Case Report

Diarrhea, nephrotic syndrome and hidradenitis suppurativa: an unusual case

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Introduction

In contrast to AL amyloidosis, where clonal plasma cells in bone marrow produce immunoglobulins that are amyloidogenic, and familial amyloidoses in which a mutant protein forms amyloid fibrils, the incidence of AA amyloidoses has been reduced since the treatment of infectious diseases and rheumatoid arthritis improved. AA amyloidoses are due to amyloid formed from serum amyloid A, an acute phase protein produced in response to inflammation. With the reduction of chronic infectious diseases such as tuberculosis or osteomyelitis from the western hemisphere, AA amyloidosis is rarely seen; however, it still occurs in patients with rheumatoid arthritis, inflammatory bowel disease or untreated Mediterranean fever. We report an unusual case of chronic hidradenitis suppurativa leading to AA amyloidosis.

Case

A 62-year-old caucasian male presented with a 4 week history of progressive foot, leg and periorbital oedema. For 6 months, he had suffered from watery diarrhea that initially led to weight loss of 30 kg. With the appearance of oedema, his body weight increased from 60 to 91 kg, despite persisting diarrhea. Medical history included coronary heart disease with posterior myocardial infarction in 1991, long-standing arterial hypertension and hypercholesterolaemia. He was an ex-smoker (40 pack years). At age 37 years, he developed progressive abscesses and fistulizations in both axillae as well as in the inguinal and perineal area. A diagnosis of hidradenitis suppurativa was made. Since 1990, axillary fistulas were excised five times. Inguinal and perineal fistulizations were excised once in 1995. Post-operation, he suffered an acute coronary syndrome and was revascularized with an aortocoronary bypass. Severe fistulizations recurred in the inguinal and perineal region and in the left axilla. Due to his high cardiovascular risk, the patient had refused further operations. Three of the patient’s six siblings suffer from hidradenitis suppurativa. The patient has three sons, two of them (aged 31 and 41 years) suffer from recurrent axillary abscesses. There was no history of hidradenitis in his mother’s family. The personal and medical history of his father is unknown.

On examination, blood pressure was 120/70 mmHg, heart rate 92 beats per minute and temperature 36.4 °C. Body weight was 85.5 kg. He had severe foot, leg, scrotal and periorbital oedema, as well as bilateral pleural effusion. In the left axilla (Figure 1A), the inguinal and perineal region abscesses and cystic lesions were noted. There was no hepato-splenomegaly or makroglossia. He had hypalbuminaemia with dysproteinaemia (total protein 4.2 g/dl, albumin 29.7%, \(\alpha_1\)-globulin 5.3%, \(\alpha_2\)-globulin 14.7%, \(\beta\)-globulin 27.8%, \(\gamma\)-globulin 22.5%). Immunoglobulin A (IgA) was 759 mg/dl (normal 400 mg/dl) with polyclonal distribution, while IgG, IgM and IgE were normal. He had proteinuria (total urinary protein 7.1 g/dl, 38.9% albumin, 61.1% globulins). There were no light chains detectable in the patient’s blood and no Bence–Jones protein was found in his urine. Antithrombin III was reduced. Diagnostic thoracocentesis revealed a transudate. Creatinine and serum electrolytes were normal, creatinine clearance was 72.0 ml/min and urinary sediment was without haematuria or cellular casts. He had normocytic anaemia (haemoglobin 9.5 g/dl)
and leukocytosis (13 100 leukocytes per μl) with mild neutrophilia (78%) and lymphopenia (18.5%). C-reactive protein was 31.1 mg l⁻¹ (normal - 5 mg l⁻¹). Alkaline phosphatase was 260 U l⁻¹ (normal - 180 U l⁻¹). Stool cultures grew no pathogens. Ingualinal, perineal and axillary swabs grew *Staphylococcus aureus* and *Escherichia coli* that were sensitive to cefuroxim.

At colonoscopy, the entire colon showed oedematous mucosa with vanished haustration. Histology (Figure 1B) showed massive intestinal and vascular amyloid deposits that were classified as AA amyloid (Table 1; for details see [1]). An additional renal biopsy was not performed.

We treated the nephrotic syndrome symptomatically with fluid restriction to 1500 ml day, a low sodium diet, 2.5 mg ramipril and diuretics (2 × 25 mg hydrochlorothiazide and 2 × 12.5 mg triamteren). Previous therapy with 0.2 mg digoxin and 100 mg aspirin was continued. Within 2½ weeks, a 13 kg decrease in body weight was obtained and oedema were largely reduced. The hidradenitis was treated with sit baths and antiseptic bandages. The secondary bacterial infection was treated with 1 × 1.5 g cefuroxim i.v. Antibiotic therapy reduced the non-specific inflammatory markers (C-reactive protein 6 mg l⁻¹, leukocytes 8900 μl⁻¹).

The patient again refused a surgical intervention and was discharged. Follow-up visits in an outpatient clinic revealed progressive renal disease (creatinine 3.1 mg dl⁻¹, creatinine clearance 29 ml min⁻¹, urinary albumin excretion 5.3 g day⁻¹ and urinary protein excretion 8.9 g dl⁻¹, 8 months after discharge). Body weight (75.0 kg) was stable under diuretic drug therapy.

**Table 1. Immunostaining of intestinal amyloid**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Code</th>
<th>Reaction</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-AA, monoclonal (mc)</td>
<td>mc1</td>
<td>++ +</td>
<td>AA amyloidosis</td>
</tr>
<tr>
<td>Anti-ALλ (HAR)</td>
<td>936</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Anti-ALλ (ULI/LAT)</td>
<td>702/1049</td>
<td>0 (+)</td>
<td></td>
</tr>
<tr>
<td>Anti-ALκ (SIN)</td>
<td>880</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Anti-ALκ (KRA/KUN)</td>
<td>1157/1182</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Anti-ATTR (TIE)</td>
<td>831</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Anti-Aβ₂M (WOE)</td>
<td>975</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

AA, amyloid A protein; ALλ, amyloid of immunoglobulin lambda light chain origin; ALκ, amyloid of kappa light chain origin; ATTR, amyloid of transthyretin origin; Aβ₂M, amyloid of β₂-microglobulin origin.

*HAR, ULI etc. are acronyms of patients’ names from whom the antigen was derived.*

![Fig. 1. (A) Hidradenitis suppurativa: left axilla. (B) Amyloid deposits in colon submucosa (congo red).](image-url)
Discussion

The secondary AA amyloidoses are due to amyloid formed from serum amyloid A (SAA), a 12 kDa acute phase protein produced in response to inflammations after limited proteolysis. With the reduced incidence of chronic infectious diseases such as tuberculosis, osteomyelitis or bronchiectasis from the western hemisphere, AA amyloidosis has become a rare disease entity. Rheumatoid arthritis, inflammatory bowel disease and untreated familial Mediterranean fever are considered as typical chronic inflammatory diseases that sometimes coincide with AA amyloidosis [2]. AA amyloidosis presents most frequently with renal manifestation. Cardiac involvement is rare, and even if detected by echocardiography, it almost never results in heart failure [3]. Prognosis for patients with AA amyloidosis is affected greatly by the underlying chronic disease. There are reports of a dramatic response to surgical resection of the chronic inflammatory focus [4,5]. In a current review of 43 patients [6], median survival in patients with AA amyloidosis was 54 months. Median renal survival (patients alive and independent of renal replacement therapy) was only 18 months. Prognosis is poorer in male patients who have a non-rheumatological diagnosis and more advanced renal disease. Factors associated with poor survival are low albumin, high urinary albumin excretion and renal disease [7]. The rate of progression of renal disease correlates negatively with serum albumin and mean arterial pressure, and positively with urinary albumin excretion. AA amyloidosis presents with renal involvement in most patients. Gertz and Kyle [7] reported ~64 patients with AA amyloidosis. One hundred percent of renal biopsies in these patients were positive for AA amyloid, while only 82% were positive for amyloid in rectal biopsies. We conclude that AA amyloid detection in rectal biopsies of patients with nephrotic syndrome provides the strongest evidence for the coincidence of a renal AA amyloidosis. Taking into account the risks and the probability of obtaining additional information (such as additional primary glomerular disease), we decided not to take a renal biopsy in addition to rectal biopsies in our patient.

Hidradenitis suppurativa is a very unusual cause of AA amyloidosis. To our knowledge, only two cases are reported in the literature [7,8]. A concept of a familial form of hidradenitis suppurativa with autosomal dominant inheritance has been established [9]. Von der Werth et al. [9] assessed a family with 132 members. Twenty-eight relatives with hidradenitis suppurativa were detected. A further 16 relatives were judged to be possibly affected. In the group with positive family history, they found 10 affected and nine possibly affected individuals among 37 surviving first-degree relatives of hidradenitis sufferers. The family history of our patient suggests that this reported case of hidradenitis suppurativa has an autosomal dominant inheritance as well.

References


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