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Case Report

Cytoplasmic anti-neutrophil cytoplasmic antibodies (c-ANCA) in systemic lupus erythematosus: An overlapping syndrome?

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Systemic lupus erythematosus (SLE) and small-sized vessel vasculitis are usually two distinguishable autoimmune diseases. We report a case of novo SLE associated with cytoplasmatic antineutrophil cytoplasmatic antibodies (c-ANCA). A 34-year old woman was admitted to our hospital for purpura, weight loss, inflammatory polyarthralgia and nasal stuffiness with advanced renal failure. The investigations have revealed positive immunological test (ANN, anti-DNA and c-ANCA). Renal biopsy showed a diffuse proliferative lupus nephritis (class IV-G (A)) with necrotizing crescentic glomerulonephritis. We have retained the diagnosis of SLE associated to c-ANCA. She has received corticosteroids and cyclophosphamide. The evolution was marked by the occurrence of alveolar hemorrhage that caused her death.

Key words: Cytoplasmic anti-neutrophil cytoplasmic antibodies, systemic lupus erythematosus, overlapping syndrome, alveolar hemorrhage, necrotizing crescentic glomerulonephritis.

INTRODUCTION

Systemic lupus erythematosus(SLE) and small-sized vessel vasculitis are usually two distinguishable autoimmune diseases(1). Vasculitis may be found in the course of SLE but rarely corresponds to an ANCA-associated vasculitis (AAV). Anti-neutrophil cytoplasmic antibodies (ANCA) are a heterogeneous group of autoantibodies with a broad spectrum of clinically associated diseases (2). The antineutrophil cytoplasmic antibodies (ANCA) with specificity for proteinase-3 (PR3) are associated with Wegener's granulomatosis, now known as granulomatosis with polyangiitis (GPA). The ANCA directed to myeloperoxidase (MPO) are associated with other idiopathic vasculitides (3).

We report case of a patient having SLE associated to c-ANCA. Our aim is to discuss clinical significance of this association.

Case Report

A 34-year old woman, without a medical history. She presented to our hospital with four weeks history of malaise, weight loss, nasal stuffiness, and oliguria. She complained of headaches which were bifrontal, pressing in nature without blurring of vision or any focal neurological symptoms. Two weeks before her admission to our service, she has developed inflammatory polyarthralgia associated with purpura extended at lower limbs and back, nausea, and vomiting. She has also complained of oral ulcers and fever without chills.

On examination, she was conscious and distorted, blood pressure was 140/70 mmhg, pulse was 80 beats/min, respiratory rate was 25b/min, and weight was 50kg. She was afebrile, oliguric(500cc/24H). Urinalysis showed blood (3+) and protein (3+).

She had an edema of lower limbs, purpura, and an extensive hyperpigmented rash over the face and the neck. Pulmonary auscultation and neurological test were normal.

On initial evaluation, kidney function included a serum creatinine level more than 1000µmol/l, and blood urea nitrogen at 8.4 mg/dl. Sodium was at 133 mEq/L, potassium at 4.9 mEq/L, chloride at 102 mEq/L, CO2 at 18mEq/L, glucose was at 93 mg/dl, calcium at 7.5 mg/dl.

Proteinuria was at 2g/day with microscopic hematuria.

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Table 1. Clinical data.

Initial symptoms	Inflammatory polyarthralgia, purpura, oral ulcers, nasal stuffiness, oliguria, malaise, weight loss, fever.
Clinical findings	edema of lower limbs, purpura, extensive hyper pigmented rash over the face and the neck
	Urinalysis: blood (3+) and protein (3+).
Initial laboratory values	Creatinine:1000µmol/l, urea nitrogen : 8.4 mg/dl
	Proteinuria: 2g/day with microscopic hematuria.
	Hemolytic anemia and leucopeniawithout thrombocytopenia
autoantibodies	ANA: 1/320, antiDNA: 140.
	c-ANCA (antiPR3) positive, p-ANCA negative
Initial investigations	rhinoscopic examination : mouth ulceration.
	The Chest x-ray :normal
histology	lupus nephritis class IV-G (A) with necrotizing crescentic glomerulonephritis
Treatment	intravenous methylprednisolone and cyclophosphamide

She had an hemolytic anemia at 10g/dl and leucopenia at 3000 per cubic millimeter without thrombocytopenia.
Hepatitis B and C serology were negative, procalcitonin was also negative. C3 level was low.
Immunological test was positive (Antinuclear antibody (ANA) was at 1/320 and anti–double-stranded (anti DNA) was at 140(negative< 20iu/ml)).

c-ANCA was also positive, while p-ANCA was negative. The ANCA anti-proteinase 3 (anti-PR3) were detected by ELISA. Cryoglobulin test was negative.

The rhinoscopic examination has only showed mouth ulceration.The Chest x-ray was normal.

Kidney failure was explored by the realization of renal biopsy, which revealed a diffuse proliferative lupus nephritis (class IV-G (A)) with necrotizing crescentic glomerulonephritis, fibrinoid necrosis, glomerular basement membrane rupture, endocapillary and extracapillary fibrin. There were global glomeruli deposits of C3, C1q, C4 and IgG, IgM on immune fluorescence.

Diagnosis of lupus has been retained according to criteria of American College of Rheumatology. SLE disease activity (SLEDAI) was 21 at the time of admission.
In our case, diagnostic of SLE associated to c-ANCA was retained because of the presence of varied clinical symptoms and the presence of positive immunological test (ANN, anti-DNA and c-ANCA).

She was emergency pulsed with intravenous methylprednisolone 1 gram daily for 3 days, and subsequently oral prednisolone 60 mg/day. She has received also bolus of cyclophosphamide. In parallel, she has required hemodialysis for advanced renal failure (Table 1).

After 2 weeks of hospitalization. She has presented diffuse alveolar hemorrhage confirmed at CT scan**,** infectious test performed was negative. The evolution was marked by her death before any treatment.

DISCUSSION

Antineutrophil cytoplasmatic antibodies (ANCA) are a group of autoantibodies found in several inflammatory disorders (4). They are directly implicated in the pathogenesis of pauci-immune crescentic GN and pauci-immune small-vessel vasculitis(5). Two different ANCA subtypes have been recognized c-ANCA and p-ANCA. C-ANCA mainly reacts with a serine proteinase called proteinase-3(PR3), and p-ANCA mainly reacts with myeloperoxidase (MPO).

Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease with involvement of predominantly small-sized blood vessels in a variety of organ systems (6). The auto antibodies classically associated with SLE are anti-double-stranded (anti-DNA), anti-Sm and anti-histone antibodies, ANCA have been described as well.
The prevalence of ANCA is reported to be as high as 31% in lupus patients.

The presence of ANCA in patients with SLE has been demonstrated by many studies, but only p-ANCA antibodies were present in these patients(7,8,9).

In our case several clinical, histological and immunological features support the hypothesis of the existence of SLE- cANCA overlapping syndrome. In literature, few studies have shown the association of lupus with cANCA. Chin et al. (2000) (10) have examined 51 patients in South Korea with LN. They have found ANCA positivity by IIF in 37.3% of these patients, including p-ANCA in 31.4% and c-ANCA in 5.9%. Other study of 21 children with lupus has shown that only two children had c-ANCA positive (11). Another case report of this association was published by Dafina B (2004)(12). All these studies suggest that MPO is a rare antigen for ANCA in LN.

The pathogenesis of LN associated to c-ANCA is not clear (13), LN is generally regarded as a classic immune

complex GN. Several investigators have suggested the possibility of a pauci-immune mechanism in subgroup of LN IV and LN III with extensive segmental necrosis and crescent formation. But ANCA testing was not performed in any of these series (14,15). Etiopathogenic mechanisms of such an association remains to be more precisely described.

Alveolar hemorrhage leading to respiratory failure is uncommon. Various vascularitis have been reported, which is generally presented as pulmonary-renal syndrome (16).

Diffuse alveolar hemorrhage is an uncommon but lethal complication of SLE, with higher mortality rates between 70 and 90 % (17). In our case both severe lupus and c-ANCA may contribute to the onset of alveolar hemorrhage.

CONCLUSION

The role of c-ANCA in SLE has no demonstrable significance. Etiopathogenic mechanisms of such an association remainsto be more precisely described.

In our study, several clinical, histological and immunological features support the hypothesis of the existence of a SLE-cANCAoverlapping syndrome.

Clinicians must be aware of such an overlapping syndrome, notably because its initial presentation can be very severe.

REFERENCE

Bakkaloglu A, Topaloglu R, Saatçi U(1998). Antineutrophil cytoplasmic antibodies in childhood systemic lupus erythematosus. Clin Rheumatol. 17: 265-7.

Bar J, Ehrenfeld M, Rozenman J (2001). Pulmonary-renal syndrome in systemic sclerosis. Semin. Arthritis. Rheum. 30: 403-10.

Bartunkova J, Tesar V, Sediva A (2003). Diagnostic and pathogenetic role of antineutrophil cytoplasmic autoantibodies. Clin-Immunol. 106: 73-82.

Charney DA, Nassar G, Truong L (2000). Pauci- Immune proliferative and necrotizing glomerulonephritis with thrombotic microangiopathy in patients with systemiclupus erythematosus and lupus-like syndrome. Am. J. Kidney. Dis. 35: 1193–1206.

Chin HJ, Ahn C, Lim CS (2000). Clinical implications of antineutrophil cytoplasmic antibody test in lupus nephritis. Am. J. Nephrol. 20: 57–63.

Dafina B Kuzmanovska, Emilija M Sahpazova (2004). Renal infarction in a child with systemic lupus erythematosus.Pediatric Nephrology.19: 685-687

Falah S, Husam M (2009). Frequency of Antineutrophil Cytoplasmic Antibodies (ANCA) in some Autoimmune Diseases Abbas Iraqi J. Pharm. Sci. 18(2): 423-8. suppl.

Hervier B, Hamidou M, Haroche J, Durant C, Mathian A, Amoura Z (2012). Systemic lupus erythematosus associated with ANCA-associated vasculitis Rheumatology International. 32: 3285-3290.

Hill GS, Delahousse M (2005). Class IV-S versus class IV-G lupus nephritis: Clinical and morphologic differences suggesting different pathogenesis. Kidney. Int. 68: 2288–2297.

Hill GS, Delahousse M, Nochy D, Bariety J (2005). Class IV-S versus class IV-G lupus nephritis: Clinical and morphologic differences suggesting different pathogenesis. Kidney. Int. 68: 2288–2297.

Hughson MD, He Z, Henegar J (2001).Alveolar hemorrhage and renal microangiopathy in systemic lupus erythematosus. Arch. Pathol. Lab. Med. 125: 475-83.

Lee JG, Joo KW, Chung WK (2001). Diffuse alveolar hemorrhage in lupus nephritis. Clin. Nephrol. 55: 282-8.

Nishiya K, Chikazawa H, Nishimura S, Hisakawa N, Hashimoto K (1997). Anti-neutrophil cytoplasmic antibody in patients with systemic lupus erythematosus is unrelated to clinical features. Clin. Rheumato. l16 :70– 75.

Pediatric Nephrology

Schwartz MM, Roberts JL (1999). Necrotizing glomerulitis of systemic lupus erythematosus. Hum. Pathol. 14:158–167.

Sen D, Isenberg DA (2003). Antineutrophil cytoplasmic autoantibodies in systemic lupus erythematosus. Ann. Int. Med. 12: 651– 658.

Spoerl D, Pers Y (2012). Anti-neutrophil cytoplasmic antibodies in rheumatoid arthritis. Allergy. Asthma. Clinical Immunology. 8: 19.

Weening JJ, D'Agati VD, Schwartz MM (2004). The classification of glomerulonephritis in systemic lupus erythematosus revisited. Kidney. Int. 65: 521– 530.