Respiratory Medicine Case Reports 39 (2022) 101727

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

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

Case Report

Pulmonary calcinosis associated with Alport syndrome

Valentine Mismetti, Marie-Pierre Perquis, Lina Hamdi, Marios E. Froudarakis *, Jean-Michel Vergnon

Department of Pulmonology and Thoracic Oncology, North Hospital, University Hospital of Saint-Etienne, France

ARTICLE INFO

Keywords:
Pulmonary calcinosis
Alport syndrome
Renal failure
Bone scan

ABSTRACT

We report the case of a 48-year-old woman under dialysis from chronic renal failure (CRF) since the age of 27, due to Alport syndrome. The patient underwent routine chest X-ray on which diffuse micronodules were shown. Chest computed tomography showed partially calcified micronodules with centrilobular distribution respecting the subpleural spaces and predominant in the upper lobar regions. Metastatic pulmonary calcinosis was confirmed by the bone scan with an overall course of 29 years. This is the first reported case of pulmonary calcinosis from CRF due to Alport syndrome.

1. Introduction

Mineral and bone disorders are common during chronic renal failure (CRF) and may include extra-osseous calcinosis. However, pulmonary localization of these calcinosis remains rare. We report herein for the first time a case of metastatic pulmonary calcinosis (MPC) in a 48-year-old female with chronic renal failure in the context of Alport syndrome (AS), which is a genetic condition characterized by kidney disease, hearing loss, and eye abnormalities.

2. Case report

A 48-year-old female was admitted to our department in June 2009, for stage II mMRC dyspnea associated to diffuse pulmonary opacities on chest X-ray (Fig. 1A). Her medical history was notable for Alport syndrome in dialysis since 1988 with kidney transplantation in 2007, thyroidectomy with parathyroidectomy for papillary carcinoma in 1993, cerebral hemorrhage with left hemiparesis and post-vascular epilepsy in 2005, hepatitis C and deep vein thrombosis of the right lower limb in 2008. Its treatment included an immunosuppressive therapy (ADVAGRAF® 2,5 mg/24h + CELLCEPT® 500 mg/12h), an antiepileptic (DEPAKINE® 90mg/24h), a statin (ATORVASTATINE® 10mg/24h) a beta-blocker (BISOPROLOL® 1,25 mg/24h) and an angiotensin receptor inhibitor (LOSARTAN® 25mg/24h).

At presentation, the patient had normal pulmonary auscultation, arterial blood gases on room air and at rest were PaO2 = 73 mmHg, PaCO2 = 36 mmHg and pH = 7,44. Lung function tests (LFT), showed irreversible bronchial obstruction with Forced Expiratory Volume in 1 s (FEV_1) at 1,01L (45% of predicted), Vital Capacity (VC) at 1,59L (59% of predicted), Total Lung Capacity (TLC) at 78% of predicted, Diffusion Capacity for Carbon monoxide (DLCO) at 48%, with carbon monoxide transfer coefficient (KCO) at 79%. Laboratory tests showed: calcemia = 1.9 mmol/L (normal = 2.2–2.6) with parathormone (PTH) dosage of 3ng/L (n = 150–300), creatinine = 62 μmol/L (GFR 75mL/min) and proteinuria = 0.10 g/day.

* Corresponding author. Department of Pulmonology and Thoracic Oncology, North Hospital, University Hospital of Saint-Etienne, 42055, Saint-Etienne Cedex 2, France.
E-mail address: marfroud@gmail.com (M.E. Froudarakis).

https://doi.org/10.1016/j.rmcr.2022.101727
Received 18 June 2022; Received in revised form 21 July 2022; Accepted 8 August 2022
Available online 24 August 2022

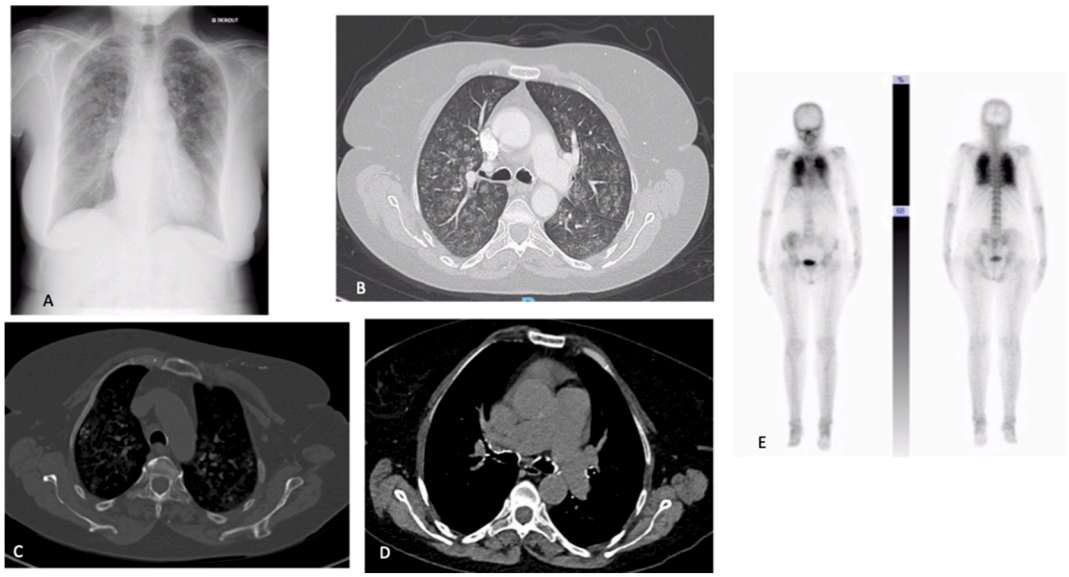

Fig. 1. Patient's imaging: **A**/chest X-ray with diffuse bilateral opacities, predominant in the upper lobes, **B and C**/chest computed tomography (CCT) with diffuse centrilobular micronodules, respecting subpleural, fissural and peribronchovascular spaces (parenchymal and bone windows respectively), **D**/CCT (mediastinal window) showing calcified tracheobronchial tree **E**/bone scan with bilateral lung fixation.

Chest computed tomography (CCT) showed partially calcified confluent ground glass micronodules with a central lobular distribution respecting the sub-pleural spaces, and predominant in the upper lobar regions (Fig. 1B and C). Calcifications were also present at the tracheobronchial tree (Fig. 1C and D). A flexible bronchoscopy was then performed to exclude any infection, finding a diffuse micronodular appearance of the bronchial mucosa. Histology of the biopsies did not suggest a specific cause. Direct examination of bronchial aspiration fluid with cultures and PCR excluded any microorganism.

A bone scan was then performed, which showed bilateral and diffuse pulmonary hyperfixation (Fig. 1E). In her medical records we found a CT and bone scans performed in 1993 before thyroidectomy, showing exactly the same pattern as in 2009. The final diagnosis retained was metastatic pulmonary calcinosis (MPC) in the context of chronic renal failure (CRF) from Alport syndrome. As the patient presented a 16-year disease and parathyroids were already removed, no further treatment was proposed, except a regular follow-up. In 2020 and after 13 years of follow-up, and 29 since the MPC image discovering, the patient is in good shape with clinical and radiological stability.

3. Discussion

Alport syndrome (AS), from which suffers our patient, is a progressive inherited disease, resulting in chronic renal failure, deafness and eye damage. It is caused by an abnormality of type IV collagen of the cells' basement membrane. The management of AS aims to delay renal failure, by associating diuretics, angiotensin-converting-enzyme inhibitors, and low-salt diet. Severe cases require dialysis and renal transplantation, as in the case of our patient. Although pulmonary calcinosis is known to be associated with chronic renal failure, no cases have been reported in CRF from AS, therefore, the case of our patient is the first reported in the literature.

Pulmonary calcinosis is a known complication of CRF due to secondary hyperparathyroidism, in patients with primary hyperparathyroidism or during vitamin D intoxication, due to imbalance of phosphocalcic metabolism [1,2]. Other contributing factors are hypercalcemia, local alkaline environment, and previous lung damage [3]. The distribution pattern of calcifications in our case happened to be diffuse, called metastatic pulmonary calcifications (MPC), in which imaging findings are somewhat unique and potentially confusing with other more frequently occurring entities. Therefore, CCT findings of MPC are characterized by a progressive pattern described as multiple diffuse nodules, fluffy, poorly defined unless calcified [4], diffuse or patchy areas of ground glass opacities, and confluent parenchymal consolidations, easily misdiagnosed as diffuse severe pneumonia, metastatic disease or congestive heart failure (CHF) [5]. The relative stability of pulmonary consolidations and no effect of the antibiotics or diuretics might be useful to differentiate MPC from infectious disease or CHF.

Other causes of MPC are granulomatous diseases such as tuberculosis, sarcoidosis, pulmonary amyloidosis, infections from viruses or parasites, vascular calcinosis, idiopathic alveolar micro-lithiasis, treatment with intravenous calcium, multiple myeloma, hemosiderosis, and pneumoconiosis [3,6]. Also, calcified pulmonary metastases in the context of a neoplastic disease may occur, either by osseous formation from the tumor itself, or by secondary deposition of calcium within the tissue due to hypercalcemia or by secondary calcinosis after chemotherapy treatment, or by mucoid calcinosis from a muco-secreting adenocarcinoma [7]. Flexible bronchoscopy is useful to overrule other entities and transbronchial biopsies may show the presence of calcifications [8]. Bronchoalveolar lavage (BAL) during bronchoscopy shows a macrophagic and lymphocytic predominance associated to microliths which contribute to

diagnosis [9]. Biochemical analysis of the lavage fluid showed elevated total protein, phospholipids, without affecting surfactant apoprotein-A which tend to be normal [10].

Bone scan is frequently overlooked, although it is a pertinent imaging technique for the diagnosis of this entity [11]. When performed, shows bilateral lung diffuse hyperfixation, strongly suggestive of MPC [11]. Ventilation/perfusion scan, may also contribute to diagnosis by estimating the ventilation dysfunction. Spirometry usually shows restriction [12], however, obstruction may also occur due to calcinosis located in the airways [6], as was the case of our patient. Lung function tests may reveal a diffusion defect, as well as from mild to severe hypoxemia with respiratory failure [12].

Autopsies from CRF patients showed pulmonary calcinosis in 60–80% of the cases. Calcifications were found in the alveolar septa, in the bronchiolar and bronchial walls, but also in the walls of the pulmonary vessels [6,11], which suggest participation in the development of pulmonary hypertension and right heart failure [11]. Most of the patients with MPC are asymptomatic with favorable prognosis, while few cases may need parathyroidectomy for rapidly developing respiratory failure leading to death [6,12]. Indeed, in our patient's case, a possible explanation for MPC stability was that he had been removed the parathyroids during thyroidectomy for papillary carcinoma in 1993.

To conclude, our patient's MPC from CRF due to AS had an overall 29 years course. Although the course of MPC is benign, early diagnosis is essential to prevent clinical and metabolic complications. Bone scan is a noninvasive method, useful to differentiate MPC from other entities.

Informed consent

The patient has provided a signed consent which is available upon request.

Authors' contribution

Patient's recruitment: JM Vergnon, Data acquisition: all authors, Manuscript Draft: all authors, Review and corrections: all authors, Approval of final version: all authors.

Statement of ethics

This case report was conducted ethically in accordance with the world medical association declaration of Helsinki. The authors state that the patient gave her written informed consent to publish her case, including images.

Funding source

None.

Declaration of competing interest

The authors have no conflicts of interest to declare in relation to this manuscript.

References

[1] M. Bestetti-Bosisio, F. Cotelli, E. Schiaffino, G. Sorgato, C. Schmid, Lung calcification in long-term dialysed patients: a light and electronmicroscopic study, Histopathology 8 (1) (1984) 69–79.
[2] A.K. Abdullah, G. Jarrar, G.C. Ejeckam, Idiopathic pulmonary calcinosis: a variant of alveolar microlithiasis, East Afr. Med. J. 71 (8) (1994) 543–544.
[3] E.D. Chan, D.V. Morales, C.H. Welsh, M.T. McDermott, M.I. Schwarz, Calcium deposition with or without bone formation in the lung, Am. J. Respir. Crit. Care Med. 165 (12) (2002) 1654–1669.
[4] T.E. Hartman, N.L. Muller, S.L. Primack, T. Johkoh, N. Takeuchi, J. Ikezoe, et al., Metastatic pulmonary calcification in patients with hypercalcemia: findings on chest radiographs and CT scans, AJR Am. J. Roentgenol. 162 (4) (1994) 799–802.
[5] H.M. Sun, F. Chen, H.L. Yin, X.Y. Xu, H.B. Liu, B.L. Zhao, Rapid development of metastatic pulmonary calcifications in primary hyperparathyroidism: a case report and literature review, Diagn. Pathol. 12 (1) (2017) 38.
[6] E. Marchiori, A.S. Souza Jr, T. Franquet, N.L. Muller, Diffuse high-attenuation pulmonary abnormalities: a pattern-oriented diagnostic approach on high-resolution CT, AJR Am. J. Roentgenol. 184 (1) (2005) 273–282.
[7] J.B. Seo, J.G. Im, J.M. Goo, M.J. Chung, M.Y. Kim, Atypical pulmonary metastases: spectrum of radiologic findings, Radiographics 21 (2) (2001) 403–417.
[8] D. Samolski, R. Dure, G. Bentolila, T. Castiglioni, Metastatic pulmonary calcification diagnosed by transbronchial cryobiopsy, Monaldi Arch. Chest Dis. 90 (4) (2020).
[9] S. Mariotta, A. Ricci, M. Papale, F. De Clementi, B. Sposato, L. Guidi, et al., Pulmonary alveolar microlithiasis: report on 576 cases published in the literature, Sarcoidosis Vasc. Diffuse Lung Dis. 21 (3) (2004) 173–181.
[10] J.B. Pracyk, S.G. Simonson, S.L. Young, A.J. Ghio, V.L. Roggli, C.A. Piantadosi, Composition of lung lavage in pulmonary alveolar microlithiasis, Respiration 63 (4) (1996) 254–260.
[11] Z. Rajkovaca, P. Kovacevic, B. Jakovljevic, Z. Eric, Detection of pulmonary calcification in haemodialised patients by whole-body scintigraphy and the impact of the calcification to parameters of spirometry, Bosn. J. Basic Med. Sci. 10 (4) (2010) 303–306.
[12] M. Pasquier, M.D. Schaller, M. Abdou, P. Eckert, [Pulmonary metastatic calcification], Rev. Mal. Respir. 29 (6) (2012) 775–784.