that showed that 10–30% of SS patients suffer from ATD [3, 4]. However, most of these results had been published before the AEC for SS were established. Two of the largest studies used European Classification Criteria (ECC) for SS. In one of the studies, the prevalence of ATD in SS patients was 20% [5]. Another follow-up study found ATD to be more frequent in the SS patients than in the controls (30% vs 4%) [6]. AEC were used to diagnose SS. They found that the prevalence of ATD was 10%. We found a significantly higher prevalence of ATD in sicca subjects than in SS patients and HS (P < 0.01). Although ATD is a common diagnosis in clinical practice, the prevalence of ATD is not known in our country. On the other hand, we found no difference in the frequency of clinical features of sicca syndrome between SS patients with ATD and sicca subjects with ATD (P > 0.05). Based on similar clinical findings, ATD could be misdiagnosed as SS, and vice versa. Therefore the symptoms of dryness should always be given serious consideration as possible signs of either SS or ATD (sometimes both). High prevalence of ATD in sicca subjects suggests that all subjects with sicca symptoms should be screened for ATD.

Rheumatology key message

- Prevalence of ATD is high in subjects with sicca symptoms without SS.

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come up represent an interesting point of discussion. In this clinical case report, we present a patient with coexistence of A1ATD and granulomatosis with polyangiitis and discuss the role that A1AT replacement therapy could play in such patients [6].

An 84-year-old woman with a history of arterial hypertension and ischaemic cardiopathy had presented two years earlier with an air flow limitation and a predicted forced expiratory volume in 1 second (FEV1) of 63%. Computed axial tomography was consistent with pulmonary emphysema. Further evaluation revealed the patient to have a severe A1ATD, which was associated with a PiZZ genotype. At that time, the patient declined replacement therapy.

The patient subsequently was admitted to the emergency unit with a 4-week illness characterized by malaise, arthralgia and anorexia. On physical examination, mild signs of dehydration and several skin lesions on the trunk and limbs (purpuric macules, some of them palpable, of several days of evolution) were observed.

Laboratory evaluation revealed evidence for renal dysfunction [blood urea nitrogen (BUN) = 160 mg/dl, creatinine = 4 mg/dl, urine sediment, haematuria and proteinuria], anaemia (haemoglobin = 11.7 g/dl) and moderately elevated CRP (11 mg/dl). Thorax radiograph revealed the presence of a parenchymal infiltrate and pleural effusion. The presence of acute renal failure together with skin lesions and the suspicion of a rheumatological disease led to further immunological evaluation (ANCA-MPO = 1.3 U/ml, ANCA-PR3 > 100 U/ml, C3 = 132 mg/dl, C4 = 29.5 mg/dl and negative ANA, anti-DNA, anti-RNP, anti-SCL70, anti-Jo1, anti-Sm, anti-Ro and anti-La). Other causes accountable for the observed acute renal impairment were ruled out during the hospital stay. A biopsy of the skin lesions revealed cutaneous and subcutaneous haemorrhage with necrosis and acute inflammation and vascular thrombus suggesting vasculitis (Fig. 1). In the light of all these findings, granulomatosis with PR3-positive microscopic polyangiitis was diagnosed.

Because of the patient’s renal function impairment, it was decided to start therapy with i.v. methylprednisolone (250 mg/24 h for 3 consecutive days). There was subsequent improvement in the patient’s renal function (creatinine = 2.8 mg/dl) and normalization of the thorax radiograph. During the next month, oral prednisone was administered (1 mg/kg, tapering off to 10 mg/24 h). Subsequent analysis showed decreased ANCA-PR3 (<10 U/ml) and CRP (~0 mg/dl). Because of the patient’s age and associated medical history, we decided to avoid cyclophosphamide in favour of therapy with glucocorticoids and replacement therapy with A1AT (Trypsone; Grifols Institute, Barcelona, Spain) at 60 mg/kg/weight weekly. This treatment resulted in a notable improvement of the skin lesions and normalization of renal function. At the present time, the patient is still alive and continues to receive the replacement therapy. She has not suffered a recurrence of granulomatosis with polyangiitis vasculitis and has stable respiratory function.

Several studies reveal a strong association of granulomatosis with polyangiitis with A1ATD [7–10]. This association, together with the fact that replacement therapy with A1AT has been effective in our patient, further indicates that an absolute or relative A1ATD plays a contributory role in many granulomatosis with polyangiitis cases.

It is known that up to 95% of granulomatosis with polyangiitis cases present positive with ANCAs when the disease is active, and that the principal inhibitor of PR3 in humans is A1AT [11, 12]. It has also been demonstrated that in patients with active granulomatosis with polyangiitis, A1AT levels are high in response to the increase in PR3 [13, 14] and decrease when the acute phase remits. However, this response to an increase in PR3 would be attenuated in the presence of a deficient SS, SZ or ZZ phenotype, supporting the observation that granulomatosis with polyangiitis is exacerbated in patients with A1ATD [13, 15, 16] as a result of an imbalance between active PR3 and A1AT [13]. Thus, A1ATD is not

Fig. 1 Skin biopsy of the limb lesions.

A vessel that has lost its normal structure, with symptoms that suggest vasculitis, such as deep necrosis, acute inflammation and thrombosis, can be observed.
only a risk factor for the development of granulomatosis with polyangiitis but also potentially a prognostic marker of its severity. Therefore, it seems reasonable to posit that A1ATD represents an important pathophysiological contributor to the development of granulomatosis with polyangiitis, and that replacement therapy for A1ATD patients could be of benefit via restoration of the protease–A1AT balance. We believe the present case supports this hypothesis.

Rheumatology key message

- An A1AT-deficient patient with lung damage who developed granulomatosis with polyangiitis-like vasculitis resolved with A1AT replacement therapy.

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