Forensic Science International 262 (2016) e1–e4

Contents lists available at ScienceDirect

Forensic Science International

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

Case report

Nodular pulmonary amyloidosis with spontaneous fatal blood aspiration

S. Morgenthal [a,*], R. Bayer [b], E. Schneider [c], M. Zachäus [d], C. Röcken [e], J. Dreßler [b], B. Ondruschka [b]

[a] Institute of Legal Medicine, University Hospital Jena, Friedrich-Schiller-University of Jena, Jena, Germany
[b] Institute of Legal Medicine, Medical Faculty, University of Leipzig, Leipzig, Germany
[c] Department of Pathology, Group Practice, Leipzig, Germany
[d] Department of Internal Medicine, Helios Park-Klinikum Leipzig, Leipzig, Germany
[e] Department of Pathology, Christian-Albrechts-University of Kiel, Kiel, Germany

ARTICLE INFO

Article history:
Received 27 October 2015
Received in revised form 22 February 2016
Accepted 10 March 2016
Available online 17 March 2016

Keywords:
Localized amyloidosis
Nodular pulmonary amyloidosis
Fatal hemorrhage
Blood aspiration

ABSTRACT

Amyloidosis is a multisystem disease, which is characterized by the extracellular deposition of insoluble abnormal fibrils. Histological and subsequent immunohistochemical examinations are necessary for the determination of the diagnosis and the classification of the amyloid type. The most common systemic variant is immunoglobulin-derived light chain (AL) amyloidosis. However, local or organ-limited AL amyloidosis can occur. Isolated pulmonary amyloidosis is a rare condition and frequently an incidental finding at chest scans or during autopsy. Generally, it is associated with a benign prognosis.

Here, we present two fatal cases, in which the cause of death was asphyxiation due to severe blood aspiration. During autopsy, several nodules were found in the lungs. Based on histological and immunohistochemical analysis, the diagnosis of an isolated nodular pulmonary AL amyloidosis lambda light chain was made. Amyloid was also present in pulmonary blood vessels, which lead to fragility and finally fatal hemorrhage.

1. Introduction

Amyloidosis is a generic term for a heterogeneous group of protein folding disorders caused by extracellular deposition of insoluble abnormal fibrils, derived from aggregation of misfolded, normally soluble, proteins [1]. These accumulated amyloid fibrils progressively disrupt the structure and function of tissue and organs [2]. Amyloidosis can be hereditary or acquired, localized or systemic and is potentially lethal [3]. The rareness of this disease and the variable involvement of different organs and tissues are often responsible for missed or delayed diagnosis [1]. Histological assessment reveals eosinophilic amorphous deposits in the tissue, which exhibit fluorescence when examined under fluorescence microscopy. Under polarizing microscopy Congo red-stained amyloid exhibits anomalous colors. In daily practice, these are more often color mixtures due to strain birefringence or uncrossing of polarizer and analyzer, beside the usually mentioned 'apple-green birefringence'. According to Howie and Owen-Casey all the other anomalous colors are just as characteristic of amyloid as the pure green one, but are more common and of great diagnostic value [4].

Using immunohistochemistry, the amyloid protein can be determined, which is necessary for the classification of the amyloidosis. The amyloid fibrils derive from a variety of precursor proteins, frequently serum amyloid A protein (AA) or monoclonal immunglobulin light chains (AL) [5]. To date more than 31 different proteins are identified, which can form amyloid [6].

Amyloidosis may involve the lungs as part of a systemic process or may be confined solely to the lungs. Clinically, patients with localized pulmonary amyloidosis can be asymptomatic or present a wide spectrum of symptoms which are frequently similar to those caused by different airway disorders [3,7]. Pulmonary amyloidosis can be classified into three forms: submucosal deposits in the airways (tracheobronchial form), diffuse alveolar septal deposits and pulmonary nodules [8]. Nodular parenchymal amyloid is often detected incidentally as single or multiple lung nodules and is presumed to be a disease with a benign prognosis [9,10]. Radiographically, it cannot be distinguished from other malignant or benign neoplasms, chronic inflammatory or granulomatous lesions [11], although spots of calcification are found in

* Corresponding author. Tel.: +49 3641 935551.
E-mail address: Sylvia.Morgenthal@gmx.de (S. Morgenthal).

http://dx.doi.org/10.1016/j.forsciint.2016.03.017
0379-0738/

about 50% of the cases [9]. Evidence of a systemic disease should be sought clinically, including examination and immunofixation of serum and urine for a monoclonal protein [5].

Here, we report about two autopsy cases of sudden unexpected death in unclear circumstances with underlying lethal hemoptysis due to nodular pulmonary amyloidosis.

2. Case reports

2.1. Case 1

A 70-year-old man was found drifting lifeless in a lake approximately 100 m from the bank. Other bathers stated that they saw him going into the water to swim several times before the incident. During recovery and resuscitation, fresh blood leaking from mouth and nose was observed. A relevant medical history was not known.

Forensic autopsy revealed a brittle yellow-brownish nodule in the right lower lung lobe with a maximum of 30 mm in diameter, which was surrounded by a measured hemorrhage approximately $100 \times 80 \times 80$ mm. Additionally, there was another nodule of maximum 30 mm in diameter in the left upper lung and further multiple brittle yellow-brownish nodules bilateral in the lung parenchyma with a maximum of 5 mm in diameter. A lot of fresh blood was detected in the respiratory system. The cut surfaces of the lungs showed typical spots of blood aspiration. There was no characteristic evidence of drowning, e.g. froth around the mouth and nostrils or an emphysema aquosum could not be detected.

By order of the investigative authority, additional toxicological investigations were performed. Applying the gas chromatography (GC) analysis in peripheral venous blood, no ethanol was detected. Using the high-performance liquid chromatography (HPLC), no drugs or medication could be detected.

2.2. Case 2

An 81-year-old female was admitted to hospital because of a deterioration of her general condition. The medical history included a severe general arteriosclerosis and hypertensive heart disease with cardiac insufficiency. A chest CT scan revealed multiple coarse up to plump roundish, space-occupying infiltrates in both lungs with small spots of calcification and a wedge-shaped infarction zone next to confluent consolidations located predominantly in the subpleural areas (see Fig. 1). These radiologic findings were interpreted as: pneumonia, due to the infection of a lung infarction that was caused by pulmonary embolism; furthermore a lung malignancy was suspected. Samples of bronchoalveolar lavage showed signs of inflammation (masses of neutrophilic granulocytes) and siderophages. Specimens taken from a transbronchial biopsy showed no characteristics of malignancy. Electrophoresis (with immunofixation) of serum and urine were normal with no evidence of monoclonal bands. After five weeks of clinical treatment, the patient was discharged in good general condition.

Four days later, the patient was re-admitted to hospital because of fever, dehydration and hypotension. Clinical examination revealed a severe multifocal infection. In addition to pneumonia the patient suffered from pyelonephritis with infection of the urinary tract and pseudomembranous colitis. Seven days later, the patient became acutely anxious and disoriented. She showed 'bubbling respiration' and massive hemoptysis. The patient died in spite of immediate resuscitation efforts. Due to a full clotting screen four days before death, a coagulation disorder was excluded.

Pathological autopsy revealed multiple white-yellowish and waxy nodules in both lungs with fragile structure up to 20 mm in greatest diameter, mainly subpleural and basal, which were suspected to be bilateral pulmonary metastases of an unknown primary. A lot of fresh and older blood was detected in the respiratory system and approximately 1 l of blood in the stomach and the small bowel. The cut surfaces of the lungs showed typical spots of blood aspiration.

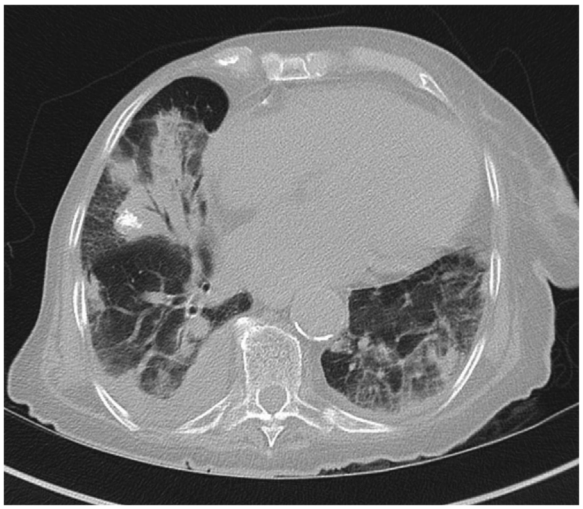

Fig. 1. Axial CT image showing multiple nodules with some spots of calcification in spatial proximity to the airway and vessel courses. The nodules vary in sizes and shape and are distributed bilaterally (slice thickness 0.3 cm, lung window setting).

2.3. Histological and immunohistochemical examinations

In both cases, histological and subsequent immunohistochemical assessment of lung specimens, especially the lung nodules (see Fig. 2), revealed a similar pattern. Histological, there were alveolar-septal and interstitial depositions of homogenous eosinophilic amorphous material, which stained positive with Congo red and showed an anomalous color in polarized light. Under fluorescence, the deposits revealed a yellowish-orange color. Several amyloid deposits presented ossification and calcification. Amyloid deposits were also found within and next to pulmonary blood vessels, especially when they were embedded or close to the nodules. Furthermore, massive extravasated erythrocytes and iron-positive siderophages were detected. The airways did not show any deposits of amyloid.

As proposed by Schönland et al., a full immunohistochemical examination was done [12]: The amyloid deposits immunoreacted

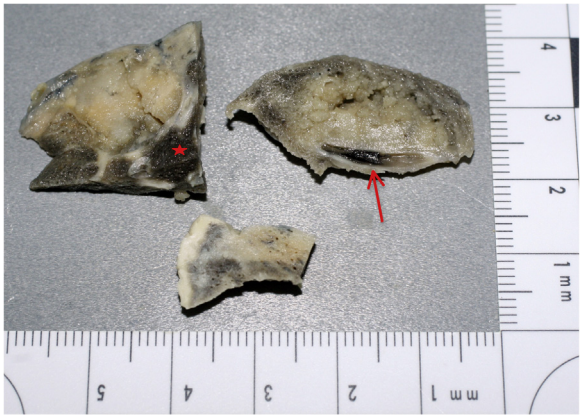

Fig. 2. Macroscopic appearance of three formalin-fixed tissue specimen showing tumor-like pulmonary nodules in varying size. Please note the little tissue hemorrhage top left (asterisk) and the proximity between a small blood vessel and the amyloid depots top right (arrow).