
A case of generalised myasthenia gravis with membranous nephropathy

K P Ruwan C Prasad¹, D G S Alahakoon² and U Vidanagama³

Abstract

We report a 40-year old woman with bilateral partial ptosis, complete external ophthalmoplegia, and weakness and fatigability of upper limbs. She was on treatment for hypertension for 5 months at the time of admission. She was found to have generalised myasthenia gravis and membranous nephropathy with end-stage renal disease. Her symptoms and signs improved within 2 months on treatment with neostigmine and prednisolone. It is postulated that either thymic hyperplasia or the subclinical stage of a thymoma may be the underlying aetiological factor in this patient.

Introduction

Myasthenia gravis is an autoimmune syndrome that is rarely associated with glomerulonephritis [1, 2]. The types of glomerulonephritis described in association with myasthenia gravis include minimal change disease, focal segmental glomerulosclerosis and membranous nephropathy [1, 3, 4]. We report here a patient with generalised myasthenia gravis and membranous nephropathy.

Case report

A 40-year old Sri Lankan woman with hypertension for 5 months, presented with a 6 weeks' history of involuntary closure of both eyes. Examination revealed bilateral partial ptosis and bilateral complete external ophthalmoplegia. There was fatigability of both eye lids. Muscle power was reduced to grade IV in abductors and extensors of the right arm. All tendon reflexes were normal. Blood pressure was elevated.

The diagnosis of myasthenia gravis was confirmed by a positive edrophonium test and a decremental response

of 23% in facial muscles by the repetitive nerve stimulation test. Acetylcholine receptor antibody assay and single fibre electromyogram were not available locally. Urine analysis revealed a urinary protein excretion of 4.3g/day. Creatinine clearance was 12.7 ml/ per minute. There was hypoalbuminaemia and hypercholesterolaemia. Renal ultrasound scan revealed normal sized kidneys with increased cortical echogenicity. Renal biopsy established membranous nephropathy (figure 1). Extensive glomerular sclerosis and capillaries with spiking of the basement membrane, extensive lymphocytic interstitial inflammation and fibrosis are evident. Immunofluorescent staining was positive for IgG and negative for IgA, IgM and C3. Chest xray and CT scan of the head and orbits were normal. CT scan of the thorax showed a normal sized thymic hyperdensity (figure 2). The ESR was 60mm/hour. Antinuclear antibodies, rheumatoid factor, and hepatitis B, hepatitis C, VDRL and HIV antibodies were negative. Screening for malignancy with stools for occult blood, CT abdomen, carcinoembryonic antigen and CA 125 were negative.

Ptosis and external ophthalmoplegia showed complete improvement after about 2 months of neostigmine and prednisolone. The patient is now completely free of myasthenia gravis symptoms on a prednisolone dose of 7.5mg daily. She is being prepared for renal transplantation.

Discussion

Myasthenia gravis with membranous nephropathy is a rare association [1, 4, 5, 6]. Their observations tally with the natural history of membranous nephropathy. In contrast our patient was already in end-stage kidney disease at the time of diagnosis. Two large case series comprising of 206 myasthenia gravis patients have failed to detect any with the combination of myasthenia gravis and membranous nephropathy.

¹Registrar in Medicine, ²Physician, ³Senior Registrar in Medicine, Teaching Hospital, Kandy, Sri Lanka.

Correspondence: KPRCP, e-mail <ruwan@med.ruh.ac.lk>. Received 10 September 2007, and accepted 15 December 2007. Conflicts of interest: none declared.

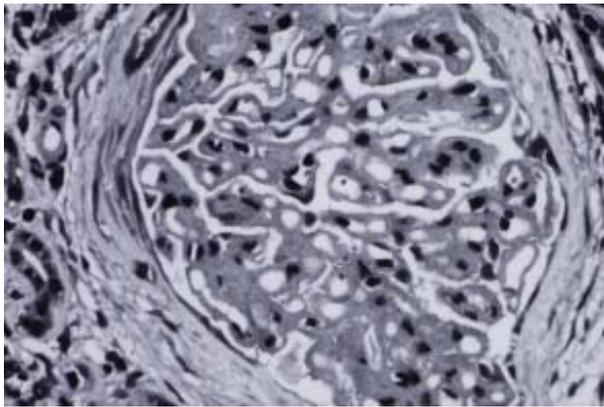


Figure 1. Light microscopic view showing a glomerulus with basement membrane thickening and lymphocytic infiltration. (Haematoxylin and eosin stain, ×400)



Figure 2. Contrast enhanced CT scan of thorax showing a normal sized thymic shadow without any radiological evidence of a thymoma.

Both myasthenia gravis and membranous nephropathy are mediated via immunoglobulin G and the membrane attack complex of the complement system. The most likely common link that triggers the autoimmune response is the abnormal thymus gland. Autoimmune diseases result from an imbalance between autoreactive lymphocytes and immunoregulatory mechanisms [3]. As the thymus gland suppresses the immune response against autoantigens, when its function is compromised, autoimmune syndromes may result. Two patients with the combination of myasthenia gravis and membranous

nephropathy had thymomas [1, 6]. Two others had thymic hyperplasia [1, 4]. In one patient both disorders showed improvement after thymectomy favouring the possible aetiological role of the deranged thymus [4].

When associated with nephropathy thymoma is known to be discovered several years after the diagnosis of glomerulonephritis [3], but thymic hyperplasia can occur with a normal sized thymus gland. It is likely that our patient with myasthenia gravis and membranous nephropathy has either thymic hyperplasia or a subclinical stage of thymoma.

Acknowledgements

We thank Dr A W M Wazil, Professor N Ranatunga and Dr Irani Dissanayake for advice and providing the renal biopsy images.

References

1. Valli G, Rogazzi GB, Cappellari A, Rivolta E. Glomerulonephritis associated with myasthenia gravis. *American Journal of Kidney Diseases* 1998; **31**: 350-5.
2. Scadding GK, Sweny P, Wilson SG, Havard CWH, Newsom-Davis J. Glomerulonephritis, thymoma and myasthenia gravis. *Quarterly Journal of Medicine* 1983; **52**: 187-93.
3. Karras A, Montpreville V, Fakhouri F, Griinfeld J, Leasavre P. Renal and thymic pathology in thymoma-associated nephropathy: report of 21 cases and review of the literature. *Nephrology, Dialysis and Transplantation* 2005; **20**: 1075-82.
4. Matsluda M, Miki J, Tabata K, Ikezoe M, Nishizawa N, et al. Myasthenia gravis with membranous nephropathy, successfully treated with extended total thymectomy. *Internal Medicine* 2000; **39**: 490-4.
5. Konishi T, Mikis, Yoshida A, Tei M. A post-thymomectomy case of myasthenia gravis which developed nephritic syndrome with membranous nephropathy during azathioprine administration. *Rinsho Shinkeigaku* 1996; **36**: 864-8.
6. Tomida C, Yamagata K, Ishizu T, Nakajima M, Doi M, et al. A case of nephritic syndrome associated with myasthenia gravis and malignant thymoma. *Nippon Jinso Gakkai Shi* 1999; **41**: 77-82.
7. Peiris JB, Gunathikake S, Wijeratne C, Gunatillake N. Myasthenia gravis in Sri Lanka. *Ceylon Medical Journal* 1991; **36**: 155-8.
8. Gunaratne PS, Larsen HA, Manatunga AK. Effectiveness of immunotherapy in myasthenia gravis: epidemiological evidence from Sri Lanka. *Neurology Asia* 2005; **10**: 39-45.