

Clinical case

Pneumomediastinum and diffuse alveolar pain. Severe interstitial pneumopathy due to dermatomyositis

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ARTICLE INFO

Article history:

Received March 11, 2008

Accepted September 4, 2008

Keywords:

Dermatomyositis

Pneumomediastinum

Subcutaneous emphysema

ABSTRACT

We have recently observed the case of a 36-year-old man with dermatomyositis of recent onset, who developed massive pneumomediastinum and subcutaneous emphysema at the onset of a progressive and severe pulmonary disease. Although there were no sign of parenchymal cysts, after the bronchoscopy it was possible to observe endobronchial necrotic injury, which was considered as the likely source of the air leak. He was treated with high dose of corticosteroids, cyclophosphamide and cyclosporin A that resulted in the disappearance of the pneumomediastinum and subcutaneous emphysema and the progressive improvement of both parenchymal lung disease and respiratory insufficiency, enabled us to progressively taper the dose of corticosteroids.

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Neumomediastino y daño alveolar difuso. Afección pulmonar severa por dermatomiositis

RESUMEN

Presentamos el caso de un varón de 36 años con dermatomiositis de reciente comienzo, que desarrolló neumomediastino y enfisema subcutáneo masivo al inicio de una neumopatía intersticial progresiva y severa. En el momento del diagnóstico no había imágenes parenquimatosas quísticas evidentes; sin embargo, la broncoscopia permitió evidenciar una lesión endobronquial de aspecto necrótico que se consideró como probable origen de la fuga aérea. El paciente se trató con corticoides a dosis altas, ciclofosfamida y ciclosporina A, con resolución del neumomediastino y del enfisema subcutáneo. Con el tratamiento se observó una mejoría progresiva de la afección parenquimatosa pulmonar y de la insuficiencia respiratoria, lo que permitió la disminución progresiva de los corticoides.

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Palabras clave:

Dermatomiositis

Neumomediastino

Enfisema subcutáneo

Introduction

Spontaneous pneumomediastinum (SP) is a clinical entity of unknown origin and a benign progression which affects young individuals. It usually resolves in the course of a few days with conservative treatment. It occasionally produces an alveolar rupture as a result of parenchymal peripheral affection in interstitial disease

that produces peripheral honeycombing, as occurs in dermatomyositis, associated frequently to the amyopathic presentation. Lung affection in these cases can be specifically severe, with an elevated mortality that is only reduced if potent immunosuppressive treatment is installed at an early stage.

Clinical case

A 36-year old male with no particular history of interest presented fever, erythematous, and desquamative skin lesions on the face, hands and elbows as well as hair loss and weakness with considerable weight loss. Laboratory testing revealed a normal

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hemogram and an erythrocyte sedimentation rate of 20 mm for the first hour (normal, 0–10). Biochemistry determinations that included creatinphosphokinase (CPK), lactate dehydrogenase (LDH), aldolase, THS, proteinogram, immunoglobulin, complement, tumor markers, CRP, coagulation, and urine testing were normal. The immunology studies showed: ANA+ 1/320. The rest of the determinations, including anti-dsDNA, ENA, AMA, ASMA, ANCA, rheumatoid factor, and anticardiolipin were negative.

The patient was diagnosed with systemic lupus erythematosus (SLE) and treatment was begun with hydroxicloroquine 200 mg TID and prednisone 30 mg daily, with marked improvement of the skin lesions on the face and scalp, a reduction in hair loss and the constitutional symptoms.

He comes into the emergency room 6 months later presenting hoarseness, increase in the neck diameter and crepitus sensation. He referred neither previous trauma nor other respiratory or digestive symptoms. Upon physical examination he presented: fever (37.5°C); heart rate, 105 beats/min; normal respiratory rate and blood pressure (BP). Pulse oximetry showed normal oxygen saturation. No finger deformity or skin vasculopathy was seen. Skin lesions compatible with Gottron's papules were found on the hands and elbows as well as subcutaneous emphysema on the face, neck, trunk and upper extremities. The rest of the examination showed no alterations. A chest x-ray and thoraco-abdominal computed tomography (CT) showed pneumomediastinum, pneumorrhachis, extensive subcutaneous emphysema, a small bilateral apex pneumothorax, and bilateral mild lung parenchymal affection with a peripheral distribution (Figure 1). In addition, an esophagogram, bronchoscopy, electrocardiogram, and echocardiogram were performed and found normal. No functional lung study was performed due to the risk that the thoracic hyperpressure technique involved. A magnetic resonance (MR) of the pelvis and muscles showed bilateral, symmetric perifascial fluid affecting the semimembranosus, vastus lateralis, and rectus anterioris muscles, without evidence of muscle edema. An electromyogram (EMG) showed spontaneous, sporadic activity with motor unit potentials of myopathic aspect in the proximal muscles of the upper and lower extremities.

Conservative treatment based on 30 mg prednisone in a descending dose was installed. After reducing the dose of prednisone to 15 mg/day, the subcutaneous emphysema and fever (38.5–39°C) increased and there was a progressive gasometrical deterioration, which merited oxygen treatment at an elevated FiO₂. A new chest CT manifested extensive mediastinal, subcutaneous,

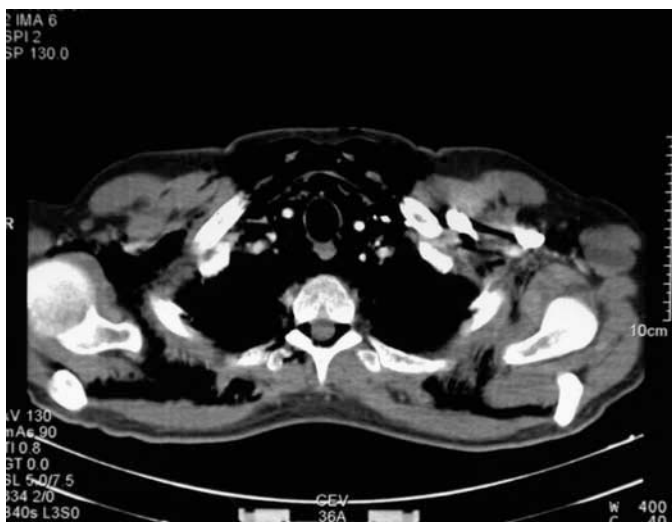


Figure 1. Pneumomediastinum with extensive emphysema.



Figure 2. Interstitial lung disease with bilateral "honeycombing."

subpleural and cervical emphysema, lung fibrosis and areas with a "ground-glass" appearance in the left inferior lung lobe parenchyma. A search for possible foci of infection was carried out and turned out negative. A bronchoscopy found a necrotic lesion in the intermediate bronchi. This lesion was considered to be the origin of the pneumomediastinum.

The patient was treated with oxygen and ample-spectrum antibiotics (piperacyllin-tazobactam and clarytromicine) without remission of the fever. With the diagnosis of dermatomyositis and spontaneous pneumomediastinum secondary to interstitial lung disease and after ruling out a concomitant infection, treatment with high-dose steroids (3 pulses of 1000 mg methylprednisolone followed by 2 mg/kg/day of prednisone), and intravenous cyclophosphamide (CFM) at a dose of 750 mg/m² (6 monthly pulses and then 6 trimestral pulses). In addition, prophylaxis for *Pneumocystis carinii* was performed. At 2 months, after an initial clinical and radiological improvement, fever reappeared and led to radiological and gasometrical worsening, obliging treatment with cyclosporine A (CyA) at a dose of 5 mg/kg/day. After 1 month of combined therapy, the patient experimented slow but progressive improvement, both clinical and radiological, with disappearance of the emphysema and pneumomediastinum, as well as of the skin lesions and the muscle weakness.

After 9 months of immunosuppressive treatment (trimestral pulse CFM, CyA at a dose of 5 mg/kg/day and steroids in a diminishing dose), there was no recidivating pneumomediastinum, the patient remained stable and was able to walk again. Arterial blood gases showed PO₂ 60 mm Hg and PCO₂ 37 mm Hg, 91% oxygen saturation. Respiratory function tests revealed a restrictive pattern with a reduction in the lung diffusion of oxygen. There was extensive bilateral honeycombing on the (Figure 2), with the disappearance of the ground glass lesions. Because of the severity of the residual lung alterations and the stability of the radiological images, the patient was sent to a hospital of reference in order to evaluate lung transplantation.

Discussion

Spontaneous pneumomediastinum is a clinical entity of unknown origin and benign progression that affects young individuals and is resolved in a few days with conservative treatment. The most probable cause is the rupture of the alveolar walls caused by thoracic hyperpressure maneuvers, with the consequential escape of air into the interstitium and a further centripetal dissection along the bronchovascular sheaths until it reaches the mediastinum through the hyllum.

Table
Current recommendations for the treatment of interstitial lung disease

Clinical progression	Histology	Treatment
Localized. Non progressive. Asymptomatic Chronic	UIP	Postpone According to ATS/ERS guidelines. Prednisone 0.5 mg/kg/day+AZA 1–2 mg/kg/day or CFM (can try CyA or tacrolimus)
Acute or subacute (including exacerbation of chronic ILD) DAD	COP (or suspicion after high resolution CT) High dose steroid* + pulse IV CFM + CyA or tacrolimus	High dose steroid
Acute or subacute	NSIP (predominantly cellular)	High dose steroid* + CyA or tacrolimus+CFM if unresponsive
NSIP (predominantly fibrosis)	High dose steroid* + IV pulse CFM+CyA if unresponsive	

Abbreviations: ATS, American Thoracic Society; AZA, azathioprine; CFM, cyclophosphamide; CyA, cyclosporin A; DAD, diffuse alveolar damage; NSIP, non specific interstitial pneumonia; UIP, usual interstitial pneumonia; COP, cryptogenic organizing pneumonia; CT, computerized tomography.

* Once CFM and CyA are combined, doses of steroid should be reduced as rapidly as possible to reduce the risk of severe infectious complications.

Occasionally, alveolar rupture can occur during an attack of asthma or as the result of a peripheral parenchymal affection of interstitial processes that lead to honeycombing. Among these latter cases, an association with dermatomyositis and polymyositis has been described, which in some cases can also be accompanied by necrotizing tracheobronchial lesions of a vasculitic nature that lead to perforation and constitute the origin of air leakage into the mediastinum.¹

Dermatomyositis is a connective tissue disease with a predominant affection of the skin and muscles, although the lung is affected in 5%–40% of cases,^{1,2} in the form of interstitial lung disease (ILD),^{3,4} with 4 clinical forms, each with a different underlying histology:

- Asymptomatic, diagnosed only through radiological or functional studies.
- Cryptogenic organizing pneumonia (COP).
- Interstitial lung disease with slow progression and occasional exacerbation. The underlying histology is usually non-specific interstitial pneumonia (NSIP).
- Acute-subacute interstitial pneumonia, with a rapidly progressive deterioration, usually exhibiting a biopsy with a diffuse alveolar damage pattern (DAD).

Spontaneous pneumomediastinum is a rare complication of dermatomyositis,⁴ with an incidence of 2/100 000, but frequently accompanying those cases with a greater clinical aggressiveness. Eighty-eight per cent of cases are present in patients under 40 years of age and occasionally can be complicated with spontaneous pneumothorax.⁵ The profile of the patient at risk for the appearance of SP has been described. They are usually young,¹ with recent-onset disease,² interstitial lung disease,⁷ skin vasculopathy (nail infarcts, erosive/ulcerative lesions on the tip of the fingers),¹ mild or no elevation of CPK,⁶ and receiving treatment with steroids.^{1,7} Our patient, with the exception of the skin vasculopathy, had all of these risk factors.

The presence of anti-Jo-1 antibodies increases the risk of interstitial lung disease in patients with dermatomyositis. This antibody is present in 20% of cases and in 70% of patients with interstitial lung disease; it is usually negative in amyopathic dermatomyositis, even when interstitial lung disease is present. Other potential markers for dermatomyositis are KL-6, anti-ADAM 10, D protein of serum surfactant and PL12.¹³

It has been proposed that the appearance of SP could be due to a hypothetical weakening of interstitial lung tissue due to treatment with steroids,⁷ although for most authors, the true cause would be the severity of the interstitial affection itself. In any way, the absence of this affection in some cases of SP leads to the postulation of other pathogenic hypothesis,^{1,6,8} among which would be the perforation

of necrotic tracheobronchial lesions of a vasculitic nature, as was described above.^{1,2}

The therapeutic management of the cases of dermatomyositis and polymyositis with lung affection varies according to their severity. The treatment decision is based always on the extension and speed of progression of the disease.

In the case of localized, non progressive and asymptomatic disease, treatment should be postponed.

In the case of chronic interstitial lung disease with a histology suggestive of usual interstitial lung disease (UIILD), according to the proposal of the ATS/ERS⁹, treatment with prednisone 0,5 mg/kg/day and azathioprine 1–2 mg/kg/day or cyclophosphamide is suggested (although cyclosporine A or tacrolimus can be considered also).

In the case of acute-subacute interstitial lung disease with NSIP histology (cellular predominance), the treatment suggested is high dose steroids, cyclosporin A or tacrolimus and cyclophosphamide (if unresponsive to the first ones).

In the case of acute-subacute interstitial lung disease with organizing pneumonia histology, treatment suggested is high-dose steroids.

In the case of acute-subacute interstitial pneumonia with DAD histology, suggested treatment is pulse cyclophosphamide and cyclosporin A or tacrolimus.

Once cyclophosphamide and cyclosporin A have been combined, steroids should be reduced as rapidly as possible in order to reduce the risk of serious infectious complications. Current treatment recommendations are summarized in Table.

The experience with cases of dermatomyositis presenting SP is scarce, with only 42 cases described^{1,2,9,12} treated with high dose steroids by themselves (22 patients with a mortality >50%) or in combination with different immunosuppressive agents, which show a clearly superior response during progression.

Conclusions

The appearance of SP in a patient with a collagen-related disease must always alert the clinician to the possibility of dermatomyositis with severe lung parenchyma disease. In spite of the limited number of cases described and that in other studies the progression has been favorable,⁴ given the poor prognosis faced by patients with dermatomyositis, interstitial lung disease and pneumomediastinum,^{9,10} control of disease activity is recommended with intense and early immunosuppressive treatment, in this case, intravenous CFM and oral CyA, after ruling out infectious causes and with a progressive reduction of steroids. Treatment in this case has been effective, with a resolution of the pneumomediastinum in 3 months and a clinical improvement at 5 months, corroborating the results of other studies.^{10,11}

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