Grave's disease associated with immunoglobulin A nephropathy: A rare association

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ABSTRACT

Immunoglobulin A (Ig A) nephropathy is the most common form of primary glomerulonephritis. The association of Ig A nephropathy with Grave's disease has not been reported so far. We report a case of 20-year-old female with Grave's disease who presented with edema, facial puffiness, and decreased urine output. She was found to be hypertensive with renal failure and nephrotic range proteinuria. Renal biopsy revealed features of Ig A nephropathy. The patient was treated with oral corticosteroids (1 mg/kg/day). To our knowledge, this is the first case showing association of Grave's disease with Ig A nephropathy.

Key words: Autoimmunity, grave's disease, immunoglobulin A nephropathy

Introduction

Thyroid diseases have been shown to have association with various immunological diseases involving kidneys like immunoglobulin A (Ig A) nephropathy,[1] membranoproliferative glomerulonephritis[2] and minimal change disease.[3] Hyperthyroid state exerts various non-immunological effects on kidneys functionally and structurally.[4,5]

This report is being presented as a first case report to show the association between Grave's disease and Ig A nephropathy, which to the best of our knowledge has not been shown so far.

Case Report

A 22-year-old unmarried female was diagnosed as a case of Grave's disease and was put on methamizole 10 mg twice daily. Her investigations done in previous 1 month showed serum free thyroxine level of 1.05 ng/dl (normal range 0.95–1.74 ng/dl), thyroid-stimulating hormone level of <0.001 μU/mL (0.34–3.88 μU/mL), and anti-thyroid-peroxidase antibody titer of 1738 units/ml (<100 units/ml). Ultrasonography neck revealed diffuse enlargement of thyroid gland. Thyroid scan showed 42% uptake in thyroid gland. She presented to our department with complaints of periorbital puffiness, swelling of feet, and decreased urine output. Her examination revealed blood pressure (BP) of 180/100 mmHg, pulse rate of 100 beats/m in and temperature of 98.8°F. She had periorbital puffiness, pedal edema, and diffuse midline neck swelling. Her hands were warm and moist, and there were no tremors or skin changes. Rest of the systemic examination was normal. Patient was continued on methamizol as the disease was in remission. Her investigations showed hemoglobin 10.3 g/dl, total leukocyte count 6500/mm3, serum creatinine 2.4 mg/dl, bilirubin 0.4 mg/dl, normal AST, ALT and alkaline phosphatase, albumin 2.8 g/dl, uric acid 6.8 mg/dl, blood sugar 89 mg/dl, calcium 8.7 mg/dl and phosphate 4.6 g/dl.

Urine exam ination revealed 6–8 pus cells/HPF; red blood cells of 10–12/hpf; protein - +++, sugar-nil. 24 h urinary protein estimation revealed protein of 13 g/day. Hepatitis B surface antigen/hepatitis C virus serology was negative. Anti-nuclear antibodies and anti-double-stranded DNA were negative. Serum and urine electrophoresis was also negative.

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Renal biopsy revealed 23 glomeruli, 12 (52.1%) of which were globally sclerosed. Among the remaining glomeruli, 7 (30.4%) revealed segmental tuft sclerosis and three glomeruli (13%) revealed segmental endocapillary cellularity. Extracapillary proliferation and partial fibrocellular crescents were seen in 2 (8.69%) glomeruli. Tubular atrophy and interstitial fibrosis involved 40–45% of the sample. Viable tubules showed prominent cytoplasmic vacuolar changes and evidence of patchy acute injury with epithelial simplification and loss of brush borders. Arteries showed medial thickening and fibrointimal sclerosis with duplication of internal elastic lamina and focal mucoid degeneration while arterioles revealed variably thickened walls with subendothelial transmural hyalinosis 1 [Figure 1].

Differential immunofluorescence study revealed Ig A-3^+ mesangial deposits, IgG negative, Ig M 1^+, C3 2^+, C1q negative, kappa 2^+, lambda 3^+ mesangial deposits. Biopsy was suggestive of focal endocapillary proliferative Ig A nephropathy with M0E1S1T1 Oxford score [Figure 2].

The patient was treated with oral corticosteroids 1 mg/kg and amlodipine. Angiotensin converting enzyme inhibitors were not given initially. Her repeat investigations on follow-up showed improvement in disease course clinically and biochemically with 24 h urinary protein of 2 g/day and serum creatinine level of 1.6 mg/dl. The patient is on amlodipine 10 mg/day and continues on tapering doses of steroid.

Discussion

Hyperthyroidism results in increased renal blood flow and glomerular filtration rate (GFR).[6] The reason is increased renal blood flow and activation of renin-angiotensin-aldosterone system.[7] Furthermore on treating the hyperthyroidism, these effects are reversed and the GFR returns to normal.[6] Serum creatinine is significantly decreased in hyperthyroid patients due to an increase in GFR and due to the reduction in overall muscle mass. Also urinary protein excretion in hyperthyroidism is increased due to increase in GFR.[4]

Hyperthyroidism also affects tubular function. It causes direct down-regulation of aquaporin 1 and 2 channels. This along with increased BP, cardiac output, and renal blood flow results in polyuria.[5] Thyroid diseases are associated with several glomerulonephritides. The most commonly observed association is with membranous nephropathy[8,9] followed by Ig A nephropathy,[1] membranoproliferative glomerulonephritis[2] and minimal change disease.[3] So for no report of Grave's disease associated with Ig A nephropathy has been reported.

The association of Hashimoto's thyroiditis and membranous nephropathy with immune complex deposition in the glomerular as well as thyroid epithelial basement membrane has been reported.[10] The likely mechanism for association of Grave's disease with Ig A nephropathy beyond chance being the presence of circulating immune complexes can only be speculated.[11] Similarly, the occurrence of thyroid and renal disease in association with other autoimmune diseases such as type 1 diabetes mellitus has been suggested as an autoimmune etiology.[12] Given the fact that hyperthyroid state influences a lot of functional and structural changes in kidneys both at glomerular and tubular levels, pathophysiological mechanisms beyond autoimmunity need to be studied further.

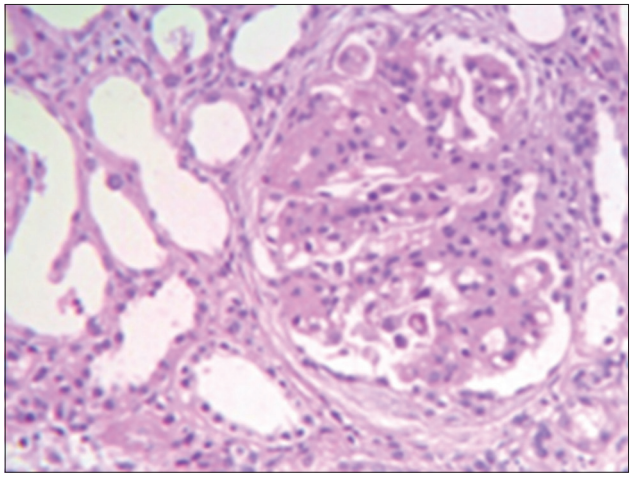

Figure 1: Microphotograph showing histopathological examination showing globally sclerosed glomeruli tuft sclerosis with segmental endocapillary cellularity. Tubular atrophy with loss of brush borders is evident

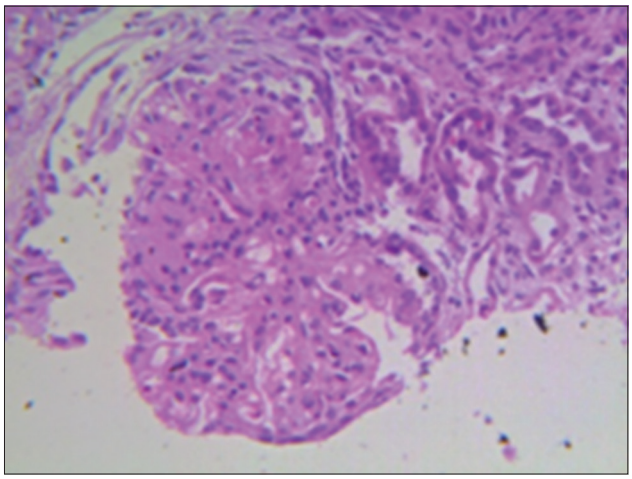

Figure 2: Microphotograph showing immunofluorescence examination depicting Ig A-3^+ mesangial deposits granular as well as confluent, Ig G negative, Ig M 1^+, C3 2^+, C1q negative, Kappa 2^+, lambda 3^+ mesangial deposits

Conclusion

This case report is the first in the literature, which shows association of two autoimmune diseases with different pathophysiological mechanisms with no clear-cut explanation. Further studies are needed to study this association and possible mechanisms. Also non-immune mechanisms in this association need elucidation.

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