



## Atypical Presentation of C1q Nephropathy in an Adolescent with Initial Hypertension

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### Abstract:

**Background:** Hypertension is the leading cause of mortality worldwide. Besides its already high disease burden, also the prevalence in children is increasing. Major presentation of hypertension among young patients is as essential or primary hypertension, while only a minority of patients present as secondary hypertension. Characterized by mesangial immune deposits, C1q nephropathy is a relatively rare glomerular disease with a dominant or co-dominant staining for C1q, presenting often with proteinuria in the nephrotic range. **Case Report:** We present an 18-year-old Turkish boy who presented with hypertension five years ago in the absence of proteinuria followed by a renal biopsy five years later demonstrating dominant mesangial deposits of C1q. **Conclusion:** We suggest that C1q nephropathy may present with hypertension before the manifestation of proteinuria and thus, C1q nephropathy should be kept in mind in patients presenting with hypertension. More specialized tests should be performed when diagnosing primary hypertension. We suggest that every patient with hypertension should be carefully followed up for C1q nephropathy.

**Key words:** Biopsy, Humans, Hypertension, Kidney Glomerulus, Proteinuria.

### Introduction

Pediatric hypertension often emerges from underlying renal, cardiovascular, or endocrine disease. Thirty to 60 percent of hypertensive children have an identifiable etiology [1]. Most common causes of pediatric hypertension are renal parenchymal diseases, while cardiovascular and endocrine etiologies are less frequent. Compared to adults, pediatric hypertension is more frequently secondary. Hence, children should undergo vigorous laboratory and radiologic evaluation [2]. Forty to 70 percent of hypertensive children do not have an identifiable etiology and are diagnosed with

primary hypertension. C1q nephropathy is an uncommon glomerular disease. It is characterized by mesangial immune deposits with dominant or co-dominant staining for C1q. The entity was first described by Jennette and Hipp in 1985 [3]. C1q nephropathy is usually encountered in teens and young adults during the evaluation of nephrotic range proteinuria [4]. It is claimed that C1q nephropathy frequently presents with proteinuria in the nephrotic range and its response to corticosteroid therapy is unpredictable or poor [5]. In this paper we present a patient who was followed up with the diagnosis of

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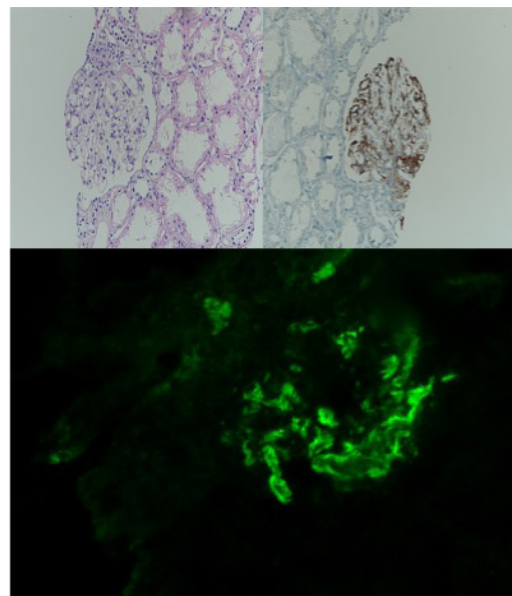
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primary hypertension for five years and ultimately emerged as C1q nephropathy with proteinuria.

### Case Report

A 12 years-old boy presented with hypertension. His past medical history was not significant. He was delivered as a full-term baby without complications and all his mental milestones were according to his age. He was not taking any medicines nor had any known drug allergies. Family history of hypertension or renal disease was negative. His physical examination at admission was unremarkable, except for high blood pressure. During his physical examination, his body weight, height and blood pressure were recorded as 48 kg (50-75<sup>th</sup> percentile), 149 cm (25-50<sup>th</sup> percentile), and 123/81 mmHg (stage 1) respectively. His body mass index (BMI) was calculated as 21.9 kg/m<sup>2</sup> (50-75<sup>th</sup> percentile) and femoral pulses were equal. Other physical findings of the patient were normal. Laboratory investigations were performed to elucidate causes of hypertension and possible target organ injury. All renal function tests, blood gas analysis, electrolytes, and urinary findings were in the normal range. A significant obliteration was not detected in renal artery on renal Doppler ultrasonography. His fundus examination findings were consistent with grade-one hypertensive retinopathy. On his cardiac examination, 40.9 g/m<sup>2</sup> increase was detected in left ventricle wall thickness. Microalbuminuria level examined for renal involvement was found normal. Ocular and cardiac involvements related to hypertension were observed. Plasma renin (1.1 ng/ml/hour) and aldosterone (120 pg/mL) levels were in the normal range. Endocrine causes of hypertension were excluded as diurnal ACTH, cortisol, thyroid function tests, and VMA were detected normal. Biochemical investigations revealed the following results: total protein 6.2 g/dL, albumin 4.2 g/dL, total cholesterol 196 mg/dL (90-95<sup>th</sup> percentile), triglyceride 93 mg/dL (75-90<sup>th</sup> percentile), high-



**Fig.1 (A):** Light microscopy showing unremarkable looking glomeruli. **(B):** Light microscopy with normal renal interstitium and tubules and a normal-looking arteriole (Trichrome stain). **(C):** Immunofluorescence staining presenting dominant (3+) mesangial C1q deposits.

density lipoprotein 50 mg/dL (75-90<sup>th</sup> percentile), low-density lipoprotein 107 mg/dL (50-75<sup>th</sup> percentile), and lipoprotein A level 101 mg/dL ( $n < 30$  mg/dL), serum urea 22 mg/dL, creatinine 0.4 mg/dL. Urine-specific gravity was 1.015. Urinalysis revealed a proteinuria of 2 mg/m<sup>2</sup>/hour. Treatment with an angiotensin receptor inhibitor was initiated and the patient was scheduled for regular followed up.

The patient's blood pressure was under control during the follow-up period. Five years later the patient developed proteinuria of 22 mg/m<sup>2</sup>/hour. Percutaneous renal biopsy was performed on the 4<sup>th</sup> day of admission. Light microscopy examination of the biopsy showed limited numbers of glomeruli with segmental hyalinization in one glomeruli. There were no tubulointerstitial abnormalities as well as no inflammatory changes in the arterioles.

Immunofluorescence confirmed 10 glomeruli. Mixed and granular mesangial C1q (3+) positivity was detected. Some of the glomeruli showed focal, segmental mesangial deposits of IgA (1+), IgM (1+), and C3 (1+). We diagnosed the patient as having C1q nephropathy and initiated steroid therapy in a dose of 2 mg/kg per day.

## Discussion

Children with C1q nephropathy frequently present with nephrotic syndrome or proteinuria. One study reported 12 pediatric patients, from which eight presented with nephrotic syndrome, one with nephrotic range proteinuria and three had non-nephrotic proteinuria associated with microhaematuria, hypertension and renal insufficiency [6]. In 1972 Vizjak *et al.* reported 28 children with C1q nephropathy. Clinical presentations of patients with focal glomerular sclerosis include asymptomatic hematuria and or proteinuria (22%), frequently relapsing nephrotic syndrome with minimal change disease (63%) [7].

C1q nephropathy may have a mixed presentation. Many studies have revealed nephrotic syndrome as the most common finding [4,6,8,9]. However, according to another study, 30% of patients who had nephrotic-range proteinuria had no evidence of nephrotic syndrome [4]. On the other hand, Fukuma *et al.* reported 60% of C1q nephropathy patients who presented with non-nephrotic-range proteinuria [10]. One case was reported to have rapidly progressive glomerulonephritis [11]. Other case reports presented as a recurrent gross hematuria [12], association with Gitelman syndrome [13], and association with atopic dermatitis [14].

Our presented case is unique in that it initially presented with hypertension and no proteinuria but with emerging proteinuria years after the first diagnosis. As to our knowledge, this

kind of atypical presentation of C1q nephropathy has not been documented in the literature before.

## Conclusion

This is probably the first report mentioning an association between initial hypertension followed by C1q nephropathy, suggesting that the relationship might need to be further explored if other cases are identified. Additionally we suggest that more specialized tests should be performed when diagnosing primary hypertension in children with C1q nephropathy kept in mind.

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