Beyond Conventional Therapies: Navigating the Complexity of Paraneoplastic Minimal Change Disease in Recurrent Steroid-Resistant Malignant Thymoma

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INTRODUCTION: THYMOMAS AND MCD

- Thymomas are uncommon mediastinal tumors arising from the thymus, representing only 0.2-1.5% of all malignancies
- Roughly 40% of thymomas are associated with paraneoplastic syndromes, 5.7% of which are secondary to nephrotic syndrome
- Of these cases, the most common renal pathology is Minimal Change Disease (MCD) at 47%
- Approximately 49 cases of MCD associated with thymoma are cited in the literature.
- Due to their rarity, determination of a standard treatment protocols is still under investigation
- First-Line Therapy: Corticosteroids
- Second-Line Therapy: Limited to Case Reports

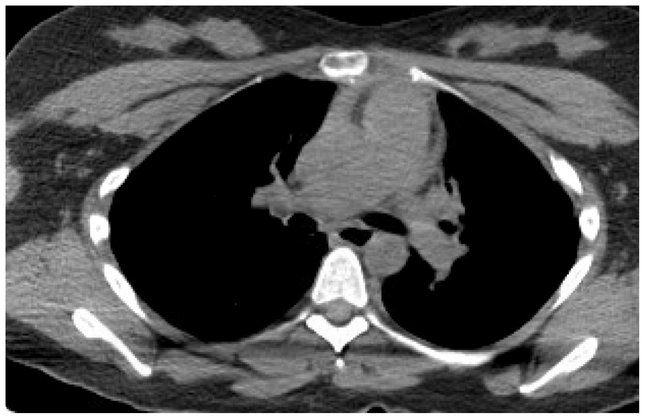

Figure 1. CT Chest concerning for metastatic pleural disease. Scarring and enlarged nodular pleural thickening of the left lung base,, and increase in multiple sub-centimeter subpleural nodules in the right upper lobe of the lung

THYMOMAS & PARANEOPLASTIC DISEASE

- Almost half of all thymomas present with paraneoplastic syndromes, most commonly myasthenia gravis (MG)
- 1/3 of patients with PNS have 2 or more conditions
- Thymus believed to be involved with immune reconstitution, thus most thymic malignancy involves autoimmune dysfunction
- Neuromuscular: MG, Limbic Encephalitis
- Hematologic: Red Cell Aplasia, Good Syndrome
- Paraneoplastic Nephropathy: MCD is most common in Thymoma vs Membranous Nephropathy in most others
- Thought secondary to systemic T cell dysfunction, though B cells may be involved
- Interestingly, Karras et al found that all patients with a B2 malignant phenotype who had thymic hyperplasia associated with MG had MCD as the associated renal disease

MINIMAL CHANGE DISEASE: WORKUP AND MANAGEMENT

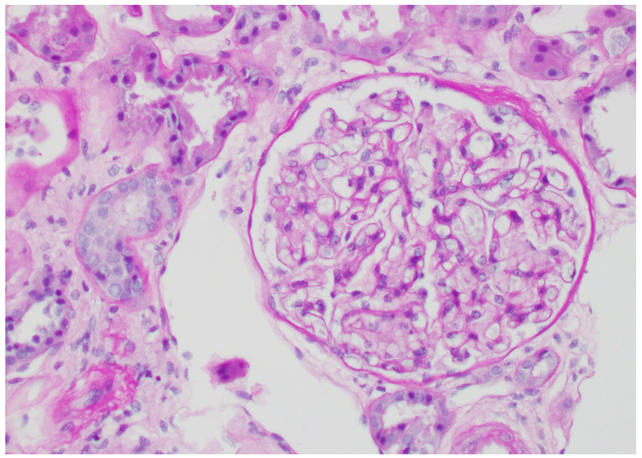

Figure 2. Renal biopsy showed diffuse podocyte effacement without immune complex deposits by electron microscopy, consistent with MCD. Mild glomerular enlargement and GBM linear attenuation also observed, likely diabetes related.

- Suspect MCD in any adult patient presenting with acute-onset signs and symptoms of nephrotic syndrome
- Nephrotic Syndrome: Edema, Substantial Proteinuria >3.5g/24hr, Hypoalbuminemia <30g/L
- Microscopic hematuria is common
- Recall: Hypercoagulability, Hyperlipidemia, Increased risk of Infection
- Biopsy: diffuse podocyte effacement
- Glucocorticoid Therapy leads to complete remission in 80-95% of adults with MCD
- Glucocorticoid-sparing regimens are available

CASE DESCRIPTION

- 37-year-old female with PMHx significant for metastatic thymoma (Stage IIB, 2012), status-post resection, with subsequent recurrence (2016), and paraneoplastic myasthenia gravis presented with periorbital, abdominal and lower extremity swelling
- Workup revealed nephrotic-range proteinuria (25g in 24hrs) and urine protein/creatinine >9.4
- Renal biopsy showed MCD
- Treatment with steroids was initiated, but her hospital course became complicated with concerns for myasthenic crisis and shock
- She underwent two rounds of IVIG in conjunction with corticosteroids, but her renal function continued to deteriorate. Pro/Cr Ratio worsened to >12
- Other complications: transudative pleural effusions, blood loss anemia secondary to hemorrhoids, abdominal cellulitis, neutropenia,
- She was offered various chemotherapeutic interventions, most of which she declined.
- She was ultimately started on Rituximab with resulting stabilization of her renal disease, and Lanreotide for treatment of her recurrent thymoma

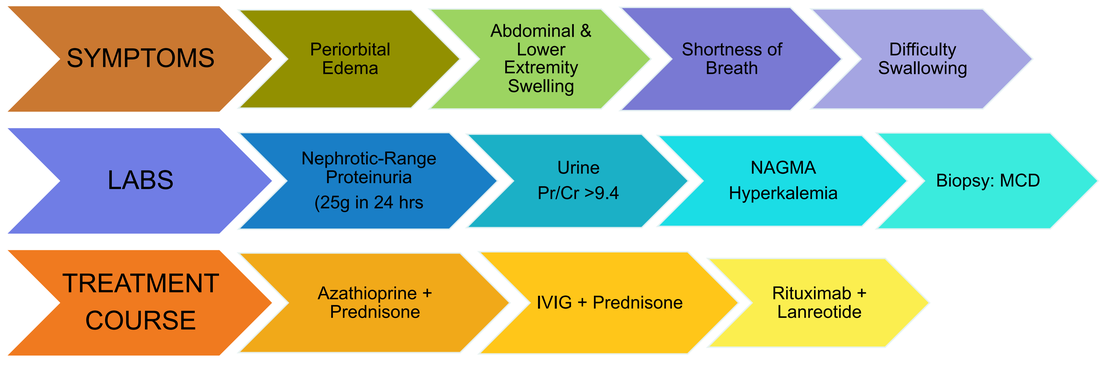

Figure 3. Visual summary of the patient's presenting symptoms, lab work, and treatment course. Treatment options limited by patient's agreement with with choice of medications.

MCD & THYMOMA: TREATMENT OPTIONS

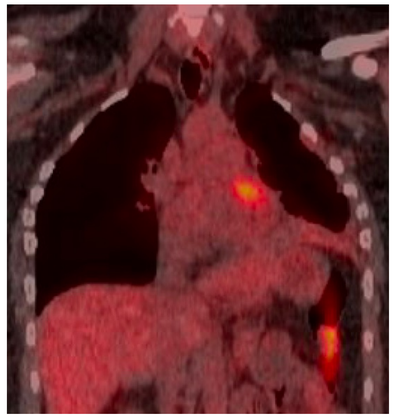

Figure 4. PET Thymus of recurrent disease. Left pleural base lesions, pleural thickening of costophrenic angle, and soft tissue density with low-grade uptake.

- High-Dose Steroids + Treatment of the Primary Tumor
- Adjunctive therapy: Cyclophosphamide, Azathioprine, etc
- Chemotherapeutic Agents: Cisplatin, Paclitaxel, etc
- Rituximab
- Prognosis: 28% may require long-term steroid or cyclosporin treatment; 17% require hemodialysis

DISCUSSION

- MCD associated with thymoma is rare, with speculation of disease course and treatment interventions largely limited to case reports
- The cause of MCD in patients with thymic disease is unclear, but evidence suggests dysregulation of the immune system may play a role.
- Steroid treatment is generally first-line, but other interventions such as chemotherapy and immunomodulators may be utilized in steroid-resistant and recurrent disease
- Responses to such immunosuppressive agents such as Rituximab, in combination with thymoma-specific management appears favorable
- Treatment requires individualized planning, discussions with patients regarding the benefits and risks of these medications, and consideration for a patient's other comorbidities.

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