A RARE REPORT OF THYMOMA ASSOCIATED MYASTHENIA GRAVIS PRESENTING AS STEROID RESISTANT NEPHROTIC SYNDROME

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INTRODUCTION

- Myasthenia Gravis (MG) superimposed with proteinuria is a rare clinical event. Association of Minimal Change Disease (MCD) with MG may be related to the common pathophysiology of T Cell dysfunction.

- Thymoma is a rare mediastinal tumor having associations with different paranseoplastic syndromes one of which is myasthenia gravis

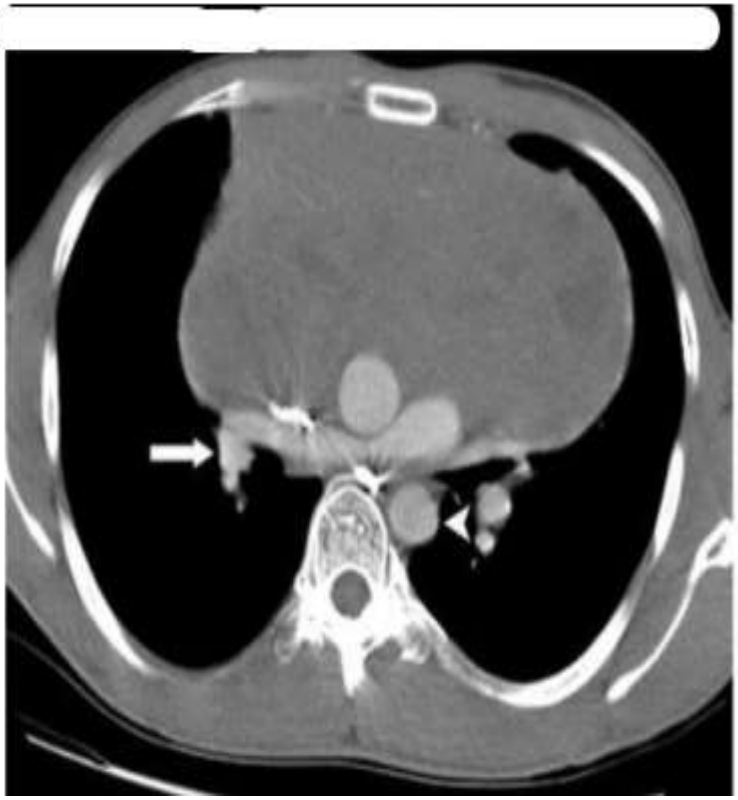
- Here we present a rare report of steroid resistant nephrotic sundrome following diagnosis of thymoma associated myasthenia gravis.

CASE REPORT

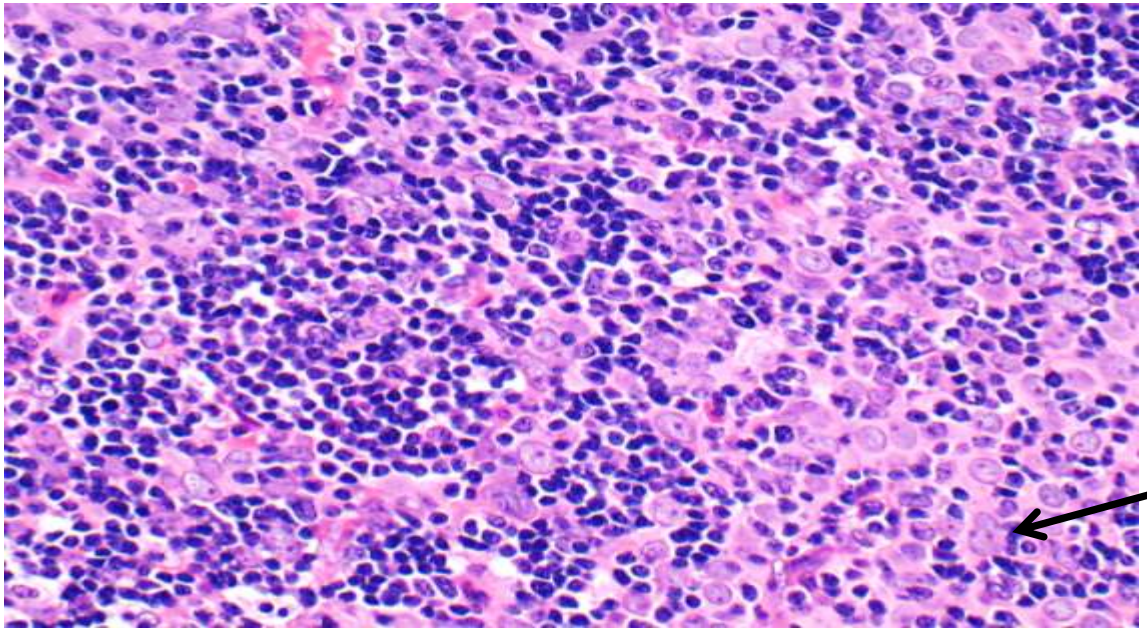
- 27 year old male was apparently well 9 months ago when he developed sudden onset weakness of facial muscles such that he had difficulty in chewing food and slurring of speech.
- Within one week of onset of these symptoms he had sudden onset simultaneous progressive weakness of all four limbs
- in suspicion of myasthenia gravis he underwent serological testing for Acetylcholine receptor antibodies which turned out to be positive.
- He also had a electrodiagnostic test performed which showed decremental response of more than 10 percent.

- He was started on pyridostigmine 60 mg four times a day and prednisolone 60 mg/day.For evaluation of underlying thymus involvement he underwent a contrast ct of chest which showed a well circumscribed anterior mediastinal mass without any necrosis or calcification.

- Subsequently a uncomplicated transternal thymectomy was performed on 2nd Jan 2021. A 12x7 fibrocystic thymoma was resected and sent for histopathological examination. The biopsy report was consistent with cystic thymoma (type B2 variant). He was also started on Azathiporine 100 mg/day. His symptoms improved over the next couple of months



- CHEST CT SHOWING ANERIOR MEDIASTINAL MASS.
- THERE WAS NO FEATURES OF CALCIFICATION OR NECROSIS



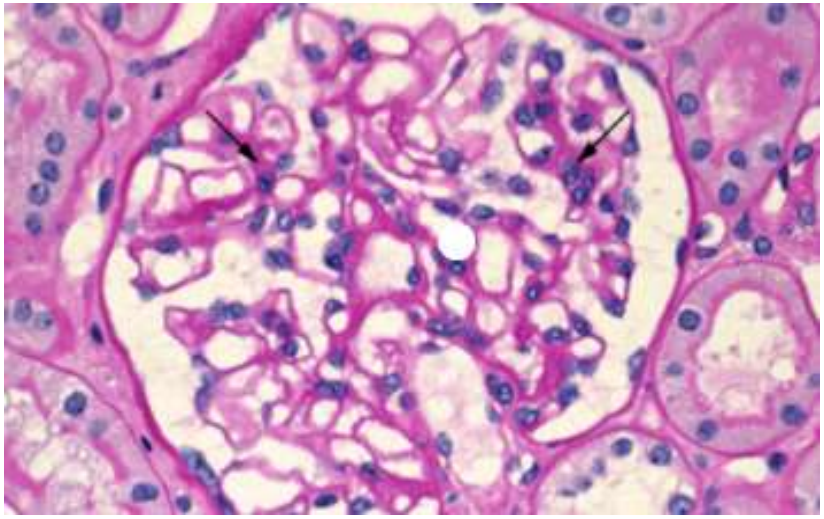
RESECTED SPECIMEN OF THYMUS
SHOWING MIXED NEOPLASTIC AND THYMUS CELLS S/O GRADE B2 THYMOMA

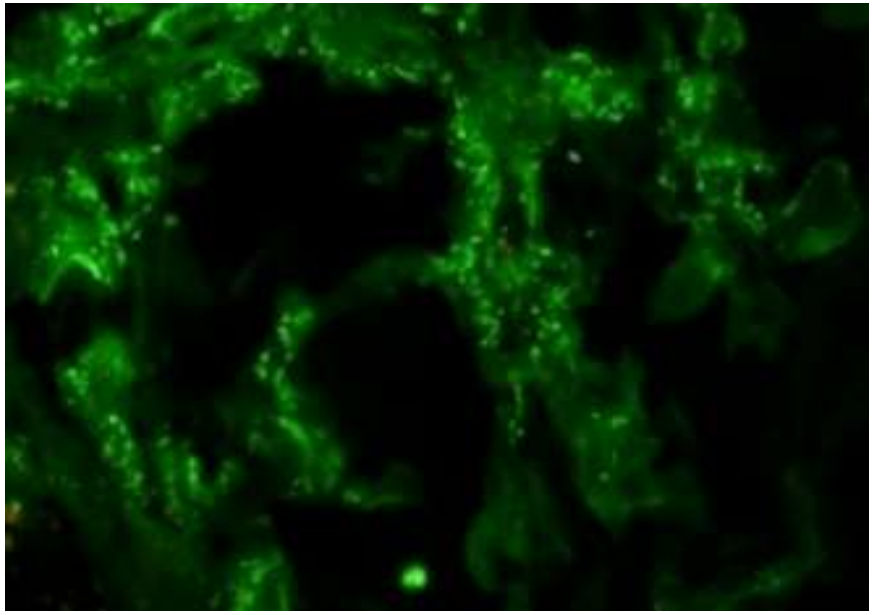
Malignant cells

- Around April 2021 he started having generalized body swelling which initially started in periorbital region and then progressed to involve bilateral lower limbs over the next one week. Simultaneously started complaining of frothuria. He was admitted in our hospital where on subsequent evaluation he was found to have

  1. Nephriotic range proteinuria (24 hour urine protein of 10.2 gm per day)
  2. hypoalbuminemia (albumin -1.9 g/dl) and
  3. dylipidemia (cholesterol 320 mg /dl and triglycerides 450)
  4. Ultrasonography of abdomen showed normal sized kidneys.

- In view of this he underwent an uneventful kidney biopsy which was suggestive of minimal change disease.





Light microscopy and Immunofluorescence findings on renal biopsy- normal findings

- Prior to this his steroid dose had been tapered to 30 mg per day. On findings of MCD on kidney biopsy his prednisolone dose was increased to 60 mg/day. He was subsequently discharged.

- On follow up after 2 months his lower limb swelling had decreased with decreased proteinuria (2.2 gm/day). However on subsequent visit couple month later his proteinuria was persistent (3 gm/day) and reappearance of swelling of both lower limbs.

- In view of this, he was labeled as steroid resistant started on second line therapy calcineurin inhibitors- tacrolimus at a dose of 0.05 mg /kg/day. With low dose Prednisolone 10 mg/day

- He was evaluated twice at one month interval and he had went to remission with proteinuria of 140 mg /day and s.albumin of 3.5 mg/dl

DISCUSSION

- In thymoma and thymic proliferation patients show immune dysregulations.
- Patients with Thymoma associated Myasthenia Gravis are started on immunosuppressants as first line therapy.
- In the presence of baseline immunosuppresed state what precipitates minimal change disease associated nephrotic syndrome in such cases is interesting.
- The pathophysiology is probably related to the shared common pathogenesis between the two disorders-an imbalance between T helper cells class 1 and 2

- From literature reviews, nephrotic syndrome as a systemic manifestation of thymic disease is rarely encountered.[4,5]

- The onset time of MCD in patients with thymoma is generally considered late. MCD had been reported to occur as late as 10 years after the diagnosis of thymoma and 15 years after MG

  - thymectomy might induce altered functions in lymphocytes and that take several years to manifest as MCD.

  - MCD-associated thymoma is caused by T cell dysfunction leading to the production of lymphokine, which increases the permeability of glomerular basement membrane.

- In our case the patient developed minimal change disease associated nephritic syndrome within 4 months of thymectomy.

- However unlike other similar case reports our patient didn't respond to steroid and was steroid resistant. He was started on second line therapy – tacrolimus to which he responded.

- Although Focal Segmental Glomerulosclerosis is a possibility it is unlikely since the thirteen glomeruli obtained for biopsy were also from the deep regions in the medulla.

- To our best of knowledge this is the second such case report from India and the only case of thymoma associated MG presenting as steroid resistant nephritic syndrome

CONCLUSION

- MCD mostly occurs in children and if diagnosed in adults, a search for a potential cause such as MG and other associated thymic disorders should be undertaken.

- In spite of its rarity, clinicians should keep in mind the association between MCD and MG and that MCD may not always occur long after the diagnosis of MG and may present as steroid resistant MCD

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