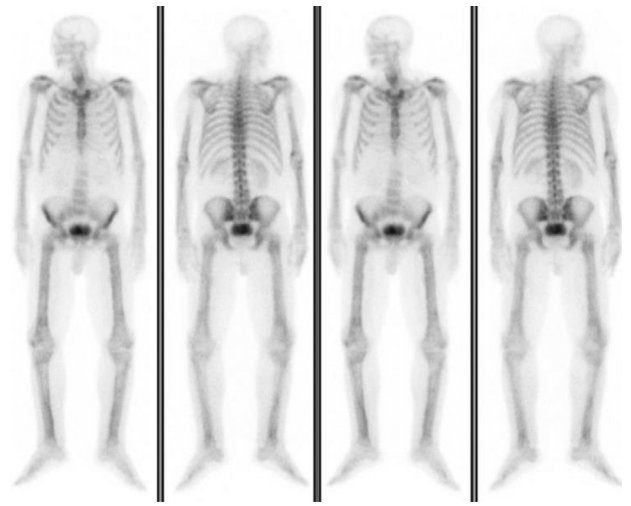

Figure 2. Bone scintigraphy showing diffuse hypercaptation of the radiopharmaceutical along the cortical of the long bones in lower limbs, less evident than in previous examination. No signs of blastic metastasis.

Our patient presented a hard control pain, and it has been described by other reports.[6,8] In this case, we used pamidronate, because literature data suggest that infusions of 30 to 90 mg of pamidronate may be used, resulting in significant analgesic benefit, sometimes just days after the treatment but may be delayed 2 to 3 months.[12]

In our patient, it is difficult to say that pain control was reached by bisphosphonates, but it could have helped, because after that patient did not need more admissions. Chemotherapy also had a very positive benefit, has described in the literature.[5,6] And in our opinion, it was the cornerstone of the case evolution. The nerve blocking also had a role in this story, showing that these patients need multidisciplinary teams helping to diminish their suffering, and a complex management of support treatment. Sometimes it is very difficult to decide to initiate chemotherapy because these patients are weakened, but we have to keep in mind that the poor performance status can be related with pain, and controlling the symptom will help to recover.

Conclusions

In conclusion, HPO is a rare paraneoplastic manifestation of lung cancer. The diagnosis is based on clinical symptoms and imaging findings.

The pain is the most worrying symptom and it is controlled by treating the underlying cause (lung cancer), but usually it is needed to manage it with strong opioids, corticosteroids, nonsteroidal anti-inflammatory, and in some cases, it has been described benefit of single dose of bisphosphonates. A multidisciplinary approach is important because of the difficulty in treatment of this rare condition.

Conflicts of interest

The authors declare no conflicts of interest.

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