A Case of Primary Amyloidosis Presenting with Massive Proteinuria and Localized Gastrointestinal Involvement

Masif Proteinüri ve Lokalize Gastrointestinal Tutulumla Prezente Olan Primer Amiloidoz Olgusu

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ABSTRACT Amyloidosis is a systemic or localized disease characterized by the extracellular accumulation of insoluble protein-like material. There are two types of it; primary and secondary. Primary amyloidosis is the accumulation of major fibril protein AL, which is derived from plasma cells and contains immunoglobulin light chains. It can be associated with myeloma and other plasma-cell dyscrasias. Although cases of amyloidosis involving different parts of gastrointestinal system were reported in the literature, there has been only one case of ampullary involvement so far. We report on a case of a female patient diagnosed at advanced age presenting with massive proteinuria and bile duct dilatation and review the relevant literature.

Key Words: Primary amyloidosis; ampulla of vater; nephrotic syndrome

ÖZET Amiloidoz, dokuların ekstrasellüler bölümünde, erimeyen protein benzeri materyalin birikimi ile karakterize sistemik veya lokalize bir hastalıktır. Primer ve sekonder amiloidoz olarak iki tipi vardır. Primer amiloidozda Ig hafif zincir birikimi olarak başlıca fibril proteini AL olup, multiple miyelom ve diğer plazma hücre diskrazileri ile birlikte bulunabilir. Literatürde gastrointestinal sistemin farklı yerlerini tutan amiloidoz vakaları bildirilse de, ampulla vater tutulumu olan tek vaka bildirilmiştir. Bizim vakamız ileri yaşta tanı alan, masif proteinüri ve safra yolları dilatasyonu ile prezente olan bir kadın hasta olup, literatür derlemesi eşliğinde sunulmuştur.

Anahtar Kelimeler: Primer amiloidoz; vater ampullası; nefrotik sendrom

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Amyloidosis is a localized or systemic disease characterized by the accumulation of insoluble protein-like material in extracellular tissues.[1] Delicate and non-branching protein fibrils comprise about 90% of amyloid deposition. Apart from the structure of fibril protein, non-fibrillary amyloid P-component always presents in all types of amyloidosis. There is accumulation of immunoglobulin light chain in primary amyloidosis. The major fibril protein is AL in primary amyloidosis and can be found with multiple myeloma or other plasma cell dyscrasias.[2] Instead, secondary amyloidosis develops along with an underlying chronic event. The major fibril protein is AA in it. Chronic inflammatory diseases (rheumatoid arthritis, ankylosing spondylitis, Behcet's diesase, Chron's disease, ulcerative colitis, etc.), infectious diseases (tuberculosis, bronchiectasis, osteomyelitis, etc.), neoplasias (carcinomas, Hodgkin's disease, medullary thyroid cancer,

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insulinoma, etc.) are the most important causes of secondary amyloidosis.[3] The best well known form of hereditary amyloidosis is Familial Meditarranean Fever (FMF). Although cases of amyloidosis involving different parts of gastrointestinal system were reported in the literature, only one case of ampullary involvement have been reported so far.[4] We report on a case of a female patient diagnosed at advanced age, presenting with massive proteinuria and bile duct dilatation and review the relevant literature.

CASE REPORT

A 82-year-old female presented with a 7-month history of edema in the lower extremities. Surgical history included coronary artery bypass grefting and total abdominal hysterectomy with bilateral salpingo-oophorectomy 15 years ago. Physical examination revealed a blood pressure of 90/50 mmHg and a heart rate of 72 beats per minute. Pretibial edema, decreased breath sounds, apical 2/6 pan-systolic murmur, minimal ascites, palpable liver 2 cm below the left costal margin and Murphy positivity were detected. The patient's biochemical parameters were as follows: hematocrit: 32.7%, hemoglobin: 10.5 mg/dL, urea: 57 mg/dL, creatinine: 1.6 mg/dL, albumin: 1.5 g/dL, alkaline phosphatase: 184 mg/dL, urinary albumin: 3+, 24h total urinary protein: 14 g, creatinine clearance: 17.8 mL/min. Protein electrophoresis showed no monoclonal band. In terms of identification of light chain disease, IgG/lambda monoclonal band (Lambda 3510 mg/L, N: 900-2100) was detected in immunofixation electrophoresis. There was no sign of a chronic (diabet, hypertension, etc.) or an autoimmune disease clarifying the etiology of nephrotic syndrome. No malignancy was identified by thoracic, abdominal and pelvic computed tomography, breast and thyroid ultrasonography and mammography. The diagnosis of lambda dominated multiple myeloma was excluded by performing bone marrow aspiration. Percutaneous renal biopsy revealed amorphous material accumulated in the glomerular mesengial matrix which was strongly positive for Congo Red histochemically and negative for Amyloid A immunohistochemically, indicating in favour of primary amyloidosis (Figure 1, 2). There was no ocular, cardiac or neurologic involvement in terms of systemic manifestation. However, endoscopic USG and endoscopic retrograd colangio pancreaticografi (ERCP) were carried out due to rapidly developed ascites, intrahepatic dilatation and hydropic gallbladder. Mild dilatation of common bile duct and Wirsung canal and bulging of papilla were demonstrated (Figure 3). Biopsies, which were taken in order to exclude ampullary tumor or amyloidosis, showed amyloid deposition positive only with Congo Red histochemically (Figure 4, 5). Melphalan was not be able to given to the patient due to poor general condition, thus only 2 cycles of chemotherapy in-

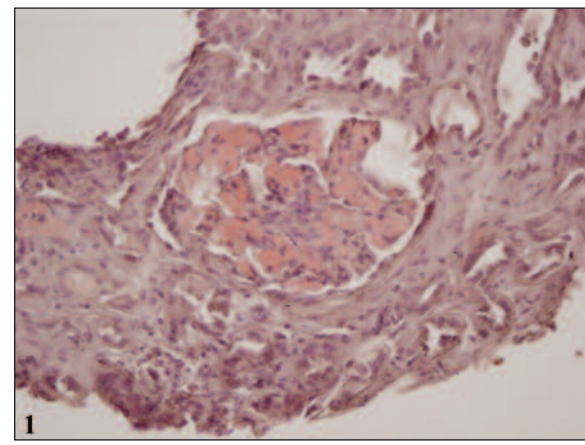

FIGURE 1: Congo-red stain revealing the glomerular amyloid depositon (Congo-Red x200).

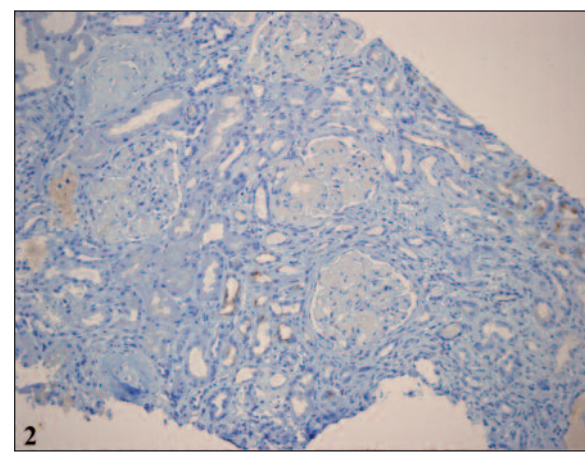

FIGURE 2: Negative in glomeruli, non-specific weak staining arround some of the tubules by immunohistochemical marker for amyloid deposition (AmiloidA x100).

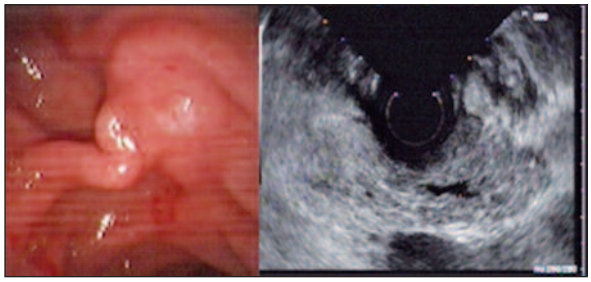

FIGURE 3: On the left, slightly bulging and fluffy appearance of ampulla Vateri is seen with ERCP, and on the right, irregularity of the papilla is seen with EUS.

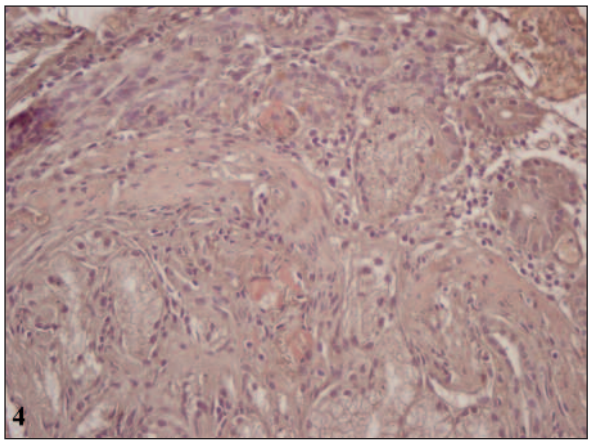

FIGURE 4: Congo-Red positive amyloid deposition in the lamina propria of a small intestinal mucosal biopsy (Congo-Redx200).

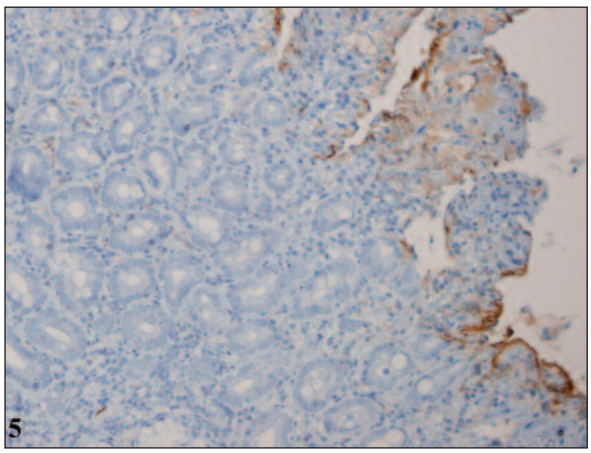

FIGURE 5: Negative immune reaction in lamina propria with immunohistochemical amyloid marker and non-specific moderate epithelial staining at some of the tips of intestinal villi (Amiloid Ax100).

cluding dexamethasone (20 mg/m^2) were administered. Because of the progression of the condition and intervening infections it was unable to continue the treatment. The patient died six months after the initial diagnosis.

DISCUSSION

Primary amyloidosis is more common in males. The average age of diagnosis is 65 and 99% of patients are over the age of 40 years.[3-7] Kidneys are the organs most likely to be the site of diagnosis with a biopsy. On average, 50% of patients with amyloidosis die within 1 year, 75% within 3 years, %84.5 within 5 years after initial diagnosis. The average survival duration is approximately 14 months. Survival is much worse which is about 4-6 months in cases of AL synchronously with Multiple Myeloma.[8-10] The average survival duration is 1 year after the histological diagnosis.

It's still controversial wheather the classifying of the amyloid type can be made exactly by immunohistochemical method. According to the literature there is a rough classification of immunohistochemical stains as Amyloid AA negative and positive ones. Therefore firstly Amyloid P positivity should be revealed by Congo Red or Cyristal Violet histochemically because P component is present in all types of amyloid.[11] In case of Amyloid P positivity and Amyloid AA negativity, possibilities including primary amyloidosis (AL type), dialysis-associated amyloidosis (beta-2 microglobulinemia) and hereditary amyloidosis should be thought.[12]

Although it is very frequent, gastrointestinal involvement is usually asymptomatic in amyloidosis.[7,13] Liver involvement is common in amyloidosis. Liver is palpable in one third of patients. A massive liver may be the first sign of it. Hepatic functions are usually normal or slightly deteriorated. In advanced cases, jaundice due to intrahepatic cholestasis have been reported. Amyloidosis is localized usually in periportal areas within liver but intrahepatic cholestasis can be seen due to centrilobular deposition.[3,14]

A male patient with recurrent cholangitis reported by Chan et al. is the only case in the literature about ampullary involvement so far. Our case becomes notable as being the case of amyloi-

dosis accompanied by nephrotic syndrome with ampullary involvement, which caused rapid progression of widespread ascites, hydropic gallbladder, bile duct dilatation, although the diagnosis is established shortly after admission. Together with IgG/lambda monoclonal band on immunofixation electrophoresis and Congo Red positive/Amyloid AA negative amyloid accumulation in kidneys and ampullary mucosa suggested primary amyloidosis in the foreground. It also comes into prominence as being the only case reported from Turkey.

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