

## Case Report

# Severe Symptomatic Proteinuria in a Patient with Polycythemia Vera

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## Abstract

We report the case of an old man with a 4-year history of Polycythemia Vera (PV) with a new proteinuria in nephrotic range. A biopsy was performed with diagnosis of Focal Segmental Glomerulosclerosis (FSGS). Glomerular proliferative or sclerotic lesions associated with proteinuria and CKD are present in patients with untreated or uncontrolled PV. This observation suggests the need for extensive studies aimed at evaluating the pathophysiology of the correlation between PV and kidney disease that is not yet clear.

**Keywords:** Proteinuria; Chronic myeloproliferative disorder; CKD

## Background

Polycythemia Vera (PV) is a one of the most common types of Philadelphia chromosome-negative chronic myeloproliferative disorder. The association between kidney disease and PV is rarely reported and remains poorly understood. It has been observed that chronic kidney disease could be a risk factor for poor prognosis in PV. The onset of proteinuria is one of the first manifestations of kidney disease in PV and the untreated or uncontrolled PV may have advanced chronic renal failure. Early screening and effective control of PV can benefit long-term renal prognosis [1-4].

## Case Presentation

An old man with a 4-year history of polycythemia Vera was referred to the nephrology unit for a new proteinuria in nephrotic range. The proteinuria progressively increased in the last two years. His medical history was remarkable for hypertension and autoimmune thyroiditis. His medications were ramipril (10 mg daily), candesartan (32 mg daily), metoprololo (50 mg daily), oncocarbide (1000 mg daily), rivaroxaban (10 mg daily). There was no personal or family history of kidney diseases. Laboratory testing revealed a white blood cell count of  $14.9 \times 10^3/\text{mm}^3$ , a hemoglobin concentration of 16.2 g/dL, and a platelet count of  $413 \times 10^3/\text{mm}^3$ . Serum Creatinine (Cr) was of 0.88 mg/dl (eGFR=78 ml/min/1.73 m<sup>2</sup>) and albumin level was 3.2 g/dL. Urinalysis was negative for red blood cell casts and leukocytes. Proteinuria was 4.7 g/24 h. Immunologic and infectious serologies were unremarkable. Abdominal ultrasonography showed normal-sized kidneys without hydronephrosis (Figure 1).

A renal biopsy was performed and reported the following description: "Double agobiopic frustule of renal tissue 1.8 cm long consisting of cortical and medulla. At the cortical level there are 15-16 glomeruli of which 5-6 sclerifying. The rest are characterized by diffuse thickening and irregularity of the capillary wall, slight collapse of the lumens of the capillaries, slight increase in mild non-specific chronic tubulo-interstitial nephropathy, remodeling of the glomeruli and poor immunofluorescence positivity". MO: Diffuse thickening and irregularity of the capillary wall with slight collapse of the lumens, slight increase in the mesangial matrix, initial fibrous thickening of Bowman's capsule. Tubules: mild/moderate atrophy, some hyaline casts. Interstitium: mild/moderate fibrosis and modest reactive lymphomonocyte inflammatory infiltrate. Arterioles: slight hypertrophy of the media. Small-caliber arteries: mild fibrous hyperplasia of the intima, multi-lamination of the internal elastic lamina. IF: mild/focal positivity for IgG, IgM, k and lambda light chains. Negatives IgA, C1q, C3, PLA2R, IgG4. Amyloid (Congo red) negative to polarized light. ME: diffuse podocytopathy, an increase in the mesangial component and segmental sclerosis, suggesting a FSGS of a probable secondary nature. Mesangial matrix and initial fibrous thickening of Bowman's capsule. Focal is observed in one glomerulus extracapillary proliferation. The tubules are the site of mild/moderate atrophy and contain some cylinders hyalines. The interstitium is the site of mild/moderate fibrosis and modest reactive lymphomonocyte inflammatory infiltrate. Arterioles are the site of mild media hypertrophy. Small caliber arteries are characterized by mild fibrous hyperplasia of the intima and multi-lamination of the internal elastic lamina. In the overall procedure, no complications were observed.

At the 3-month follow-up, on change of anti-hypertensive agents and on introduction of steroid, BP remained well controlled, and proteinuria gradually decreased (from 4.7 g/24 h to 2.4 g/24 h).

## Discussion

Myeloproliferative disorders are stem cell disorders characterized by impaired production of differentiated hematopoietic cells. According to 2008 they are subclassified into 8 groups and The Philadelphia-negative MPNs include 3 main diseases: Polycythemia Vera (PV), Essential Thrombocythemia (ET), and Myelofibrosis

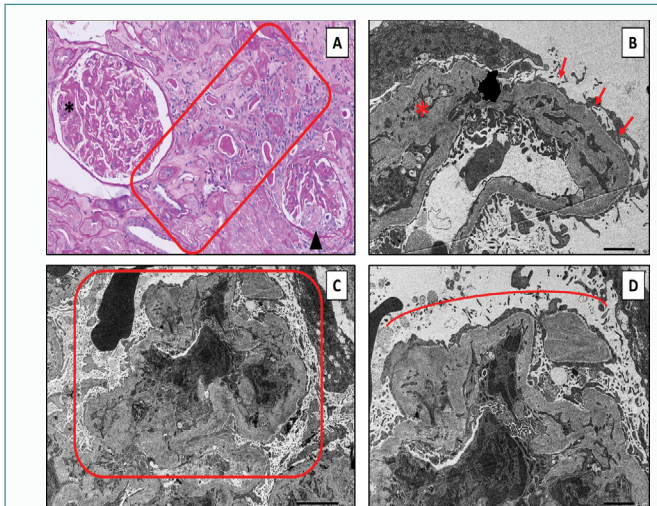
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**Figure 1:** Histology: Glomeruli characterized by variable increase in the mesangial component with an area of matrix thickening and capillary collapse in one glomerulus (asterisk) and focal extracapillary proliferation in the other (arrow). Moderate scleroatrophy (rectangle) is present at the tubulointerstitial level. EE 20x.

Electronic microscope: B) Cellular interposition in the capillary wall (arrows) with an adjacent capillary with obliteration of the lumen (asterisk). C) Collapse of the capillaries with increase of mesangial matrix and formation of area of segmental sclerosis. D) Extensive fusion of the podocytic pedicles (red line) with underlying collapse of the capillaries.

(MF). In these pathologies renal involvement is not frequent but it is possible to find both glomerular and obstructive renal involvement [5].

PV is the most common MPN, characterized by an increase in Red Blood Cell Mass (RCM) with secondary risk of thrombosis. These patients could present peripheral neurological disorders and gastrointestinal disorders [6].

One of rare complication of PV is renal involvement, characterized by glomerulonephritis and mesangial proliferation. One of the initial symptoms associated with renal involvement is the presence of proteinuria, which may also be in the nephrotic range. Although the mechanism of renal damage is not known, it has been seen that the presence of uncontrolled or inadequately treated PV predisposes to renal damage. Among the probable elements determining the damage is the presence of a microvascular stasis. So, it could be deduced that CKD has been recognized as a risk factor for thrombosis in patients with PV [1].

As already highlighted, glomerular lesions of the proliferative and/or sclerotic type, glomerulosclerotic with glomerulosclerosis, glomerular hypercellularity, associated with proteinuria and CKD, are present in patients with untreated or uncontrolled PV [2].

Said SM, et al. proposed the term ‘MPN-related glomerulopathy’, characterized by a combination of mesangial sclerosis and hypercellularity, segmental sclerosis, features of chronic Thrombotic Microangiopathy (TMA), and intracapillary hematopoietic cell infiltration. In all cases, Electron Microscopy (EM) and IF excluded immune complex-mediated glomerulonephritis [5].

Although it is hypothesized about the mechanism of the pathophysiology of the correlation between PV and kidney disease, the etiology is not yet clear and therefore further studies and insights are needed to investigate this association [1].

### Contributor Ship Statement

O. De Marco analysis and interpretation of data, drafting of the paper, final approval of the paper submitted; F. Diomedi Camassei substantial contributions to data interpretation. Substantial contributions to the critical revision of the work, final approval of the paper submitted; S. Vallese Substantial contributions to data interpretation. Substantial contributions to the critical revision of the work, final approval of the paper submitted; A. Gigante Substantial contributions to data interpretation. Substantial contributions to the critical revision of the work, final approval of the paper submitted; S. Bianchi Substantial contributions to data interpretation. Substantial contributions to the critical revision of the work, final approval of the paper submitted; R. Cianci Substantial contributions to data interpretation. Substantial contributions to the critical revision of the work, final approval of the paper submitted.

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