Case Report

AA amyloidosis in systemic lupus erythematosus: an unusual complication

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Introduction

AA amyloidosis is a complication of chronic inflammatory diseases including Crohn’s disease, rheumatoid arthritis, ankylosing spondylitis, and juvenile rheumatoid arthritis. In contrast to the past, today it is less frequently associated with chronic infectious diseases such as tuberculosis. AA amyloidosis has also been reported in cancer, Muckle–Wells disease and familial Mediterranean fever (FMT) where the incidence differs between less than 10% for Armeniens and Arabs and over 30% among Turks and Sephardic Jews.

Conversely, AA amyloidosis is not a classic complication of SLE, and fewer than 20 cases have been reported in English worldwide, although cases of SLE with monoclonal gammopathy may be complicated by AL amyloidosis.

We observed one unusual patient with SLE complicated by AA amyloidosis.

Case

A 55-year-old woman with a 4-year history of SLE without renal involvement was admitted with a nephrotic syndrome. SLE had been diagnosed when she was 51 years old, following a 10-year history of isolated dermatological problems: she presented with non-destructive and non-deforming polyarthritis, skin rash, and iliac thrombophlebitis. Laboratory investigation revealed high titres of antinuclear (1/1000) and anti-DNA (82 U/ml) antibodies. There was no haematuria, no proteinuria, the creatinine level was normal, and the C-reactive protein level (CRP) was very high (3.6 mg/dl); lupus anticoagulant and IgG anticoardiolipid (34 U GPL) were also present. She met four of the American Rheumatism Association’s criteria for SLE, and was treated with oral corticosteroid.

She was readmitted to our service 4 years later with a nephrotic syndrome. The only SLE activity she reported during this time were brief episodes of polyarthritis. Laboratory tests showed a normal creatinine level, albumin concentration at 1.79 g/dl, heavy proteinuria (3 g/day), no haematuria, antinuclear antibody titres of 1/500, no anti-DNA antibodies, no monoclonal gammopathy, and normal levels of complement factors. The CRP level was high (6.7 mg/dl) despite the presence of a nephrotic syndrome. No infectious disease was found. Although there were no signs of active SLE, a diagnosis of membranous glomerulopathy was entertained and renal biopsy was performed which revealed massive glomerular and vascular Congo-red-positive areas exhibiting green birefringence under polarized light, staining with anti-AA antibodies but not with other sera (Figure 1). Optic microscopy and immunofluorescence study detected no SLE nephritis. Electron-microscopic analysis was not performed.

The patient received colchicine (1 mg/day). Subsequently, clinical and biological findings suggested hepatic and intestinal amyloid involvement. Renal insufficiency began 2 months later and progressed in 6 months to end-stage renal disease; the patient was then

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The delay between the diagnosis of SLE and the onset of symptomatic AA amyloidosis varied from 1 to 35 years. In nearly half the observations, as in our case, AA amyloidosis appeared within 5 years after onset of SLE.

The sex ratio deviates from the usual female predominance in SLE i.e. 10:1; approximately 40% of the reported cases of SLE complicated by AA amyloidosis are men.

In the reported cases, the clinical activity of SLE varied greatly. However, CRP was high in all cases when it was tested. This was true even in cases with the nephrotic syndrome, as was also observed in our patient [6, 7].

Similarly, when SAA values were reported, they were also high and paradoxically they remained high even in the nephrotic syndrome [6, 7], although Rosenthal and Franklin [19] had shown that SAA concentrations are often normal in AA amyloidosis with nephrotic syndrome, presumably due to urinary loss. Persistently elevated concentrations of SAA in nephrotic patients suggest very high compensatory hepatic synthesis of SAA.

Discussion

SLE was the most likely cause of the AA amyloidosis documented in this 55-year-old Caucasian woman. Inherited, infectious, and inflammatory diseases, which are known to cause AA amyloidosis, were excluded with reasonable certainty. To our knowledge, fewer than 20 such cases have been reported in the English literature since 1956 [1–17]. Experimental studies, e.g. histopathological examination of the kidneys of (NZB/NZW) F1 mice which develop SLE-like disease with immune-complex glomerulonephritis has consistently failed to demonstrate amyloid deposits [18].

The type of amyloidosis has not always been ascertained among the few cases with lupus and amyloidosis described so far [1–5]. The Wright test (stability with KMNO₄, a characteristic of AA amyloidosis, but of limited specificity) was positive in some [6–8, 15, 16]. Further, the aetiological link between SLE and AA amyloidosis is not entirely convincing in some of these reports since the patients in addition to lupus had further diseases that are themselves often associated with AA amyloidosis, notably ankylosing spondylitis, rheumatoid arthritis and lymphoma [1, 2, 4]. In one further report, Huston et al. [6] described a 43-year-old Egyptian with SLE amyloidosis; despite no personal or family FMT history, it is uncertain whether FMF is totally excluded.

Nevertheless no explanation other than SLE can be found in the remaining cases, and AA amyloidosis was well characterized by immunohistochemical studies in three of them [9, 10, 12]. The general features of AA amyloidosis complicating SLE were proteinuria with nephrotic syndrome and subsequently multivisceral involvement, as in our patient. Atypical presentations included isolated symptomatic pulmonary AA amyloidosis [12, 16], and hepatomegaly without proteinuria [15].

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There is a growing body of evidence that a high concentration of the acute phase reactant SAA, is a major predisposing factor for AA amyloidosis. This constitutes a necessary, but not sufficient, condition in the complex multifactorial process that ultimately leads to amyloidogenesis.

The SAA concentration in SLE and chronic inflammatory diseases has been studied by De Beer et al. [20]. They found very high SAA concentrations in patients with rheumatoid arthritis, juvenile chronic arthritis, and Crohn’s disease. They were highly correlated with disease activity. In contrast SAA concentrations are only slightly elevated in patients with ulcerative colitis and most patients with SLE, even in those with very active disease. The concentrations of CRP in patients with SLE follow a similar pattern. Like SAA, CRP is often normal even in the presence of active disease. These differences with respect to SAA and CRP concentrations between SLE and rheumatoid arthritis, may largely account for the difference in incidence of AA amyloidosis between these two conditions.

Garcia-Tobaruela et al. [15] observed improvement of symptoms when colchicine treatment was instituted, but our patient received colchicine treatment without any benefit. They is actually no information as to whether immunosuppressants are effective.

References

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