



A Rare Case of Cryoglobulinemic Vasculitis

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INTRODUCTION

Cryoglobulins are monoclonal or polyclonal immunoglobulins which are cold precipitable. This is strongly associated with systemic vasculitis. Cryoglobulinemic vasculitis is either idiopathic or associated with a variety of underlying disorders including multiple myeloma, lymphoproliferative disorders, connective tissue diseases, infection, and liver disease.

CASE REPORT

A 74 year old male presented with complaints of breathlessness for 15 days. Dyspnoea was of grade 3, associated with orthopnoea and paroxysmal nocturnal dyspnoea. He also had reduced urine output, pedal edema and facial puffiness. Patient is a known case of hypertension and ischaemic heart disease for 10 years, diabetic for 4 years. He also had polyarthritis 4 years back which lasted for 4 months but was undiagnosed. On examination he had pallor, grade 2 clubbing, tachypnoea and generalised anasarca. His jugular venous pulse was elevated. He had tachycardia but his blood pressure was normal. His respiratory system examination revealed bilateral infraaxillary medium crepitations but the cardiac examination

was normal except for tachycardia and he had a tender liver. Clinically he was diagnosed to have a volume overload state secondary to coronary artery disease and diabetic nephropathy.

On investigation, his renal function tests were elevated: Blood Urea- 32mg/dl, S. creatinine – 3.03mg/dl, Creatinine clearance -15.48. His serum electrolytes Sodium (128mEq/L) and Potassium (5.9mEq/L) were deranged but calcium and phosphorus were normal. Urine examination revealed Alb- +++ , Pus cells – 3-5, Epi cells – 6-8 cells, RBC - 10-15 cells, Urine spot Protein / creatinine ratio – 6.23:1, 24 hr urine protein -- 3116mg. Urine culture did not grow any bacteria and USG Abdomen showed B/L increased renal cortical echoes. Ophthalmological examination did not show any features of diabetic retinopathy. Since patient had nephrotic range proteinuria but normal retina , kidney biopsy was done which showed features of Membranoproliferative Glomerulonephritis (Type I). Patient was evaluated further for the etiology of MPGN Type 1. The viral markers HbsAg, Anti-HCV, HIV I&II were negative. ANA by immunofluorescence assay and ENA blot assay were also negative. Serum protein electrophoresis was done to rule out

multiple myeloma and MGUS which was also negative. Finally patients serum was tested for cryoglobulins which turned out to be POSITIVE. Hence idiopathic cryoglobulinemic vasculitis was diagnosed. Patient was treated with supportive measures such as fluid restriction, diuretics, beta-blockers for heart rate control. He was also treated with steroids which was then tapered and stopped over 3 mon. Now the patient is doing well with no features of volume overload and his renal parameters were stable with S.creatinine less than 2 mg/dl.

DISCUSSION

Cryoglobulinemia is characterized by the presence of cryoglobulins in serum, which are immunoglobulins which precipitate reversibly at low temperatures. The clinical manifestations are many depending upon the type of cryoglobulins.⁽¹⁾ It may be idiopathic or secondary to certain diseases such as autoimmune diseases⁽²⁾, lymphoproliferative disorders⁽³⁾, infectious diseases. It is commonly associated with HCV infection⁽⁴⁾. However, 5%-48% of cases with cryoglobulinemic syndrome have still been reported as Essential mixed cryoglobulinemia. It is of three types⁽⁵⁾. Type I contains monoclonal immunoglobulin mostly IgM, rarely IgG or IgA. Type II and III contain mixed cryoglobulins both IgG and IgM. IgG is polyclonal in both whereas IgM may be monoclonal (type II) or polyclonal (type III). Further B cell clonal expansion is also seen in these disorders^(6,7).

The prevalence of cryoglobulinemia is 1:100000. The frequencies of various types are as follows: type I – 25%, type II – 25%, type III – 50%. The mean age of onset is 32-42 years with a female preponderance. The female-to-male ratio is 3:1. The clinical features are listed in Table.1.

TABLE 1.

S.NO.	SYSTEM	MANIFESTATIONS
1.	Skin	Erythematous macules, papules or ulcers
2.	Musculoskeletal	Arthralgias, arthritis, myalgia
3.	Nervous system	Sensory neuropathy, visual disturbance, pseudotumor cerebri, cerebrovascular accident
4.	Renal	Membranoproliferative glomerulonephritis(8), nephrotic range proteinuria(9)
5.	Abdomen	Abdominal pain, hepatomegaly(10), splenomegaly(10)
6.	Respiratory system	Pleurisy, pleural effusion, bronchiectasis

The investigation of choice is to look for cryoglobulins in serum. The blood specimen must be collected in warm tubes (37°C) in the absence of anticoagulants. Allow the blood sample to clot before removal of serum with centrifugation (at 37°C). Incubate the serum sample at 4° C. The period required for the appearance of cryoglobulins depends on the type present:

Type I tends to precipitate within the first 24 hours

Type III cryoglobulins may require 7 days.

In our case the cryoglobulin precipitation occurred within 24 hours, hence probably of type I. The other investigations are to be done to find the etiology which includes viral markers especially HCV, antinuclear antibody, rheumatoid factor, serum and urine protein electrophoresis which were all negative in our case.

CONCLUSION

We publish this case to stress the fact that cryoglobulinemia has to be considered in patients presenting with glomerulonephritis and massive proteinuria when other causes have been ruled out