Fibrillary Glomerulonephritis Associated with Thyroid Papillary Microcarcinoma: A Case Report

Tiroid Papiller Mikrokarsinoma Eşlik Eden Fibriller Glomerülonefrit: Olgu Sunumu

ABSTRACT

In this report, we describe a case of fibrillary glomerulonephritis associated with thyroid papillary microcarcinoma arising in a 54-year-old female patient suffering from Hashimoto's thyroiditis. The patient presented with mild edema and a palpable mass on right thyroid lobe. Examinations revealed 1053 mg daily protein excretion and an approximately 1 cm highly vascularized thyroid nodule. She underwent total thyroidectomy and histopathological examination provided evidence of the encapsulated follicular variant of multifocal thyroid papillary microcarcinoma. Thereafter, percutaneous kidney biopsy identified the fibrillary glomerulonephritis for which renin angiotensin system blockage was targeted and, in time, daily protein excretion decreased. The favorable clinical outcome after treatment of carcinoma suggests that there might be a pathophysiological link between autoimmune/malignant pathology and fibrillary glomerulonephritis development.

KEY WORDS: Fibrillary glomerulonephritis, Proteinuria, Thyroid papillary microcarcinoma

ÖZ

Bu makalede, Hashimato tiroiditi tanısı ile takip edilmekteyken, tiroid papiller mikrokarsinomuna eşlik eden fibriller glomerülonefrit tanısı alan 54 yaşında kadın hastayı sunuyoruz. Hasta, alt ekstremitede ödem ve sağ tiroid lobuna uyan boyun bölgesinde ele gelen şişlik yakınmaları ile başvurdu. Yapılan değerlendirmesinde, 1053 mg/gün proteinürisi ve yaklaşık 1 cm ebatında, yoğun damarlanma gösteren tiroid nodülü tespit edildi. Total tiroidektomi yapılan hastanın patolojisi multifokal tiroid papiller mikrokarsinomunun enkapsüle foliküler varyantı olarak raporlandı. Ardından yapılan böbrek biyopsisinde fibriller glomerülonefritle uyumlu bulgular saptandı. Renin anjiyotensin sistem inhibitörü başlanan hastanın zamanla proteinüri düzeylerinde gerileme izlendi. Kanserli dokunun ortadan kaldırılması sonrası klinik tabloda gözlenen olumlu seyir, otoimmün/malign patoloji ile fibriller glomerülonefrit gelişimi arasında patofizyolojik bir ilişki olabileceği ihtimalini akla getirmektedir.

ANAHTAR SÖZCÜKLER: Fibriller glomerülonefrit, Proteinüri, Tiroid papiller mikrokarsinomu

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INTRODUCTION

Fibrillary glomerulonephritis (FGN) is a rare glomerular pathology with an incidence of 0.8 to 1.5 % in native kidney biopsy specimens of the adults (1). The clinical involvement is almost exclusively confined to the kidney with rare exceptions and the affected patients present with increased protein excretion, hypertension, hematuria and renal insufficiency (2). The characteristic pathological appearance is deposition of straight fibrillary structures measuring generally 16-24 nanometers in thickness in the mesangium and/or glomerular basement membranes. Their larger size and lack of reactivity with Congo red staining differ these fibrils from amyloid deposits. Immunohistochemical staining is positive for immunoglobulin G and complement factor 3. FGN is generally accepted as an idiopathic glomerular pathology. However, recent data point to the association of FGN with autoimmune diseases and malignancy (3-5). In this report, we described a case

of FGN associated with thyroid papillary microcarcinoma in a 54-year-old female suffering from Hashimoto's thyroiditis.

CASE REPORT

A 54-year-old woman presented to our nephrology department with a complaint of edema. She had history of Hashimoto's thyroiditis and essential hypertension and was on 5 mg amlodipine treatment. On admission, arterial blood pressure was 154/110 mmHg. Physical examination revealed mild pretibial edema and a 1.3x0.5 cm sized palpable mass on her right thyroid lobe. Her laboratory test results were as follows; hemoglobin: 13.6 g/dl, white blood cell count: 8750/mm^3, thrombocytes: 159000/mm^3, PT-INR: 0.91, blood urea nitrogen: 17 mg/dl, serum creatinine: 0.7 mg/dl, serum albumin: 4.1 g/dl, fasting blood glucose: 82 mg/dl, free triiodothyronine (T3): 3.25 pg/mL, free thyroxine (T4): 1.19 ng/L, thyroid-stimulating hormone: 2.02 uIU/L, immunoglobulin A: 352 mg/dl, complement 3: 88 mg/dl, complement 4: 32 mg/dl. Urine examination revealed normal sediment with a pH of 5.5 and density of 1013. Daily urinary protein excretion rate was 1053 mg (NR < 150 mg/day). Serum and urine immune-fixation electrophoreses were in normal ranges. Hepatitis B, C and human immune deficiency viruses, anti-nuclear antibodies and anti-glomerular basement membrane antibodies were all negative.

Renal ultrasonography revealed normal-sized kidneys with bilaterally increased parenchymal echogenicity. Thyroid ultrasonography revealed a 1.1x0.9x1.1 cm hypoechoic, non-homogeneous, highly vascularized nodule in right lobe of thyroid gland. Fine needle aspiration biopsy detected papillary microcarcinoma and total thyroidectomy was planned. During the perioperative period, clinical follow up was scheduled for increased protein excretion and amlodipine therapy was switched to 160 mg valsartan therapy. The patient underwent total thyroidectomy and histopathological examination identified encapsulated follicular variant of multifocal thyroid papillary microcarcinoma with neither lymphovascular nor capsular invasion.

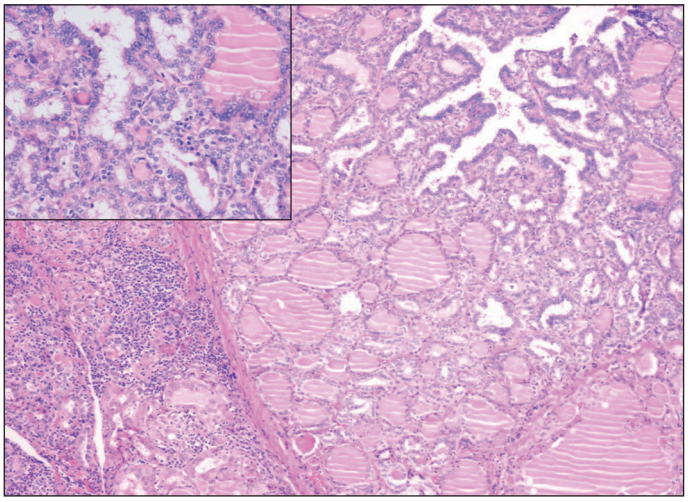

Figure 1: *Papillary microcarcinoma- encapsulated follicular variant with the surrounding thyroid parenchyma showing Hashimoto's thyroiditis, H&Ex100 (inset: orphan annie nuclei of the thyroid papillary carcinoma, H&Ex400).*

Thyroid hormone replacement therapy was started and she was put on 100 millicuries radioactive iodine therapy. No residual tumor was detected on post-ablative scanning. Eight months later, she was re-consulted to nephrology department because of increased protein excretion rate. Her arterial blood pressure was under control and physical examination was normal without pretibial edema. Renal biopsy was performed because of 2116 mg daily protein excretion. Light microscopic evaluation revealed two globally sclerotic glomeruli among 15 glomeruli. Periodic Acid-Schiff staining was positive, Congo red staining was negative and a mild increase in the mesangial cells with eosinophilic mesangial expansion was remarkable in preserved glomerular structures. Immunofluorescence staining revealed immunoglobulin G, complement factor 3 and complement factor 4 depositions in mesangium. On electron microscopy, diffuse and randomly arranged fibrillary deposits were spotted in mesangial and subendothelial areas. Focal splitting and fibrillation of glomerular basement membrane were remarkable (Figure 1, 2A-D). The diagnosis was fibrillary glomerulonephritis.

Initially, a conservative approach was planned due to papillary microcarcinoma history and her valsartan dosage was increased up to 320 mg per day. We observed a partial remission in daily protein excretion rate in time. Renal function tests are still within normal limits and the protein excretion rate is eventually 800 mg per day after twenty-four months of follow up.

DISCUSSION

In the medical literature, there are limited data regarding the association between thyroid carcinoma and glomerulopathies. Previously, Han et al. (6) published a case having simultaneous development of thyroid papillary carcinoma and membranoproliferative glomerulonephritis. We herein presented a patient who had history of Hashimoto's thyroiditis and has taken the diagnosis of thyroid papillary microcarcinoma during the investigation period of increased protein excretion. As far as we know, our case is the second reported case with thyroid papillary microcarcinoma and concomitant FGN. The first patient was one among 66 FGN patients reported by Samih et al. (5). FGN is known as an idiopathic glomerular pathology. However, the abovementioned largest study in medical literature showed that, one third of FGN patients had a history of autoimmune diseases or malignancy (5). Currently, we do not know whether this association is causal or not but the association between Hashimoto's thyroiditis and papillary thyroid carcinoma is well established. Depending on these data, in our case, we considered

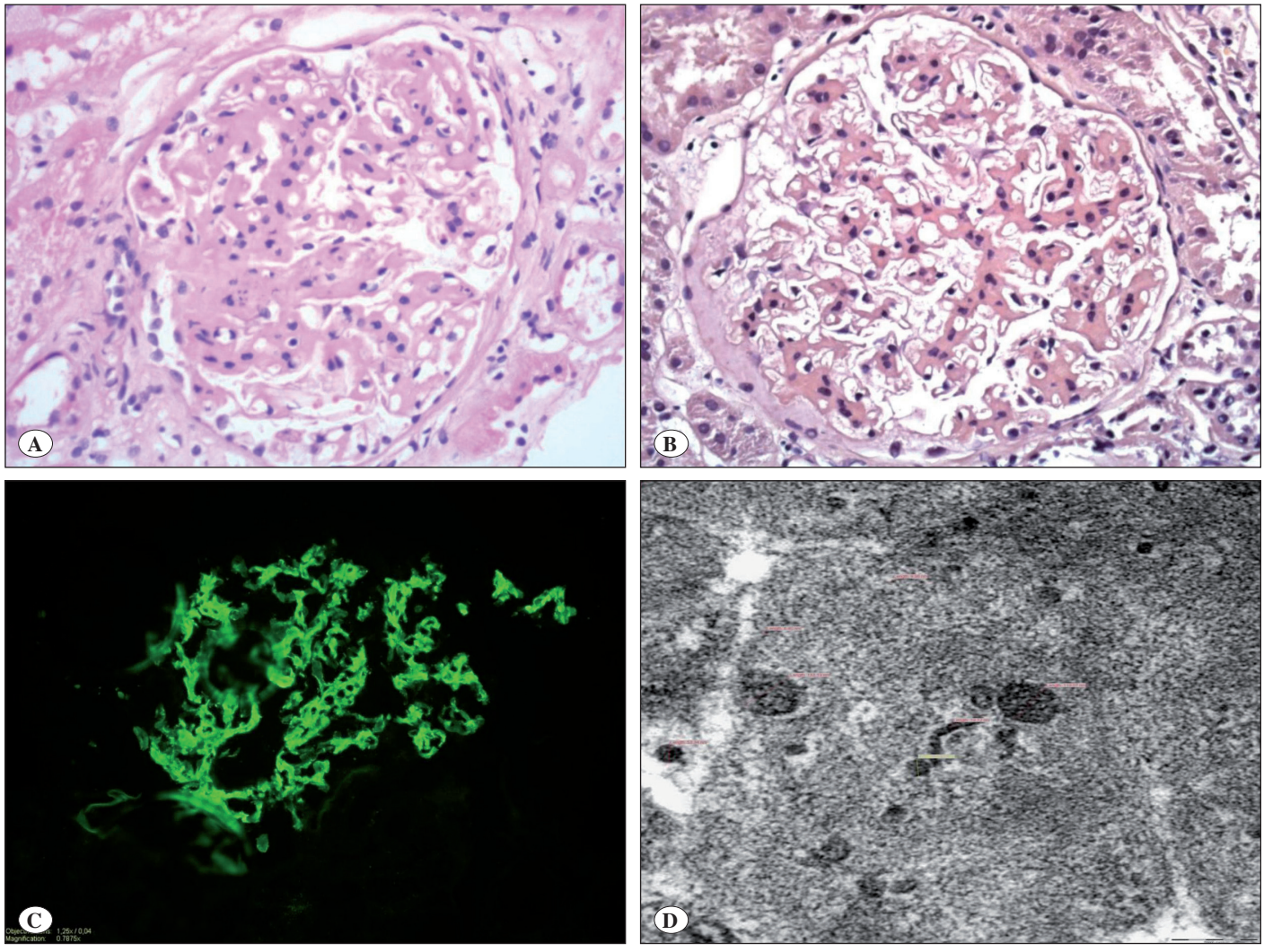

Figure 2: A) *Light microscopy showing prominent, acellular mesangial expansion partly in the form of nodular glomerulosclerosis in a patient with fibrillary glomerulonephritis, H&E x200.* ***B)*** *Congo red stain was negative in the expanded mesangium, x200.* ***C)*** *Immunofluorescence revealed 3+ staining with IgG mostly in the glomerular mesangium with accompanying partial staining along glomerular basement membrane.* ***D)*** *Electron microscopy showing randomly arranged fibrils in the glomerular mesangium, uranyl acetate x10000.*

that, chronic autoimmune activation on the basis of Hashimoto's thyroiditis could have an influence on both the pathogenesis of papillary microcarcinoma and FGN development. The favorable clinical outcome of our patient after treatment of carcinoma suggested that there might be a pathophysiological link between malignant pathology and FGN development. Nevertheless, this issue should be addressed in further observations and investigations.

Clinical remission rates are not promising for FGN patients and almost one half of the patients progress to end stage kidney disease within five years (5). In our case, the immediate schedule including thyroidectomy operation and subsequent iodine ablation therapy caused a delay in management of proteinuria and the patient received an FGN diagnosis eight months after the thyroidectomy operation. Actually, immunosuppressive agents such as corticosteroids, cyclophosphamide, cyclosporine and mycophenolate could be tried for management of idiopathic FGN cases (5, 7). However, management of patients with concomitant autoimmune disorders or malignancy is unclear. Previous data suggest that treatment of accompanying disorder could result in regression of renal histopathology and improvement in clinical findings (7). In our case, we avoided immunosuppressive therapy due to the recent carcinoma diagnosis. We initially planned a conservative approach and increased the dosage of valsartan therapy since our patient had preserved kidney functions, lower percentage of sclerotic glomeruli and no adverse clinical outcomes in the setting of proteinuria. Fortunately, we achieved a decrease in protein excretion with preserved kidney functions during the clinical course.

In conclusion, we considered that this good clinical outcome likely supporting a probable pathophysiological association between autoimmune/malignant pathology and FGN development.

REFERENCES

1. Iskandar SS, Falk RJ, Jenette JC: Clinical and pathological features of fibrillary glomerulonephritis. Kidney Int 1992;42:1401-1407
2. Hvala A, Ferluga D, Vizjak A, Koselj-Kajtna M: Fibrillary noncongophilic renal and extra-renal deposits: A report of 10 cases. Ultrastruct Pathol 2003;27:341-347
3. Abraham G, Bargman JM, Blake PG, Katz A, Oreopoulos DG: Fibrillary glomerulonephritis in a patient with metastatic carcinoma of the liver. Am J Nephrol 1990;10:251-253
4. Kim HJ, Kang SW, Park SJ, Kim TH, Kang MS, Kim YH: Fibrillary glomerulonephritis associated with Behçet's syndrome. Renal Failure 2012; 34:637-639
5. Nasr SH, Valeri AM, Cornell LD, Fidler ME, Sethi S, Leung N, Fervenza FC: Fibrillary glomerulonephritis: A report of 66 cases from a single institution. Clin J Am Soc Nephrol 2011;6:775-784
6. Han ST, Choi SO, Song SH, Kim JS, Eom MS, Lee JI, Kim MK, Han BG, Yang W: Membranoproliferative glomerulonephritis associated with papillary thyroid carcinoma. The Korean Journal of Nephrology 2011;30:183-186
7. Rosenstock JL, Markowitz GS, Valeri AM, Sacchi G, Appel GB, D'Agati VD: Fibrillary and immunotactoid glomerulonephritis: Distinct entities with different clinical and pathologic features. Kidney Int 2003;63:1450-1461