UNUSUAL PRESENTATION OF MALIGNANT THYMOMA ASSOCIATED NEPHROTIC SYNDROME WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS: A CASE REPORT

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Abstract

Paraneoplastic syndromes (PS) are the consequences of hormones or immune cross-reactivity produced by a tumor. Nephrotic syndrome (NS) is an extremely rare PS resulting from a thymoma. Here, the case of a 55-year-old woman presenting progressive generalized edema and foamy urine is reported. The patient's chest CT scan showed anterior mediastinum with intramural punctate calcification size 8.6x7.0x10.2 cm. The case was reviewed at the multi-dispensary team conference, and the clinical diagnosis was an unusual presentation of malignant thymoma known as NS. After that, a thymectomy and kidney biopsy was performed. Histopathologic examination showed Thymoma type B and focal segmental glomerulosclerosis, respectively. Therefore, we considered it paraneoplastic nephrotic syndrome (PNS), without glucocorticoids, immunosuppressants or other drugs to treat NS. After the thymectomy, her clinical spontaneous resolved at the first follow-up, proposing a causative relationship between the two conditions.

Keywords: Malignant thymoma-associated nephrotic syndrome, Paraneoplastic nephrotic syndrome

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Introduction

Undoubtedly, one-third of the patients with thymoma also present paraneoplastic syndrome. Those manifestations are the effects of hormones or immune cross-reactivity produced by malignancy. The most common condition of those manifestations is myasthenia gravis (MG). Other associated autoimmune disorders include thymoma-associated multiorgan autoimmunity, pure red cell aplasia, etc.[1] However, nephrotic syndrome (NS) is extremely rare, resulting from a thymoma. This clinical syndrome includes nephrotic range proteinuria (24-hour urine protein>3 g/24 hours), hypoalbuminemia (serum albumin <2.5 g/dL), generalized edema, and hyperlipidemia (total cholesterol >350 mg/dL).[2] In the related reports of paraneoplastic nephrotic syndrome (PNS), almost all (80% of cases) of glomerular lesions involve minimal change disease or membranous glomerulonephritis.[3-10]

Moreover, focal segmental glomerulosclerosis (FSGS) is a type of kidney disease characterized by scarring or sclerosis in specific areas (segments) of the kidneys' filtering units called glomeruli, one of the leading causes of NS among children and adults. However, the relationship between the two conditions as PNS of thymoma is scarce. Here, we present a case report of NS associated with thymoma, kidney biopsy-proven FSGS, and clinical improvement after performing a thymectomy.

A case report

A 55-year-old female was referred to an Internal Medicine Inpatient Department for a consultation based on suspicion of NS. The patient reported the onset of progressive generalized edema and foamy urine for two weeks. Her family history showed no particular diseases, and she was physically fit in the past. Her physical examination showed that she had eyelid edema and pitting edema in both legs and arms. She attended a primary care hospital for a workup. The laboratory data at admission are shown in **Table 1.** The following symptoms were associated with this case: albuminuria, hyperlipidemia, edema and hypoalbuminemia. These clinical findings are consistent with the diagnosis of NS.

Unfortunately, initial chest x-ray images showed a heterogeneous well-circumscribed mass

Table 1. Laboratory data

Variable	At admission	After thymectomy
Blood urea nitrogen (BUN) (mg/dL)	31	10
Creatinine (Cr) (mg/dL)	1.59	1.03
Albumin (g/dL)	1.4	1.7
Globulin (g/dL)	2.5	3.2
Total cholesterol (mg/dL)	619	
Urine protein 24 hours --g/24 hours	5.3	
urine protein creatinine ratio (UPCR) (g/g Cr)	4.6	1.4
Urine analysis		
- Urine protein	3+	
- Urine red blood cells (cells/HPF)	3-5 (no dysmorphic RBC)	
- Urine white blood cells (cells/HPF)	5-10	
HBsAg, Anti-HCV, Anti-HIV	negative	
Antinuclear antibody (ANA)	Positive 1:80	
Beta-human chorionic gonadotropin (beta-HCG) (MU/ml)	1.31	
Alpha-fetoprotein (ng/ml)	2.75	

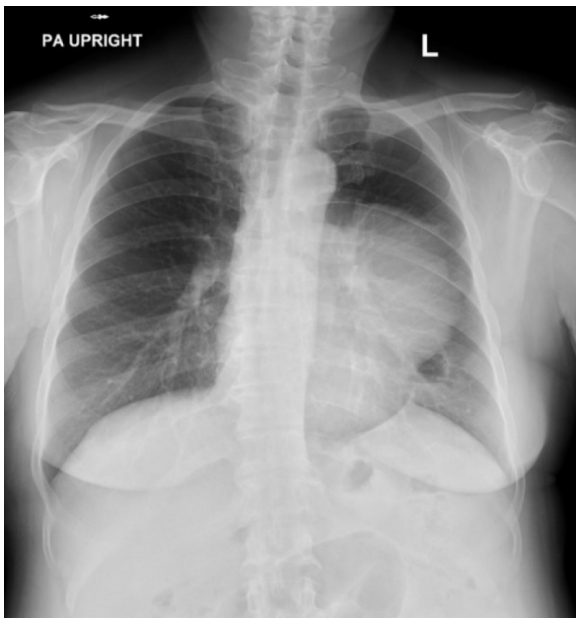

Figure 1. Chest x-ray images showed a heterogeneous well-circumscribed mass at the left upper lung, of which the silhouette lay on the left heart border with an obtuse angle. The estimated diameter from the chest X-ray was 10.3 cm.

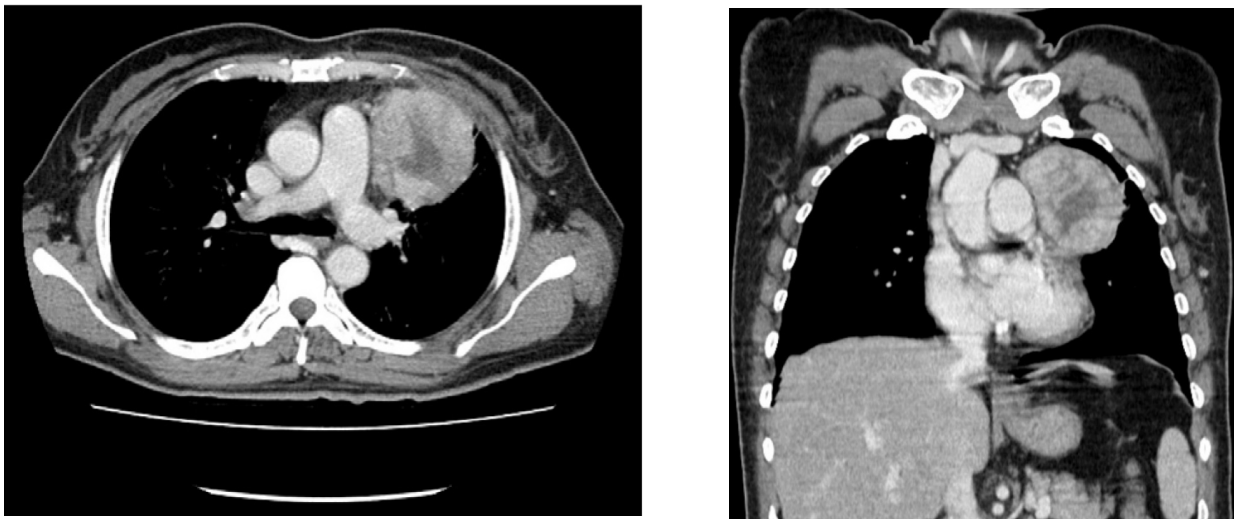

Figure 2. CT chest with the whole abdomen showed the lobular shape of heterogeneously enhancing necrotic mass at the left-sided anterior mediastinum with intramural punctate calcification size 8.6x7.0x10.2 cm

at the left upper lung, of which the silhouette lay on the left heart border with an obtuse angle. The estimated diameter from the chest X-ray was 10.3 cm **(Figure 1).** Then she underwent a computerized tomography (CT) scan of the chest including the whole abdomen, to work up the mediastinal mass. The CT chest with the whole abdomen showed the lobular shape of heterogeneously enhancing necrotic mass at the left-sided anterior mediastinum with intramural punctate calcification size 8.6x7.0x10.2 cm **(Figure 2).** No obviously observed uterine mass, lungs, liver, or bone metastasis was shown. Her clinical data and CT scan were reviewed during a multidisciplinary team conference, and the consensus summary concluded an NS was associated with a thymic tumor. Finally, she underwent a thymectomy for total tumor removal. A kidney biopsy was performed for a further workup to determine the cause of NS. The kidney biopsy suggested FSGS **(Figure 3)** and immunofluorescence microscopy findings. All

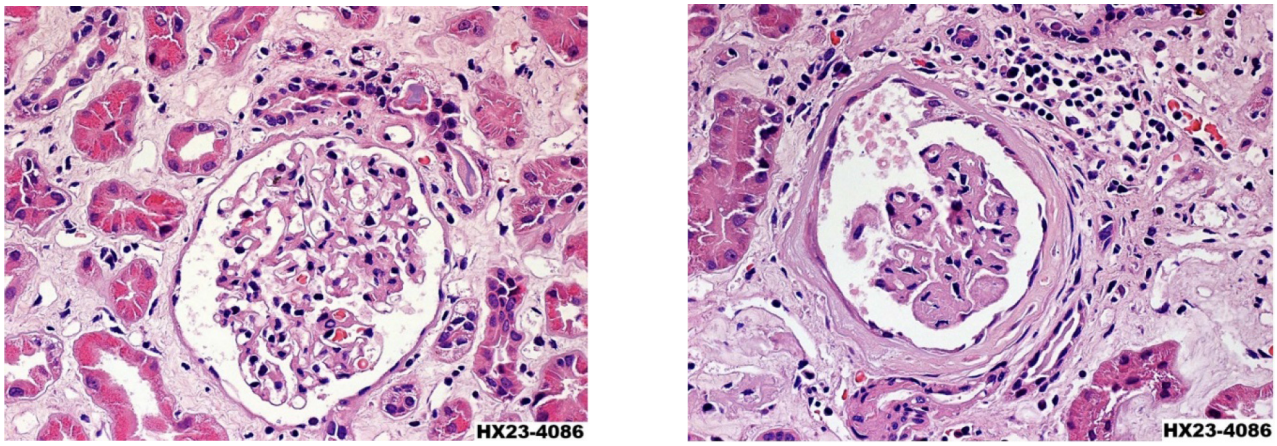

Figure 3. Light microscopy findings of the kidney biopsy identified seven glomeruli. Six glomeruli showed mild expansion of some mesangial areas with no definite change in the thickness of the capillary wall. One glomerulus with periglomerular fibrosis showed mesangial sclerosis. Interstitial edema and mild diffuse with focal dense lymphomonocytic infiltrate were observed. No vasculopathy was present. Immunofluorescence microscopy findings: all nine glomeruli in each frozen section showed no immune complex deposition.

nine glomeruli in each frozen section showed no deposition of the immune complex. Unfortunately, electron microscopy was unavailable to diagnose and evaluate the FSGS. The thymectomy pathology results showed a thymic epithelial tumor, consistent with thymoma type B **(Figures 4 and 5).**

We diagnosed it as PNS without glucocorticoids, immunosuppressants or other drugs used to treat the NS. After the thymectomy, the first follow-up on her urine protein creatinine ratio (UPCR) at the outpatient unit decreased from 4.6 at the first visit to 1.4, and generalized edema was improved, consistent with the body weight lowering from 70 to 62 kg. Moreover, the serum albumin continued rising from 1.4 gm/dL to 2.2 gm/dL. Consequently, in long-term follow-up, the overall clinical of NS remained in remission.

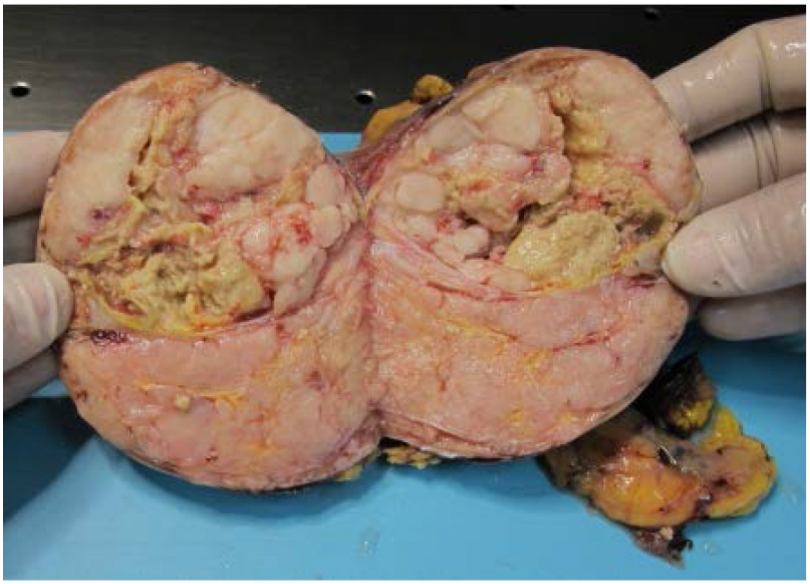

Figure 4. Gross examination of the thymoma showed a well-circumscribed mass surrounded by a partial fibrous capsule and focal irregular borders. Cut surfaces showed a grey, tan mass with lobulated and variegated appearance and revealed hemorrhage and necrosis.

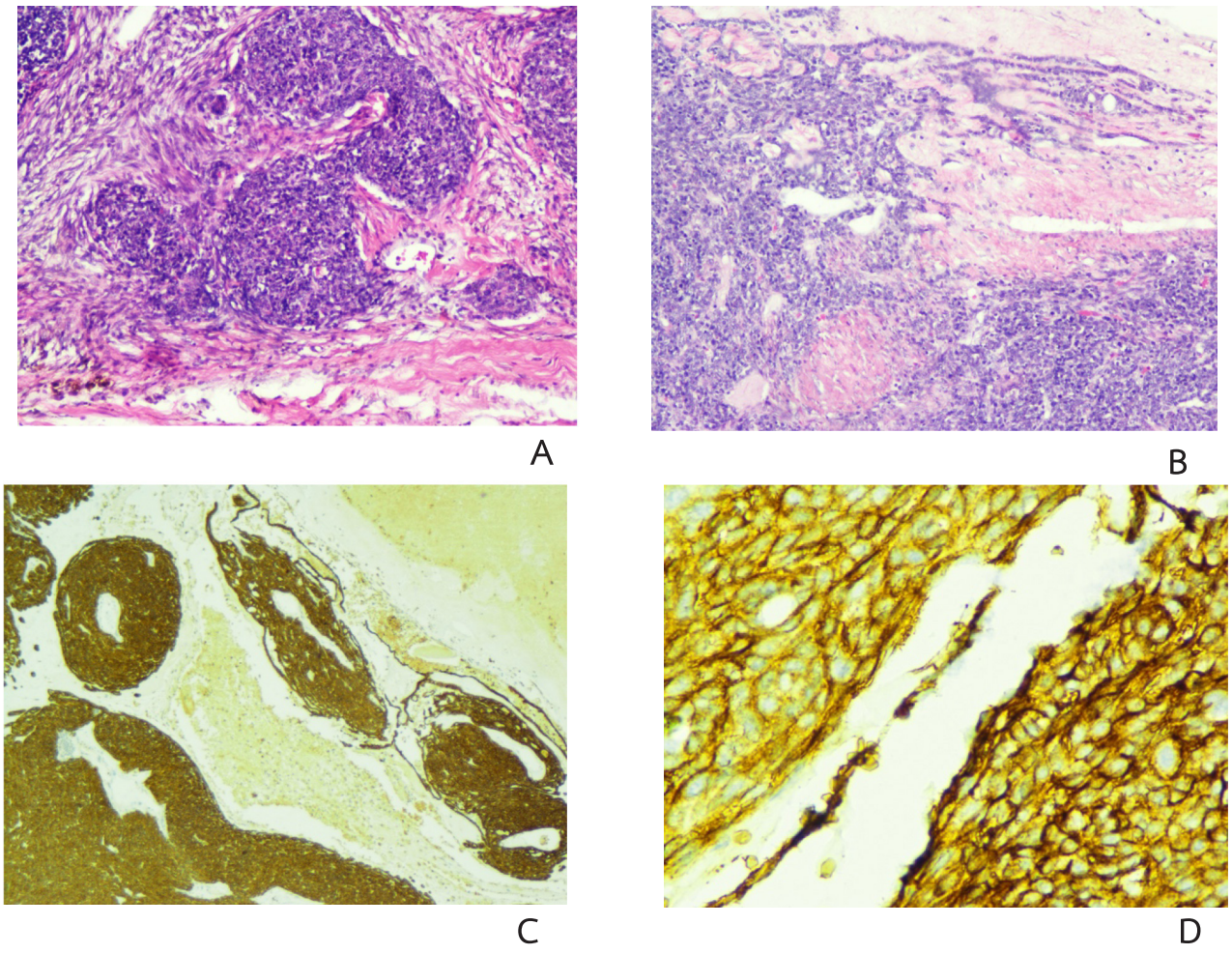

Figure 5. Thymectomy pathology results showed a thymic epithelial tumor, consistent with thymoma type B (A, B), and GLUT1 was strongly positive in thymic carcinoma (C, D).

Thymoma is associated with varied paraneoplastic syndromes such as MG and pure red cell aplasia [1] including case reports of PNS from thymoma. The first reported association of cancer and NS by Lee JC in 1966[11] showed the incidence of PNS during ten years of study was 10%, and nine of eleven histopathologic kidneys were membranous glomerulonephritis. Although the relationship between malignancy to NS remains unclear, the study was the first to describe this relationship due to the immunologic response. Thymoma and NS caused by T-cell mediated are associated with the paraneoplastic explanation.[3-7] Thus, cross-reaction has been observed between eluates from glomeruli and tumor antigens, providing evidence for the role of the immune complex in paraneoplastic glomerulopathy. [12]

Nevertheless, in this case, the patient uncovered a thymoma, and then she developed NS. The kidney biopsy showed FSGS. In this case, clinical findings were like the ordinary NS; the histopathologic result was unusual as PNS. After the thymectomy, overall clinical symptoms improved, suggesting a causative relationship between the two conditions. Accordingly, dysfunction of the immune system, particularly T lymphocytes caused PNS and damaged the podocytes by inflammation due to substances produced by the tumor cells such as cytokines or growth factors that could damage the kidney tissue and disrupt the normal functioning of the glomeruli. This damage led to the formation of scar tissue or sclerosis. FSGS could be a more aggressive disease, with a higher risk of progression to end-stage kidney disease and the need for renal replacement therapy. This case report confirmed that FSGS was one of the PNS.

Finally, the pathophysiology of FSGS is complex and multifactorial. Therefore, further research is needed to understand this disease's mechanisms and develop effective treatments. Moreover, PNS is a rare disorder requiring a multidisciplinary approach involving oncologists and nephrologists to manage underlying cancer and any associated kidney damage.

This case report demonstrates that FSGS is one of the PNS of thymoma. The clinical of NS spontaneously resolved after thymectomy, proposing a causative relationship between the two conditions. Her UPCR decreased from 4.6 to 1.4, and the serum albumin continued rising from 1.4 to 2.2 g/dL. Therefore, when we encounter patients with PNS, maintaining awareness of FSGS is important. Thus, early recognition, work-up and treatment of underlying cancer can preserve the patient's kidneys.

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