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CASE STUDY

Pulmonary infiltrates in Costello Syndrome

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Pulmonary infiltrates in Costello Syndrome. N. Waldburg, F. Buehling, M. Evert, O. Burkhardt, T. Welte. ©ERS Journals Ltd 2004.

ABSTRACT: This paper reports on a patient with diffuse pulmonary infiltrates directly related to Costello Syndrome.

This congenital disorder is characterised by multiple congenital abnormalities, such as psychomotor retardation, short stature, redundant skin, papillomata, curly hair, relative macroencephaly, distinctive face and various defects of internal organs.

This study is the first to document the histopathological findings in the lungs.

Most conspicuous was the depositing of abnormal collagen and elastic fibres and the development of endogenous lipid pneumonia.

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In 1971, Costello described a new syndrome that involves multiple congenital abnormalities, such as psychomotor retardation, short stature, redundant skin, papillomata, curly hair, relative macroencephaly, distinctive face and various defects of internal organs [1–3]. In addition, patients with the Costello Syndrome tend to develop benign and malignant tumours [4–6]. This paper now reports on a patient with diffuse pulmonary infiltrates that are directly related to this condition.

Case history

History

The 37-yr-old male patient was born after uneventful pregnancy (birth weight 3,240 g; length 49 cm), with unremarkable family history. A gastroduodenal tube was required at the age of 9 months. Upon his last examination, at 37 yrs of age, he described exclusively progredient dyspnoea. He showed a happy outgoing nature, short stature (153 cm) and mental subnormality.

Physical findings

Characteristically, his skin was dark, with loose and redundant skin on the hands and feet. The palms were hyperkeratotic and the fingers hyperextensible with dystrophic nails. Papillomas were noted on his cheeks and fingers. His ears were low-set, protuberant and posteriorly rotated. He had curly hair, relative macroencephaly, depressed nasal bridge, pectus carinatum, long nipples and lymphedema (fig. 1).

Laboratory data

Laboratory data were unremarkable. The results of the immunological work-up showed no abnormalities, but ultrasound examination disclosed moderate hepatomegaly. ECG revealed atrial fibrillation, and echocardiography demonstrated an abnormal intraventricular septum but no hyperthrophic cardiomyopathy.

Chest examination

Chest radiographs showed bilateral diffuse interstitial infiltration predominating in lower lung zones (fig. 2). Chest CT scans displayed bilateral, diffuse areas of ground-glass attenuation, with a basal predominance (figs 3 and 4). The bronchoalveolar lavage fluid contained increased amounts of granulocytes and CD8-positive lymphocytes.

Clinical course

Despite antibiotic therapy, dyspnoea and pulmonary infiltrates continued progressing. Therefore, thoracoscopy was performed and a representative segment excised.

Histopathological examination

Histopathological examination revealed endogenous lipid pneumonia consisting of numerous intra-alveolar foamy macrophages, cholesterol clefts, surrounding giant cell reaction and hyperplasia of type II pneumocytes. Atypical collagen fibres were deposited in the pleura and septal connective tissue, particularly in the adventitia of medium-sized pulmonary veins and arteries, leading to marked thickening and compression (fig. 5). Most conspicuous was the increased deposition of atypical, fragmented, thickened, sometimes loosely organised elastic fibres in the alveolar walls (fig. 6). Continuous aspiration of lipids, virus pneumonia and malignancy were excluded.

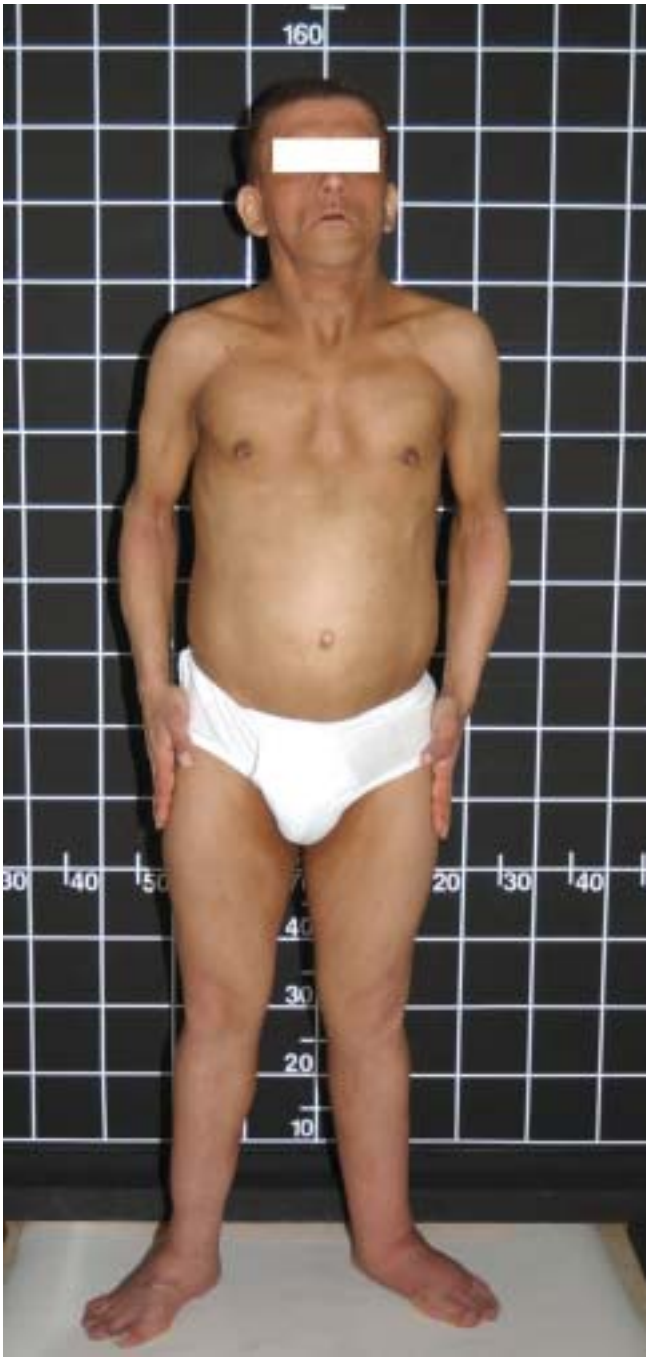

Fig. 1. – A 37-yr-old male patient with Costello Syndrome (short stature (153 cm), redundant dark skin, curly hair, relative macroencephaly, distinctive face, pectus carinatum, long nipples and lymphedema).

Discussion

Since its first description in 1971, >45 cases of Costello Syndrome have been reported, suggesting that this congenital disorder is more common than previously thought. Aetiology and genetics still need to be clarified. The clinical findings of this patient are consistent with those described previously. Some patients suffered from respiratory distress, upper respiratory infection and aspiration syndrome. Most patients died at a very young age because of cardiac complications, failure to thrive or unspecified causes [2, 7, 8].

To the best of the current authors′ knowledge, this is the first histologically proven affection of the lung structure in

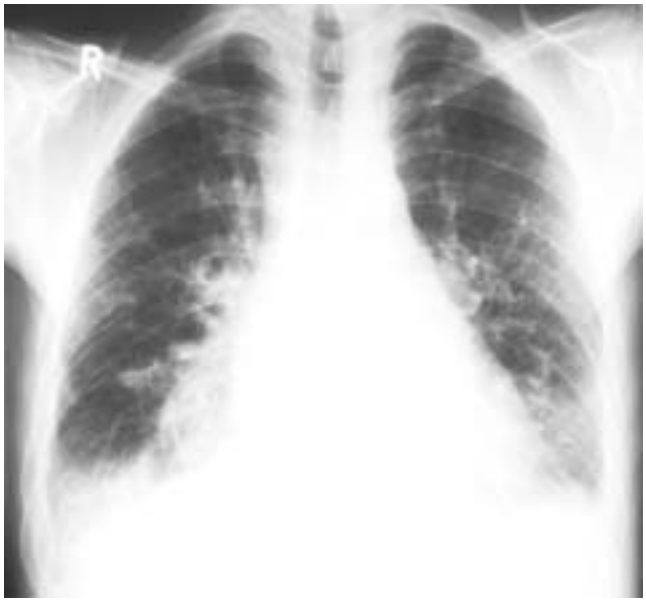

Fig. 2. – Chest radiographs showed bilateral diffuse interstitial infiltration predominating in lower lung zones.

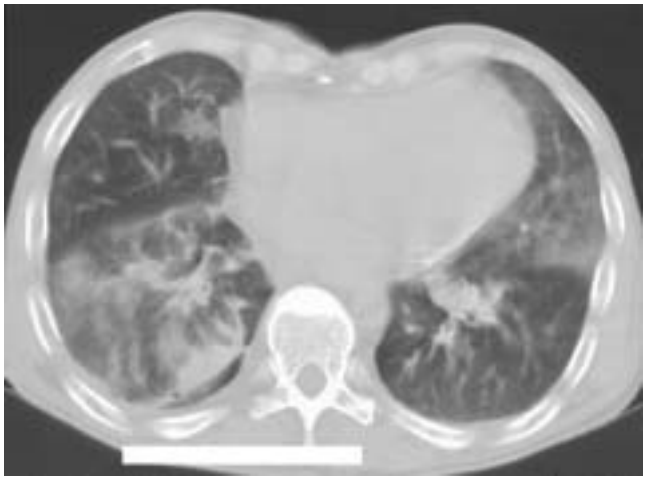

Fig. 3. – Basal chest CT scans displayed bilateral, diffuse areas of ground-glass attenuation, with a basal predominance.

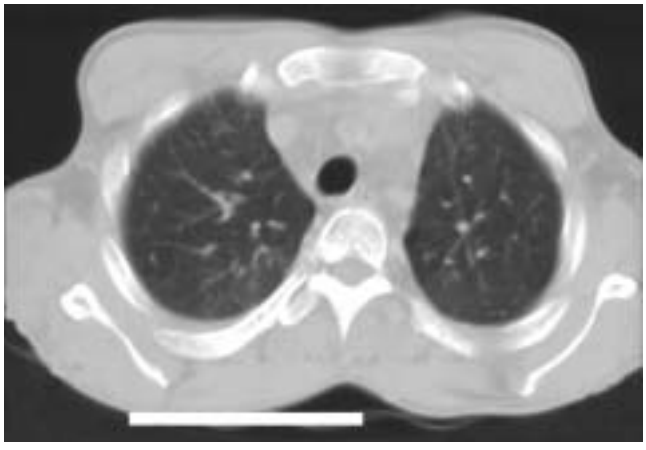

Fig. 4. – Apical Chest CT scans without significant pathologies.

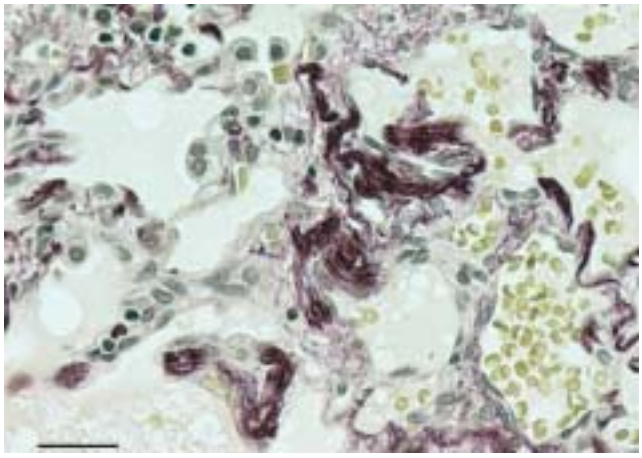

Fig. 5. – Atypical collagen fibres in the adventitia of pulmonary vessels. Elastica van Gieson. Scale bar=310 μm.

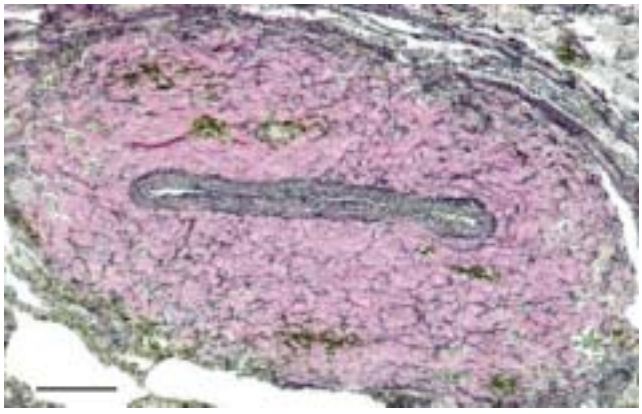

Fig. 6. – Atypical elastic fibres in alveolar walls. Elastica van Gieson Scale bar=40 μm.

Costello Syndrome. However, abnormal elastic fibres in the skin are a common feature [9, 10]. In addition, autopsy cases revealed an impaired deposition of elastic fibres in the tongue, pharynx and upper oesophagus [11]. The authors believe that the respiratory problems seen in this patient result from an impaired clearance of the airspaces from lipoproteins, caused by a structural damage of the lung parenchyma. Therefore, a direct relationship to the primary disease, which could have been revealed only by histopathological examination, seems to exist. There might be a causal link between the functional deficiency of the 67-kD elastin-binding protein, as previously described for Costello Syndrome [10], the depositing of abnormal collagen and elastic fibres, and the development of endogenous lipid pneumonia.

Future examinations of patients with Costello Syndrome may reveal organ manifestations that are unknown at present but may be clinically relevant or even play a decisive role for prognosis, as in the case presented here.

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