# IgA Nephropathy in a Patient with IgG Myeloma

Sir,

IgA lambda myeloma with mesangial proliferative glomerulonephritis (GN) without IgA had been reported.[1] IgA myeloma with nephritis and Henoch-Schonlein purpura (HSP) may coexist,[2] and some have suggested a causal relationship between IgA nephropathy and IgA myeloma.[3] We report a patient of diabetes mellitus with IgA nephropathy with IgG myeloma.

A 65-year-old male, type 2 diabetic and hypertensive for the past 3 years, presented with a history of swelling of feet, facial puffiness and distention of abdomen for the past 3 months. There was no antecedent history of fever, upper respiratory tract infection, allergy, insect bite, or drug intake. The swelling was gradually progressive. Fundus examination revealed the absence of diabetic retinopathy. The initial investigations revealed serum creatinine: 1.05 mg/dL, serum potassium: 3.1 mEq/L, hemoglobin: 9.0 g/dL, erythrocyte sedimentation rate: 125 mm after 1st h, total serum proteins: 5.6 g/dL, serum albumin: 1.6 g/dL, total cholesterol: 172 mg/dL, triglycerides: 276 mg/dL, serum calcium: 8.2 mg/dL, serum phosphorus: 3.4 mg/dL, serum uric acid: 8.9 mg/dL, 24 h urine protein: 3.1 g, urine albumin: 1+, urine red blood cells: nil, and urine white blood cells: 2–4/hpf.

For the indication of proteinuria, a renal biopsy was done. It revealed eleven glomeruli. Two of them were sclerosed. Remaining glomeruli revealed diffuse segmental increase in mesangial matrix without increase in cellularity. There was no thickening of basement membrane, no crescents, or necrosis. Immunofluorescence revealed IgA ++ in all glomeruli, IgM+, and lambda ++. Kappa was negative.

As IgA nephropathy in patients above 60 years requires investigation for a malignancy,[4,5] bone marrow aspiration and trephine biopsy were done. It revealed increased number of plasma cells, presence of bi- and multinucleated plasma cells, and plasmablasts. Plasma cells accounted for 24% of the cells. Serum protein electrophoresis showed the presence of "M" band. The serum levels were IgM: 95.9 mg/dL (reference range: 40–230 mg/dL), IgA: 192 mg/dL (reference range: 70–400 mg/dL), IgG: 1810 mg/dL (reference range: 700–1600 mg/dL), kappa: 68.30 mg/L (reference range: 3.3–19.4 mg/L), and lambda: 145 mg/L (reference range: 5.71–26.30 mg/L).

A bortezomib-lenalidomide-dexamethasone regimen was used for the treatment. The schedule of this regimen was on days 1, 4, 8, and 11: injection bortezomib 1.3 mg/m$^2$ IV, days 1–14: lenalidomide 25 mg orally daily, plus days 1, 2, 4, 5, 8, 9, 11, and 12: dexamethasone 20 mg orally daily. The cycle was repeated after 3 weeks for 2 cycles. We intended to give 4 cycles. However, after second cycle, the patient suffered pneumonia due to Klebsiella pneumoniae and could not be revived.

IgA nephropathy is characterized by the mesangial and blood vessel deposition of IgA1.[6] In IgA myeloma, the paraprotein is more commonly of the IgA1 than the IgA2 subclass, yet if there is renal involvement, it will typically be myeloma cast nephropathy with intratubular precipitation of excreted light chains and no evidence of glomerular immunoglobulin deposition or injury.[3] Our patient had no features of myeloma cast nephropathy on renal biopsy but had mesangial proliferative glomerulonephritis (GN) with mesangial IgA deposition, which is a characteristic pattern of IgA nephropathy and HSP nephritis. In addition, IgA was the dominant immunoglobulin in all glomeruli. It was therefore not due to incidental deposition of IgA in a patient of myeloma but simultaneous occurrence of IgA nephropathy in a patient of myeloma.

The reduction of hinge region O-glycosylation of the IgA1 molecule is involved in susceptibility to mesangial IgA deposition and to invoke an inflammatory response.[7,8] If this glycosylation abnormality of IgA1 is an unusual event in IgA1 myeloma, this may explain why IgA nephropathy and HSP so rarely complicate IgA myeloma even when the circulating IgA burden is very high.[3]

Very little is known about the relationship between IgA nephropathy and IgG myeloma; for there were only two similar reports[9,10] published [Table 1].[3,7,9-12]

The first patient[9] was a 76-year-old man who had right-sided loin pain and back pain. Magnetic resonance imaging showed a tumor mass compressing the lower part of the thoracic spinal cord. A biopsy of the tumor disclosed atypical plasma cells in the infiltrate and clear cell clonality consistent with plasmacytoma. In addition, pathologic lytic areas were discovered in several bone structures. A monoclonal component consisting of IgG light chain was found in serum and bone marrow aspiration material that consisted of 10% of plasma cells confirming multiple myeloma. When serum creatinine increased to 2.32 mg/dL, after 5 years, a renal biopsy was done. It revealed increased mesangial cellularity and mesangial matrix and granular deposition of IgA in the mesangium together with mesangial positivity to kappa and lambda light chain. There was no evidence of multiple myeloma. A year later, a second renal biopsy was done. It showed slightly more mesangial matrix material with no IgA deposits. There was no evidence of multiple myeloma in the second biopsy also. The patient received intensive bortezomib treatment. It resulted in recovery of kidney function.

**Table 1: Published reports of IgA nephropathy and Henoch-Schonlein syndrome and multiple myeloma**

| Reference | Myeloma type | Renal manifestation | Age/sex | Treatment | Outcome |
|---|---|---|---|---|---|
| [7] | IgA (K) paraprotein | Relapsing Henoch-Schonlein syndrome[#] | 42/female | BCNU, melphalan, cyclophosphamide, prednisolone | Achieved remission |
| [8] | IgA multiple myeloma | Henoch-Schonlein purpura and polyarteritis nodosa[@] | 50/male | Steroid and cyclophosphamide | ESRD<br>died due to staphylococcal pneumonia |
| [11] | IgA myeloma | IgA nephropathy* | 56/female | Melphalan and prednisolone | ESRD 2 years after the diagnosis of myeloma |
| [3] | IgA kappa myeloma | Henoch-Schonlein purpura[^] | 50/male | Vincristine, adriamycin, methylprednisolone, and cyclophosphamide | Serum creatinine: 1.4 mg/dL |
| [12] | IgG lambda light-chain plasmacytoma | IgA nephropathy[$] | 76/male | Local irradiation, methylprednisolone, vincristine, lomustine (CCNU), cyclophosphamide, melphalan (MOCCA-regimen), dinatrium chlodronate, dinatrium pamidronate, zoledronic acid, and bortezomib | Serum creatinine after 6 years: 1.8 mg/dL |
| [13] | IgG kappa type myeloma | IgA nephropathy[^] | 55/male | Bortezomib and dexamethasone | Reduction of proteinuria |

[#]IgA nephropathy preceded the IgA myeloma by 1 year, [@]Renal manifestations preceded the IgA myeloma by 4 years, *Renal biopsy not done. IgA nephropathy preceded the IgA myeloma by 30 years, [^]The diagnosis of IgA nephropathy and the myeloma was simultaneous, [$]The diagnosis of myeloma was 5 years before the diagnosis of IgA nephropathy. ESRD: End-stage renal disease, BCNU: Carmustine, CCNU: Lomustine, MOCCA: Methylprednisolone, vincristine, CCNU, cyclophosphamide and melphalan

The second patient[10] was a 55-year-old man presented with facial puffiness and edema in lower limbs, low backache, and generalized weakness for 4 months. The patient had anemia, hypercalcemia, hypoalbuminemia, hyperuricemia, high lactate dehydrogenase levels, altered albumin-protein ratio, with mildly enlarged kidneys. Serum immunoelectrophoresis showed M band in the gamma region, which on immunofixation was IgG kappa type. Bone marrow biopsy showed 13%–15% plasma cells. A renal biopsy was done for the indication of active urine sediment and nephrotic-range proteinuria. Light microscopy showed focally and segmentally accentuated increase in mesangial cellularity and matrix. Malignant cells or fractured casts were absent. Immunofluorescence revealed diffuse mesangial granular staining in the glomeruli for anti-IgA (3+) and C3 (2–3+), staining for lambda light chain was positive, and staining for kappa light chain was negative. The kidney function improved with the bortezomib.

In both the patients, multiple myeloma was identified before the IgA nephropathy. In our patient, it was simultaneous. However, it was reported that malignancy was not uncommon among older patients with IgA nephropathy. Of 26 patients aged 60 or older, 6 (23%) had cancer compared with none of the 158 patients younger than age 60.[4]

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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