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CASE BASED REVIEWS

Spontaneous pneumomediastinum, a rare manifestation of clinically amyopathic dermatomyositis

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ABSTRACT

Clinically amyopathic dermatomyositis (CADM) is a rare condition characterized by dermatomyositis skin lesions without clinically apparent muscle involvement. Respiratory involvement is common, occurring in about half of the cases. Spontaneous pneumomediastinum (PnM) is a rare, and often fatal, complication of CADM. We report a case of a 61-year-old female patient who was diagnosed with anti-melanoma differentiation-associated gene 5 antibody-associated CADM and interstitial lung disease. She developed an extensive spontaneous PnM with subcutaneous emphysema. The patient was treated with a conservative approach which was, initially, successful in reducing the size of the PnM. However, the patient died from an eventual nosocomial pneumonia requiring mechanical ventilation. This case illustrates that improving the management of CADM associated PnM, remains a major unmet need.

Keywords: Myositis; Muscle disease.

INTRODUCTION

Clinically amyopathic dermatomyositis (CADM) is a rare rheumatic and musculoskeletal disease (RMD) characterized by skin lesions, such as heliotrope rash and Gottron´s papules, without clinically apparent muscle involvement[1,2]. CADM corresponds to approximately 20% of all cases of dermatomyositis[3]. Respiratory involvement occurs in about half of the cases. Rapidly progressive interstitial lung disease (ILD) is the most common form of respiratory involvement, which is strongly associated with the presence of the anti-melanoma differentiation-associated gene 5 antibody (anti-MDA5) and with a worse prognosis. Spontaneous pneumomediastinum (PnM), pneumothorax and subcutaneous emphysema are rare and often fatal complications of CADM-associated lung disease[1,2,4]. So far, there is no consensus for the management of PnM associated with CADM or any other RMDs. Herein we report the case of a patient recently diagnosed with CADM with positivity for anti-MDA5 and with ILD complicated by PnM with subcutaneous emphysema.

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CASE REPORT

A 61-year-old non-smoker black female patient, with a five-year history of asymmetric additive polyarticular joint pain and with Gottron papules on the metacarpal and proximal interphalangeal joints was evaluated in our department. She had also a 6-month history of non-productive cough, fatigue and dyspnoea for moderate efforts. On physical examination she did not have arthritis. She had bilateral velcro crackles in the lower third of the thorax. The muscle strength was normal (manual muscle testing - MMT-8: 150/150) as were the muscle enzymes (creatine kinase: 26 IU/l), liver enzymes (aspartate aminotransferase: 16 IU/l, alanine aminotransferase: 20 IU/l) and lactate dehydrogenase (192 IU/l) values. The HEp-2 immunofluorescence assay was positive for antinuclear antibodies (cytoplasmic fine speckled, weak positive value: 1/160) and for anti-MDA5 and negative for extractable nuclear antigens as well as for other inflammatory myopathies antibodies, tested with the immunodot assay. The patient did not have any vascular symptom. A ground glass pattern and organizing pneumonitis on chest high-resolution computed tomography (HRCT) was compatible with a nonspecific interstitial pneumonia (NSIP). Pulmonary function tests showed a moderate restrictive respiratory pattern (decreased total lung capacity of 3.0 l, 61% of the predicted value and a normal forced expiratory volume to forced vital capacity ratio) and moderate decreased diffusing capacity of the lung for carbon monoxide (DLCO), 45% of the predicted value, with hypoxemia at rest.

The diagnosis of CADM with ILD was made and the screening for an underlying malignancy was negative.

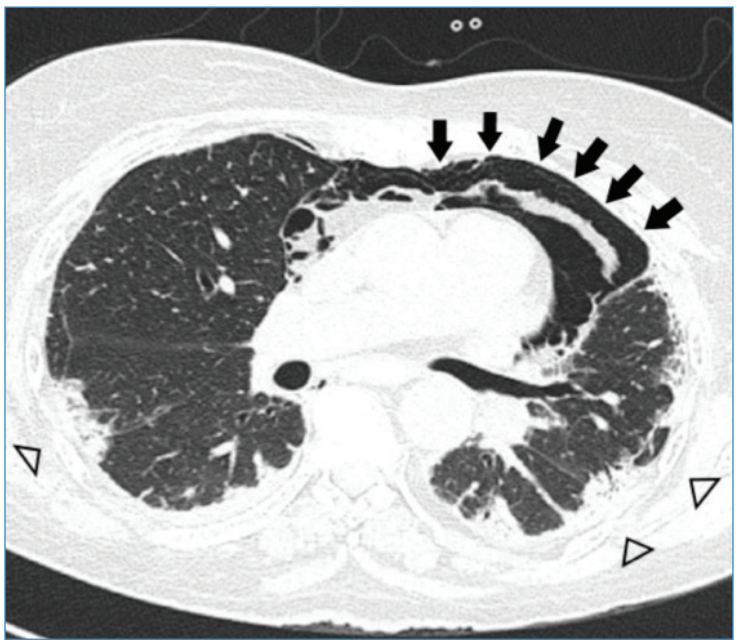

Figure 1. Axial image of chest computed tomography showing interstitial peripheral lesions, irregular thickening of pulmonary septum and ground glass pattern areas compatible with a nonspecific interstitial pneumonia - NSIP (arrow heads). Pneumomediastinum (black arrows).

Treatment with mycophenolate mofetil (MMF) 1500 mg/day, prednisolone (PDN) 1 mg/kg/day and oxygen therapy (2 l/min for 16 hours per day) was started. Four months later, when PDN had already been tapered to 30 mg/day, she complained of insidious onset of severe dysphagia for solids and liquids. An upper digestive endoscopy revealed esophageal candidiasis which was successfully treated with intravenous fluconazole 400 mg/day for 2 weeks. Six days after the endoscopic procedure, the patient complained of moderate chest pain with accompanying cervical and upper thoracic subcutaneous emphysema. She had no fever and no elevation of inflammatory markers. An urgent thoracic HRCT scan revealed an extensive PnM without pneumothorax (Figure 1). A ventilation/perfusion scintigraphy identified a possible leak at the level of the posterior wall of the trachea, which was not confirmed by bronchoscopy. In addition, no evidence supporting paraesophageal infectious collections or an esophagus perforation was found in the chest HRCT performed with oral iodinated contrast. All blood and bronchoalveolar fluid cultural exams were negative.

Despite the extensive PnM, the patient remained asymptomatic under treatment with continuous oxygen and bronchodilators. Bed rest was needed as any effort resulted in a decline of the oxygen saturation as a consequence of an increase of the PnM. Even though she was receiving enoxaparin in prophylactic dose, the patient suffered an acute pulmonary thromboembolism, due to long-term immobilization, which resolved with enoxaparin in therapeutic dose and supplementary oxygen. For treating the PnM, neither a surgical procedure nor a transthoracic drainage was considered in a multidisciplinary meeting due to the absence of pneumothorax. For the CADM, the dose of MMF was increase to 2000 mg/day, approximately 5 months after initiation, with a deescalating dose of PDN up to 25 mg/day. Upon discharge, the patient was under 4 l/min of continuous oxygen therapy and was already able to walk short distances without desaturating and could perform physical therapy in order to prevent muscle atrophy.

The chest HRCT performed 4 months after the onset of the PnM (Figure 2A) shows a marked reduction of its dimensions and absence of subcutaneous emphysema. However, multiple dispersed interstitial peripheral lesions and ground glass pattern areas were still evident, especially in the lower lung lobes. Five months after the diagnosis of PnM, the patient was hospitalized due to emphysematous cystitis. Later, the patient developed hypoxemic nosocomial pneumonia, requiring broad spectrum antibiotics. Despite invasive ventilation, the patient showed progressive worsening of respiratory failure as a consequence of an increase of the PnM (Figure 2B), which resulted in her death 6 months after the initial diagnosis.

DISCUSSION

PnM is a rare complication of RMD-associated lung disease. In patients with CADM, it usually occurs within one year after the diagnosis and is rarely the presenting

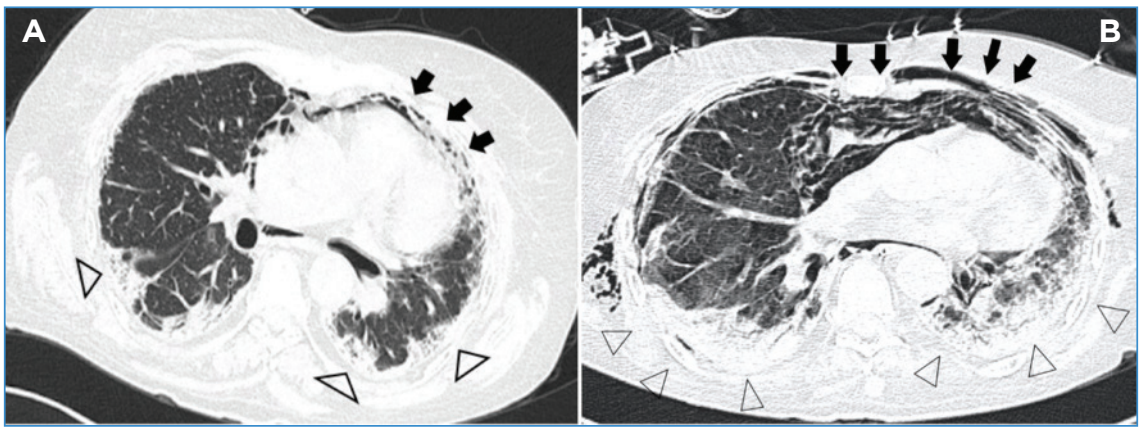

Figure 2. A) Axial image of chest computed tomography 4 months after pneumomediastinum (PnM) diagnosis with a significant reduction of the size of the PnM (black arrows). NSIP (arrow heads). B) Axial image of last performed chest computed tomography 6 months after pneumomediastinum (PnM) diagnosis with a significant worsening of parenchymal lesions and consolidation areas (arrow heads). It is also evident an increase in the size of the PnM (black arrows) and subcutaneous emphysema.

manifestation[4,5]. The mortality rate is high, with one in each four patients dying within one month[1]. Patients with dermatomyositis have a particularly high risk of PnM (prevalence of 2.2 to 8.3%), with more than half of the cases occurring in patients with CADM[2,5-7]. Positivity for anti-MDA5 is a risk factor for PnM[7,8]. Interestingly, MDA-5 antibodies often present with negative antinuclear antibodies.

The mechanism underlying spontaneous PnM remains largely unknown. One hypothesis holds that PnM results from the rupture of subpleural bullae that form due to an increase in intra alveolar pressure driven by interstitial fibrosis. This, in theory, can lead to dissection of air around perivascular sheaths and into the mediastinum through the so-called Macklin effect[2,6,7,9,10]. The development of either pneumothorax and/or PnM probably depends on the location of the rupture (peripheral for pneumothorax and adjacent to vessels for PnM)[11]. Systemic glucocorticoids (GCs) also seem to predispose to PnM through the weakening of pulmonary alveoli wall[2,7]. MDA-5 antibodies are often associated with vasculitic lesions of the skin and it is though that bronchial necrosis due to vasculopathy could be another explanation to CADM-associated PnM[12].

The evidence supporting the efficacy of interventions for PnM associated with CADM is yet scarce. Supportive measures, including bed rest, oxygen and analgesic therapy are often prescribed for the PnM as in our case. Cozzani *et al.* reviewed 55 cases of CADM with pulmonary involvement and reported that high doses of systemic GCs and immunosuppressive agents, such as MMF can be effective if initiated early[1,13]. In theory the use of these drugs to treat rapidly progressive ILD could reduce the risk of complications such as PnM as suggested by previous case reports[1,13].

The role of systemic GCs is less clear. On one hand GCs might weaken the alveoli wall and consequently predispose to PnM. On the other hand, they are, as mentioned above, often and successfully used a first-line therapy in rapidly progressive ILD, especially if poor prognosis risk factors are present (anti-MDA5 positivity, muscle weakness absence, decreased vital capacity and DLCO)[1,2]. Surgical interventions have been rarely described in cases of PnM, with only a few successful case reports of percutaneous decompression[14].

Unfortunately, our patient was under-treated with MMF before being referred to our department. In our case we opted for not increasing the dose of GCs. We did, however, increase the dose of MMF to 2000 mg/day which was followed by a reduction of the PnM. Even though this improvement happened after MMF dose increase, it is unlikely due to MMF, given its slow therapeutic effect. Besides, the follow-up HRCT did show a worsening of parenchymal lesions and a major increase in the dimensions of the PnM. Whether or not the new increase in the size of the PnM could have been a consequence of mechanical ventilation remains uncertain.

There is an urgent need of high quality evidence informing the management of PnM associated with RMDs. Even though this is a rare complication, it is often fatal especially in patients with bad prognosis factors as the one reported here.

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