Lung Cancer 86 (2014) 105–111

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Case report

Pleuropulmonary angiosarcoma involving the liver, the jejunum and the spine, developed from chronic tuberculosis pyothorax: Multidisciplinary approach and review of literature

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ARTICLE INFO

Article history:
Received 27 April 2014
Received in revised form 4 July 2014
Accepted 15 July 2014

Keywords:
Angiosarcoma
Pleura
Chemotherapy
Sarcoma
Tuberculosis
Pyothorax

ABSTRACT

Pleuropulmonary angiosarcomas are very rare, with less than fifty cases reported in the literature. In most cases, the etiology is unknown but the presence of a chronic tuberculous pyothorax has been reported in several Asian case reports as a possible risk factor.

We report the case of a Caucasian 68-year old man who presented with a pleuropulmonary angiosarcoma that arose from a chronic tuberculous pyothorax and which involved the ribs and the vertebrae, the psoas muscle, and the jejunum. The patient received adapted anti-tuberculosis treatment, embolization of the mass in the small bowel, palliative external beam radiotherapy on the spine and systemic chemotherapy with liposomal non-pegylated doxorubicin and ifosfamide. With this multidisciplinary approach the patient's symptoms were well controlled and he achieved a complete metabolic response after six cycles of chemotherapy. Unfortunately, the patient died after eight months from the beginning of chemotherapy due to an acute lung injury secondary to extensive bilateral interstitial infiltrates. Opportunistic pathogens or drug-induced lung toxicity were the most probable causes.

Treatment with liposomal non-pegylated doxorubicin and ifosfamide could be a reasonable option in pleuropulmonary angiosarcoma but it should be validated in clinical trials. Chronic pyothorax seems to be a predisposing factor for the development of pleural angiosarcoma but further investigations are required to assess a causal association.

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1. Introduction

Vascular sarcomas are considered an uncommon type of sarcomas, representing overall 2 to 3% of all soft-tissue tumours [1,2]. Under this heading, the latest WHO classification includes up to 14 different histological subtypes, categorizing them according to their degree of malignancy, from benign tumours, such as haemangiomas, to highly aggressive neoplasms, such as high-grade angiosarcomas [3].

With regards to the latter, more than half of angiosarcomas are cutaneous while the rest arise in deep soft tissues, breast, bones and solid organs, particularly the liver, spleen and heart. There are a few well-documented general predisposing factors, such as previous radiation-exposure and chronic lymphedema [4,5]. Some associations have been described with specific-site angiosarcomas, such as the link between hepatic angiosarcoma and a previous exposure to vinyl chloride, thorium dioxide or arsenic. However, in most cases, the exact mechanisms which drive the development of angiosarcomas remain obscure [5].

In the case of primary pleuropulmonary vascular sarcomas in general [6], and specifically of angiosarcomas, they are exceedingly rare, with fewer than 50 case reports described in the literature. With regards to their pathogenesis, several series of cases from Japan have reported an association with chronic tuberculosis pyothorax or other sequels of tuberculosis [7–13]. Interestingly, in Western patients, no history of tuberculosis has been described in the reported cases, possibly because of a lower incidence of mycobacterial infections in the West and/or a better antitubercular

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http://dx.doi.org/10.1016/j.lungcan.2014.07.012
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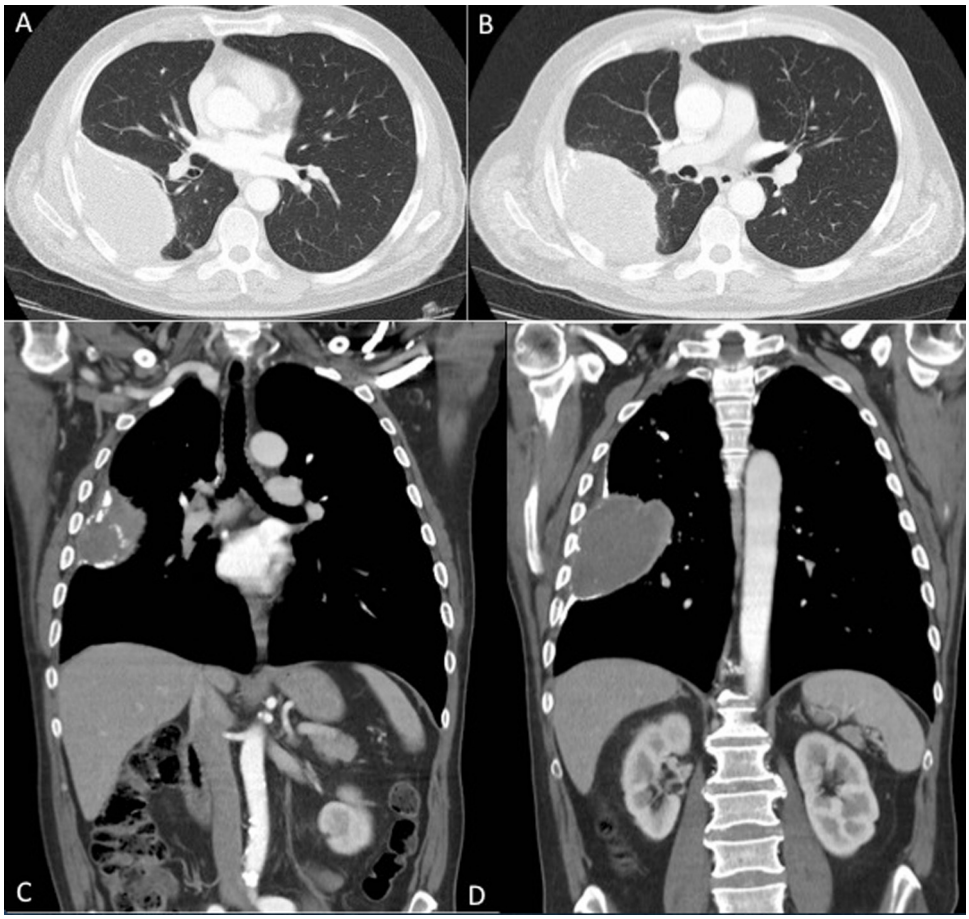

Fig. 1. Thoracic CT scan of March 2012. Axial images (Panel (A) and (B)) and coronal images (Panel (C) and (D)) from a contrast enhanced CT-scan of the chest that showed a mass in the right lower lobe, multiple granulomas and fibrous tracts in the upper lobes and calcified hiliar lymph nodes, consistent of residual tuberculosis.

treatment compliance [14,15]; in some cases, asbestos and radiation exposure have been proposed as causal factors [16] but most angiosarcomas are described as *de novo* [16].

2. Case report

Our patient was a 68-year man who presented in March 2012 with hemoptysis, pleuritic pain and occasional chills. No fever, weight loss or dyspnea were reported. The patient had a previous history of childhood pulmonary tuberculosis. He did not receive antitubercular treatment at that time and he had developed a chronic calcified pyothorax in the lower right chest that had remained stable since then. He had stopped smoking 15 years ago. There was no other personal history of interest. His family history was unremarkable.

A computed tomography (CT) of the chest showed an opacity of 5.5 by 4.5 cm, in the posterior segment of the right lower lobe of his lung that abutted the pleura and that contained hypodense material and calcified walls with multiple noncalcified pulmonary nodules ($\leq$4 mm in diameter), as well as fibrous tracts and calcified subcarinal lymph nodes. All these features were consistent with a previous granulomatous infection (Fig. 1). The skin tuberculosis test was positive and there was a mild ferropenic anaemia. Treatment with codeine, a short course of levofloxacin, and oral iron supplements were prescribed. The respiratory symptoms quickly subsided.

In June of 2012, four months after the first episode, due to the persistence of the anaemia, faecal occult-blood tests were performed. They were positive. A total-body CT scan, colonoscopy and gastroscopy did not find any new abnormalities; but a capsule endoscopy revealed a small bowel jejunal tumour. It was resected in August 2012. The pathological analysis reported an epithelioid angiosarcoma, 2 cm of diameter, with a mitotic index lower than 5%. All resection margins were free of tumour cells. No adjuvant treatment with chemotherapy or radiotherapy was prescribed.

In December 2012, ten months after the first episode, the patient developed low back pain that radiated to his right thigh and low-grade fever A magnetic resonance imaging of the dorso-lumbar spine showed a $60 \times 45 \times 18$ mm lesion at the level of L3 that extended within the L3–L4 disc, the right psoas muscle and the right iliac bone, all findings suggestive of a paravertebral abscess. An open biopsy was performed that showed a non-malignant, granulomatous fibrinous purulent synovitis. He completed a 14-day inpatient course of broad spectrum antibiotics (rifampicin, isoniazid, pyrazinamide, vancomycin and ceftriaxone). He was discharged with a two-month course of oral rifampicin and levofloxacin.

On June 2013, sixteen months after the first episode, the low back pain reappeared. There was also right chest wall pain, inability to walk, dyspnoea on exertion, low-grade nocturnal fever, and a severe anaemia (hemoglobin (Hb) 7 g/dl).

A total-body CT scan showed an enlargement in the previous described calcified residual tuberculous pyothorax. In continuity with this lesion, there was a new pleural heterogeneous contrast-enhanced mass, which infiltrated the intercostal muscle and eroded the 7th and 8th ribs. There were also lytic bone lesions in the L3 vertebral body and in the iliac bone with a soft-tissue component

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