

CASE FOR DIAGNOSIS

Rapidly growing intrathoracic mass with paraneoplastic syndrome

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A 56 year old nonsmoker presented with a 6 month history of dry cough, increasing malaise, night sweats, loss of appetite and weight loss of 10 kg. His past medical history was unremarkable. The patient was in a clearly reduced general state, his temperature was 37.5°C, blood pressure 120/80 mmHg and heart rate 78 beats·min⁻¹. Physical examination including cardiopulmonary and neurological systems was normal.

Laboratory analyses demonstrated an anaemia with a haemoglobin level of 8.5 g·dL⁻¹ but with normal erythrocyte indices, a normal differential white blood cell count but a thrombocytosis of 500×10⁹ platelets·L⁻¹. Anaemia quickly recurred after transfusion of 2 units of blood. Erythrocyte sedimentation rate (ESR) (110 mm·h⁻¹) and C-reactive protein (CRP) (134 mg·L⁻¹; normal value <10 mg·L⁻¹) were elevated. Liver function tests showed significant elevations of gamma-glutamyltransferase (172 U·L⁻¹; normal value 8–66 U·L⁻¹) and of alkaline phosphatase (674 U·L⁻¹; normal value 31–108 U·L⁻¹). Other laboratory tests, including urine, three stool specimens for occult blood, parameters of haemolysis, vasculitis and tumour markers (carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), β₂-microglobulin and markers for germ cell tumours) were negative, as was a tuberculin skin test. Results of pulmonary function tests were also normal.



Fig. 1. – Posteroanterior chest radiograph.

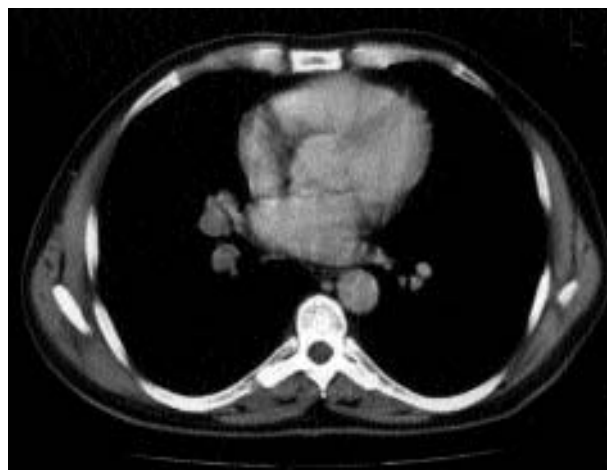


Fig. 2. – Initial computed tomographic scan (CT) scan of the thorax.

Chest radiograph and computed tomography (CT) scan of the thorax are shown in figures 1 and 2.

On fiberoptic bronchoscopy, no endobronchial pathology was seen. Cytological analyses of bronchial washings and transbronchial needle aspiration material from the middle lobe segmental carina showed no evidence of malignancy. A search for metastases, including CT-scan of the brain and bone scintigraphy was negative. As it seemed unlikely that the small hilar mass was responsible for the clinical symptoms and the anaemia, which rather suggested a systemic disease, we first ruled out occult bleeding, infection or a lymphoma. Endoscopy of the upper gastrointestinal tract, colonoscopy, bone marrow biopsy and aspiration, CT-scan of the abdomen and scintigraphy of the bone marrow were normal.

A second bronchoscopy and transbronchial needle cytology in the middle lobe showed a few malignant cells, which could not be further classified. In order to proceed to a percutaneous, CT-guided needle-biopsy, another CT-scan of the thorax was performed, 4 weeks after the first one (fig. 3). Tru-cut biopsy (with a 18-gauge needle) revealed an undifferentiated large-cell tumour with necrotic areas.

Immunohistochemically, the tumour was positive for the soft tissue marker vimentin but not for the epithelial marker LU-5. Three days later, a thoracotomy was performed. A central tumour in the middle and lower lobe was found, in the bifurcation between the middle and lower lobe arteries. A right pneumonectomy was performed. Pathology findings are given in figures 4–6.

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Fig. 3. — Computed tomographic (CT) scan of the thorax with *i.v.* contrast 4 weeks later.

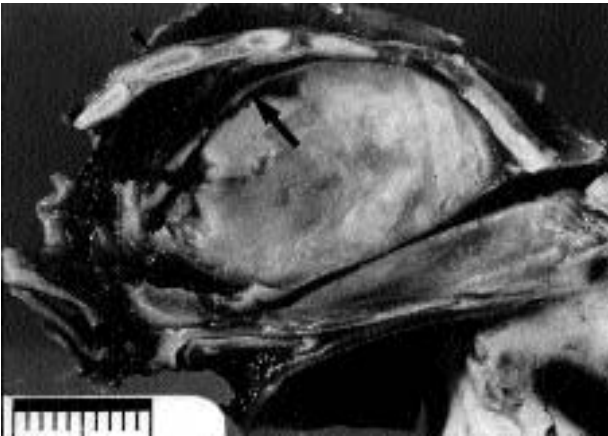


Fig. 4. — Macroscopic view of the tumour filling the pulmonary artery without infiltration into the adjacent bronchus. Large arrow: vessel wall; small arrow: bronchial wall. (Internal scale bar = 1 cm).

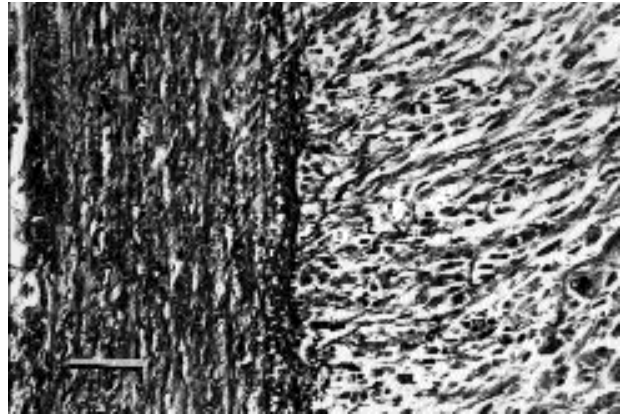


Fig. 5. — The pleomorphic tumour emerges from the intimal layer of the pulmonary artery. (Elastica-van Gieson's stain; internal scale bar = 70 µm).

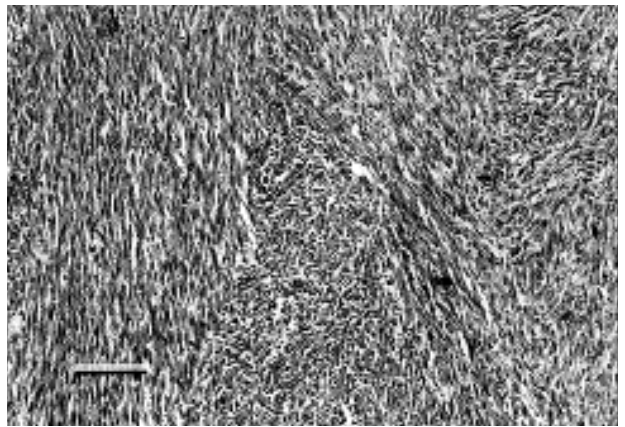


Fig. 6. — Tumour area showing fascicles of spindle cells that intersect at right angles. (Haematoxylin and eosin stain; internal scale bar = 350 µm).

BEFORE TURNING THE PAGE: INTERPRET THE CHEST RADIOGRAPH, CT SCAN AND PATHOLOGY FINDINGS. SUGGEST A DIAGNOSIS

Interpretation of chest radiograph and CT

The posteroanterior view (fig. 1) shows a slight enlargement of the right lower hilus and possibly a loss of peripheral vascularization in the right lung below the hilar level, a feature compatible with compression or obstruction of the inferior central vessels by tumour. On CT scan (fig. 2) a circular mass, 2 cm in diameter, is visible in the region of the right hilus, between the medial and lateral segmental bronchi of the middle lobe. Four weeks later (fig. 3) the circular mass measured 4.5×5.5 cm, which corresponds to a doubling-period of the tumour volume of 1 week.

Interpretation of pathology findings

Macroscopic examination of the right lung (fig. 4) showed a multilobular, homogeneous tumour originating from the right middle lobe artery and involving the central parts of the middle and lower lobe. Microscopically, the tumour originated from the intimal layer of the vessel wall (fig. 5). The resection margins were free of tumour and no metastases were detected in regional lymph nodes. The major part of the tumour showed typical features of a high grade sarcoma, consisting of focal necrosis, considerable pleomorphism, giant cells and numerous mitoses. Some areas showed the typical pattern of leiomyosarcoma, with spindle cells, forming intersecting fascicles (fig. 6). Immunohistochemically, the tumour was positive for the soft tissue marker vimentin, for muscle-specific actin, smooth muscle actin and focally for desmin.

DIAGNOSIS: "Primary high grade leiomyosarcoma of the pulmonary artery, peripherally located, presenting primarily with paraneoplastic symptoms".

Treatment and clinical course

Only a few days after the operation, the patients general condition improved dramatically. Two weeks after thoracotomy, haemoglobin, platelets, liver function tests, ESR and CRP were within normal limits. Radiotherapy (60 Gy) of the right mediastinum and hilus was performed. Twenty months after the operation the patient is still free of recurrence.

Discussion

Primary sarcomas of the pulmonary artery are rare, though highly malignant, tumours of vascular origin. Until 1990 a total of 93 cases had been reported with a median survival of 1.5 months [1]. Typically this tumour occurs at 40–50 yrs of age, with no apparent sex bias. There are no established diagnostic or therapeutic strategies for this tumour because of its rarity, nonspecific clinical presentation and wide histological heterogeneity. The poor prognosis is related mainly to the central location of the tumour and usually late diagnosis.

Most pulmonary artery sarcomas have been classified as leiomyosarcoma and undifferentiated sarcoma, though many other terms, such as intimal sarcoma, have been applied to the latter type [2]. The vast majority of these

tumours originate from the pulmonary trunk and tend to expand either distally into one or both of the pulmonary arteries or proximally, involving the pulmonary valve. Local destruction or invasion into the adjacent structures are rare but tumour emboli into peripheral pulmonary artery branches occur in 61% of cases. Systemic metastases (without organ predilection) have been reported in 19%, whilst mediastinal and hilar lymph node metastases are uncommon. Typically, the tumour will occlude pulmonary arterial branches, leading to pulmonary arterial hypertension and ultimately right heart failure. Many patients die with the clinical misdiagnosis of acute or chronic recurrent pulmonary thromboembolism [3].

Typical presenting symptoms are dyspnoea (76%), chest pain (53%), cough (52%), haemoptysis (32%) and syncope (23%), related to pulmonary vascular obstruction. The mean duration of symptoms before final diagnosis or death is 12 months.

Though the chest radiograph is abnormal in most of the published cases, it usually shows nonspecific secondary effects of the tumour, *i.e.* parenchymal infiltrates (48%), hilar or mediastinal masses (38%), enlarged cardiac silhouette (38%) and peripheral hypoperfusion (24%).

Angiography and perfusion scintigraphy show perfusion defects in all cases investigated. In a recently reported case, a peripheral pulmonary artery sarcoma was diagnosed preoperatively by magnetic resonance imaging enhanced with gadolinium and confirmed by percutaneous CT-guided needle biopsy [4]. In our patient, with the predominant systemic symptoms, we proceeded to a CT-guided needle biopsy in order to exclude a tumour, which should be treated by radiotherapy and/or chemotherapy rather than surgery. Although the advantage of a precise preoperative diagnosis is obvious, the risk of taking a biopsy sample in a centrally located lesion, adjacent to vascular structures, needs to be considered.

Complete resection is the treatment of choice. In most reported cases, radical excision was not possible due to the critical localization of the tumour at the base of the right heart. The role of adjuvant radiotherapy and/or chemotherapy remains debatable [5].

In our case we had to deal with a patient in a very significantly reduced general state, though with only a small lung tumour, which did not fit the typical picture of a bronchial carcinoma. We suggest that the disturbed liver function, thrombocytosis and anaemia were paraneoplastic phenomena, since they promptly normalized after resection of the tumour. This specific paraneoplastic syndrome with predominant malaise and anaemia has not, to our knowledge, been described in this context previously. Only one patient has been reported with a paraneoplastic picture similar to the clinical presentation of a pheochromocytoma [6]. The peripheral location of the tumour in our patient is rather exceptional and contributed to the uncomplicated surgery and the ongoing favourable outcome after 20 months of follow-up.

Keywords: Leiomyosarcoma, paraneoplastic syndrome, pulmonary artery.

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