A Unique Form of Polycythemia Associated with Minimal Change Disease

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Key Words

Polycythemia · Minimal change disease · Proteinuria

Abstract

Objective: To present a case with nephrotic syndrome due to minimal change disease and polycythemia. **Clinical Presentation and Intervention:** A 20-year-old female was admitted to our clinic for edema and severe proteinuria present with minimal change disease since the age of 7 years. Polycythemia was found during the last activation of nephrotic syndrome. The patient was placed on glucocorticoid therapy that caused disappearance of edema, proteinuria and polycythemia. Ten months later both hemoglobin and hematocrit levels were within normal range. **Conclusion:** This patient with nephrotic syndrome due to minimal change disease and polycythemia was successfully treated with glucocorticoid.

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Introduction

Systemic inflammation, urinary losses of transferrin and erythropoietin (EPO) are known causes of anemia in nephrotic syndrome [1]. Nephrotic syndrome-associated secondary polycythemia is a rare complication, and polycythemia has been described with membranous glomerulonephritis [2–4].

Case Report

A 20-year-old female was admitted to the hospital with generalized edema. She had a history of minimal change disease since she was 7 years old. Her episodes of proteinuria and edema have responded completely to corticosteroid treatment until this last one.

On admission, physical examination revealed blood pressure of 100/70 mm Hg, temperature 37.5°C and pulse 76 beats/min. Additional examinations were normal except for edema. Laboratory findings showed white blood cell count of 10,700/mm³, hemoglobin 18 g/dl, hematocrit 55%, mean corpuscular volume 84.4, platelets 363,000/mm³, glucose 82 mg/dl, BUN 20 mg/dl, creatinine 1.2 mg/dl, total protein 4 g/dl, serum albumin 1.8 g/dl, total cholesterol 552 mg/dl, HDL 63 mg/dl, LDL 422 mg/dl, triglyceride 333 mg/dl, proteinuria 11.9 g/day and arterial PO₂ was 105 mm Hg. Complements C3 and C4 were within normal limits, antinuclear antibody and anti-DNA were negative, PPD was negative. Renal ultrasonography (US) and Doppler US were normal without evi-

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Table 1. Values of hematocrit, hemoglobin and daily proteinuria during follow-up

	Days					Months				
	1	2	4	6	7	1	2	5	7	10
Red blood cells, 10 ⁶ /ml	5.99	6.51	6.18							
Hematocrit, %	51.5	55.0	51.4	50.0	54.0	41.5	43.0	41.0	43.5	30.0
Proteinuria, g/day	9.0	–	–	–	11.5	0.4	0	0	0.2	0
ACEI	+	+	+	+	+	+	+	+	+	+
Steroid	–	–	–	–	+	+	+	–	+	+

ACEI = Angiotensin-converting enzyme inhibitor.

dence of renal vein thrombosis or renal artery stenosis. A second renal biopsy was performed to evaluate the cause of heavy proteinuria. The diagnosis was minimal change disease. The patient was placed on foscinopril (10 mg/day), and later methylprednisolone (1 mg/kg/day) and acetylsalicylic acid (80 mg/day) were started. In the first month of treatment hemoglobin was 14 mg/dl, hematocrit 41.5%, total protein 5.7 g/dl, serum albumin 3.8 g/dl, and proteinuria was negative (table 1).

There was no evidence of pulmonary disease, congenital heart disease, hypoventilation, cystic renal disease, renal artery stenosis, hydronephrosis or malignancy to explain the polycythemia. Chest X-ray, arterial PO₂, renal arteriovenous Doppler US were all normal. The hemoglobin levels became normal with the disappearance of proteinuria and edema.

Discussion

The pathogenesis of polycythemia associated with nephrotic syndrome is obscure. Hypoxia caused by thromboembolism can induce the secretion of EPO and polycythemia can develop. Arterial PO₂ measurements of this case were normal and therefore hypoxia could not be the underlying cause of polycythemia. Heavy proteinuria and hypoalbuminemia can lead to renal interstitial edema and hypoxia, thereby increasing the levels of EPO. Therefore, we thought that the polycythemia of this case might be related to hypoalbuminemia. Intrarenal hypoxia activates the renin angiotensin II system that increases reabsorption of sodium from proximal tubules and increased oxygen consumption, thereby stimulating oxygen-sensitive receptors and the secretion of EPO [5]. This mechanism may be responsible in post-transplantation erythrocytosis.

Our patient received angiotensin-converting enzyme inhibitor (foscinopril) during the period of polycythemia. The levels of erythrocytosis and hemoglobin-hematocrit were high (table 1). With the regression of proteinuria and the increment of serum albumin, hemoglobin level de-

creased to 14 mg/dl where it remained during the 10-month follow-up period despite foscinopril treatment. Although we could not ignore the effect of angiotensin-converting enzyme inhibitor on hemoglobin levels; the dramatic change in hemoglobin levels was detected with the improvement of proteinuria and hypoalbuminemia in the first month. Therefore we suggest that improvement of polycythemia in this case was related to the regression of nephrotic syndrome, similar to a case of diffused cerebral hypoperfusion in a patient with steroid-resistant nephrotic syndrome that resolved with the regression of nephrotic syndrome [6].

With interleukin-8 (IL-8) infusion, alterations in the dimension and electric charge of the glomerular heparan sulfate glycosaminoglycan chain have been demonstrated [7]. It has also been shown that the serum level of IL-8 and the stability of IL-8 mRNA increase in patients with minimal change disease [8]. It has been reported that patients with polycythemia vera have high serum and bone marrow plasma levels of IL-8 and IL-11 and also increased secretion of these two interleukins from the bone marrow stromal cells [9]. In minimal change disease and polycythemia vera, the augmentation in similar cytokines may explain the occurrence of polycythemia in minimal change disease, as in our patient. But this probability is low because polycythemia is very rare in minimal change disease. We did not determine serum and bone marrow levels of IL-8 and IL-11. Anemia is more common in patients with nephrotic syndrome, and urinary losses of EPO and transferrin are known to be a cause of anemia in nephrotic syndrome.

The alteration of serum insulin-like growth factor-1 (IGF-1) has been reported in nephrotic syndrome [10] and in patients with chronic renal failure associated with polycythemia [11]. In nephrotic patients, the levels of IGF-1 and its binding protein (IGF BG3) have been found in fluid proximal tubules [10]. A high level of IGF-1

can lead to reabsorption of sodium and phosphorus and may stimulate EPO secretion similar to angiotensin II [12]. High levels of IGF BG1–2 may act like erythrocyte precursors and make the receptors of target organs sensitive to IGF-1 [13]. This effect may be independent of EPO secretion. It is possible that renal hypoperfusion might cause polycythemia by EPO production related to hypoxemia and hypoxia inducible factor-1. However, no such report exists in the literature.

Conclusion

This patient with nephrotic syndrome due to minimal change disease and polycythemia was successfully treated with glucocorticoid. During the follow-up period recurrence of polycythemia and proteinuria were not detected. The regression of nephrotic syndrome could help improvement of polycythemia.

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