Case Report

Lingual Amyloidosis—a Rare Complication of Long-Term Hemodialysis in a Patient with X-Linked Alport Syndrome

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Abstract

Dialysis-related amyloidosis (DRA) of the tongue is a rare and late complication in dialysis patients undergoing chronic hemodialysis for more than 20 years. Alport syndrome is a progressive inherited form of glomerular disease with a characteristic glomerular pathology that is often associated with neural hearing loss and ocular abnormality. A 52 year-old male was referred to our hospital with the chief complaint of gait disturbance for three days in October, 2008. He had a history of uremia of unknown etiology for which he had received regular hemodialysis thrice weekly for 26 years. After admission, he was diagnosed with DRA of the tongue, carpal tunnel syndrome of both hands and destructive spondyloarthropathy in the cervical spines as revealed by CT and MRI study. These also could have been related to DRA and his gait disturbance. X-linked Alport syndrome was diagnosed following detailed history taking, as well as ocular and auditory evaluation. To the best of our knowledge, this is the first case of a uremia patient with X-linked Alport syndrome and a rare and late complication of DRA—lingual amyloidosis. Therefore, a detailed family screening, ocular and auditory evaluation were helpful in diagnosing X-linked Alport syndrome, even in the absence of demonstrable changes in the glomerular basement membrane.

KEY WORDS: Alport syndrome, dialysis, amyloidosis, tongue

Introduction

Alport syndrome is a progressive hereditary kidney disease characterized by hematuria, sensorineural hearing loss, and ocular lesions with structural defects in the glomerular basement membrane. The frequency of the Alport gene has been estimated to be between 1:5000 and 1:10000 in the United States (1). Dialysis-related amyloidosis (DRA) is a major complication in long-term hemodialysis patients that has been recognized as being caused by amyloid deposition and derived from beta-2-microglobumin (2). It is also well known DRA predominantly involves the osteoarticular system, and is less frequently related to the other extraarticular systems (3). We report a 52 year-old male patient, who had received regular hemo-
dialysis for 26 years with unknown etiology, diagnosed with uremia due to X-linked Alport syndrome. He also experienced a rare and late complication of DRA—lingual amyloidosis after 20 years of regular hemodialysis, which was diagnosed during this admission 26 years after his initiation of regular hemodialysis.

Case Report

A 52 year-old male was referred to our hospital with the chief complaint of gait disturbance for three days in October, 2008. He had a history of uremia of unknown etiology, for which he had received regular hemodialysis thrice weekly for 26 years. He had also developed bilateral carpal tunnel syndrome 13 years after starting regular hemodialysis, for which he had surgery. The dialyzer was shifted from the cuprophan membrane to the polysulfone one following surgery. On physical examination, numbness, pain and decreased muscle power to 3 to 4 were noted over both lower extremities. Multiple pale-yellowish nodules of various sizes occupied the entire surface of his tongue (Fig. 1a). History taking revealed he suffered from pain of the tongue twenty years after initiating regular hemodialysis, which was followed by multiple small, pale-yellowish nodules scattering initially on the lateral surface of the tongue, gradually enlarging, and spreading extensively to occupy the entire surface. As the pain of the tongue progressed without lingual dysfunction, he received an excision biopsy on these tongue nodules at our hospital in December, 2006, revealing histology findings of positive Congo red stained amyloid depositions (Fig. 1b).

Macroglossia was also noted then. Following admission, as the immunoelectrophoresis did not reveal any paraproteinemina and there were no recognizable causes for amyloidosis by extensive history review, the diagnosis of this patient was presumed to be dialysis-related amyloidosis of the tongue. The dialyzer was further changed to a high-flux polysulfone one. Meanwhile, after an extensive review of the patient’s medical history and the current condition, he was presumed to have X-linked Alport syndrome. He had progressive hearing loss since young adulthood, confirmed by audiometry performed during admission, which showing moderate to severe high frequency sensorineural hearing loss. He also had visual disturbances since young adulthood. As shown in his genetic lineage (Fig. 2), mother to son transmission was noted, suggesting X-linked inheritance of Alport syndrome. This was subsequently confirmed...
by the presence of anterior lenticonus (protrusion of the central portion of the lens into the anterior capsule) after slit-lamp biomicroscopy performed during admission (Fig. 3a), which was virtually pathognomonic of Alport syndrome. Further, genetic analysis revealed the mutation point at the COL4A5 gene c.2605 G > A (p.Gly869Arg) mapped at the long arm of the X-chromosome (4), indicating the diagnosis of X-linked Alport syndrome. The image of CT in his cervical spine showed synovium thickening (one-head arrow) and odontoid process erosion with cyst formations (two-head arrow) in his axis.

Discussion

DRA is caused by tissue deposition of amyloid fibril protein identified as β-2-microglobulin in long-term dialysis patients and the occurrence of DRA is closely linked to the duration of dialysis and the use of bio-incompatible membranes (5). DRA of the tongue is a rare and late complication in dialysis patients undergoing chronic hemodialysis for more than 20 years (6). Lingual amyloid nodules are firm in consistency, whitish-yellow in color, and vary with sizes of more than 1mm in diameter (6). Some literature speculates amyloid deposition predominantly begins on the lateral side of the tongue due to frequent contact with the teeth and related stimulation (6), which was also experienced in our patient. The advanced form DRA of the tongue may lead to lingual dysfunction, such as abnormal taste, altered mobility, and articulatory dysfunction. With severe and prolonged lingual dysfunction, malnutrition and other associated comorbidity can occur (7). Our patient did not suffer from lingual dysfunction but did have macroglossia, which was also described in some literature (6). He also suffered from various forms of DRA, including bilateral carpal tunnel syndrome, lingual amyloidosis, and destructive spondyloarthropathy in the cervical spines. To prevent DRA morbidity, prolonging the duration, changing the frequency of dialysis treatment, and applying biocompatible high flux dialyzers are potentially helpful strategies.

Alport syndrome is a progressive inherited form of glomerular disease with a characteristic glomerular pathology that is often associated with neural hearing loss and ocular abnormality. Guthrie first reported a family with recurrent hematuria (8). Alport reported an additional observation on this family, the occurrence of deafness associated with hematuria, and the observation affected males died of uremia, whereas affected females lived to an old age (9). Alport syndrome is a genetically heterogeneous disease with X-linked, autosomal recessive and autosomal dominant variants. X-linked accounts for approximately 80% of affected patients. It arises from mutations in the COL4A5 gene in the X-chromosome, which encodes alpha-5(IV) chains (10). Anterior lenticonus, which is associated with thinning of the lens capsule, the basement membrane surrounding the lens, occurs in 20 to 30 percent of males with X-linked Alport syndrome (11). If present, anterior lenticonus is pathognomonic of Alport syndrome. From the clinical picture, our patient is compatible with X-linked Alport syndrome. Therefore, a detailed family screening most probably related to DRA for which he was admitted, but he refused further surgical intervention. Therefore, he was discharged.
and ocular and auditory evaluation were helpful in diagnosing X-linked Alport syndrome, even in the absence of demonstrable changes in the glomerular basement membrane (12).

Following a detailed and extensive literature review, there is no evidence confirming the incidence of lingual amyloidosis is higher in dialysis patients with Alport syndrome than those dialysis patients without Alport syndrome. However, there is a case report describing destructive spondyloarthropathy with β-2-microglobulin amyloid deposits in a patient with chronic renal insufficiency of 17-year duration and Alport syndrome before chronic hemodialysis (13). Finally, there was no genetically linked lingual amyloidosis in the involved individual who received dialysis treatment for only five to six years.

References