SELF-ASSESSMENT PROGRAMME

A 70 year old labourer presented with episodes of pain in both the legs on walking, for one year, which used to be relieved on rest. For past one month he had noticed painful black discoloration and shrivelling up of the right little finger and left second toe. Multiple bluish black discoloration of the skin with peeling off had been observed for 8 days, had started on the scrotum, the thighs, the buttocks and pinnae. Some of these broke down forming superficial ulcers. The symptoms used to get worse on exposurse to cold and were relieved by immersing the parts in warm water. The patient had been a heavy smoker and used to drink occasionally. There was no history of fever, joint pains or loss of weight or history suggestive of diabetes mellitus.

The patient was in great distress due to pain and showed multiple large areas of bluish discoloration on the thighs, the buttocks and the scrotum with superficial ulcers over some of the areas. Right little finger and left second toe showed dry gangrenous change. Both dorsalis pedis and posterior tibial pulsations were feeble. Sensations were normal. Systemic examination revealed fine crepitations in right interscapular area and liver was palpable 2 cm below the right costal margin. Lymphadenopathy was insignificant.

I. What is the likely diagnosis?

1. Generalised vasculitis
2. Connective tissue disease
3. Thromboangitis obliterans
4. Cryoglobulinemia
5. Idiopathic thrombocytopenia
6. Periarteritis nodosa

II. What are the investigations likely to help?

1. Skin biopsy
2. Urinalysis
3. Platelet count
4. Arteriography
5. Serum proteins including cryoglobulins

The skin biopsy showed acute vasculitis. Routine urine and blood examination were non-contributory. Serum showed heavy deposits of cryoproteins. The presence of cryoproteins together with changes of vasculitis warranted further investigations.

III. Which of the following would be further helpful?

1. Urine for Bence-Jones proteins
2. Bone marrow biopsy
3. Skeletal survey
4. Peripheral blood smear
5. Lymph node biopsy
6. Antinuclear factor

IV. What is the line of treatment?

1. Penicillamine
2. Cytotoxic agent
3. Systemic Corticosteroids
4. Plasmapheresis

V. What is the likely prognosis?

1. Good
2. Guarded
3. Unpredictable

ANSWERS

I. With a clinical picture of intermittent claudication and gangrene in toe and finger a diagnosis of Thromboangitis obliterans should be made, superficial skin necrosis could be due to additional, perhaps unrelated, vasculitis.

II. All of these investigations listed should be carried out. While the skin biopsy showed vasculitis, arteriography, urinalysis and serum proteins would help in excluding or clinching the other likely diagnoses. Serum did show the presence of cryoproteins.

III. A work up of vasculitis with associated cryoproteinemia should include all these investigations. Urine showed Bence-Jones proteins, Skeletal survey carried out to detect multiple myeloma did not show any abnormality. Peripheral blood smear and lymph node biopsy were normal. Antinuclear factor was negative. Bone marrow showed large number of plasma cells suggestive of myeloma.

IV. While all of these modalities have been reported to be beneficial in idiopathic cryoglobulinemia, attempts should be made to identify the underlying cause and appropriate treatment should be instituted. In the present patient plasmapheresis was carried out five times with considerable reduction in the levels of cryoglobulins and an improvement of symptoms. A combination of cytotoxic agents and systemic corticosteroids have also been employed for multiple myeloma.

V. Prognosis is guarded, though remissions with combination therapy (Vincristine, cyclophosphamide, melphalan and prednisolone) have been reported.

Comment

The present patient presented with a picture suggestive simultaneously of thromboangitis obliterans (intermittent claudication gangrene of toe and finger) and acute vasculitis (bluish painful necrotic areas). On the face of it these two would seem to be unrelated and search should therefore be made for a common denominator.

Such a picture could be seen in a connective tissue disorder or cryoglobulinemia (idiopathic or secondary). Attempts to investigate on these two lines showed the presence of cryoproteins in the serum which on further investigations was proved to be secondary to multiple myeloma. A picture simulating thromboangitis obliterans has earlier been reported and a picture of vasculitis is not uncommon. Interestingly this patient presented a combination of these two.

Cryoglobulins are serum globulins that precipitate on cooling and redissolve on warming. They occur in a variety of conditions like myeloma, macroglobulinemia, glomerulonephritis, viral infections, syphilis, leprosy, collagen disease. They may represent a homogenous protein that have been physically altered as in myelomas; a mixture of immunoglobulins or immune complexes (IgG, IgM). Cryoprotinemia may be asymptomatic or give rise to a variety of clinical manifestations chiefly attributable to vascular insufficiency because on cooling the abnormal protein may form precipitates in smaller vessels and cause increased viscosity, stasis, thrombosis or haemorrhage.

The varied cutaneous symptoms range from urticaria, Raynaud's phenomen, livedo, distal necrosis, leg ulcers and vascular purpura. Other manifestations are neurologic, articular and renal.

A direct role of cryoglobulins in the genesis of various visceral injuries found in patients with infective, renal or hepatic diseases has not been established.

The treatment of cryoprotenemia is essentially that of the underlying disease in addition to treatment for those symptoms linked to cryoglobulins. Plasmapheresis is considered an emergency treatment for acute symptoms and the response in such cases has been dramatic[3]. Plasmapheresis is done until a sizable reduction of the cryoglobulin level is maintained. The choice and effectiveness of cytotoxic agents in cryoglobulinemia associated with multiple myeloma or other malignancies are the same as for random patients with these diagnoses. In patients with autoimmune diseases, the presence of cryoglobulin usually does not modify the therapeutic attitude.

A thorough search for any other malignancy is indicated in a case like this, even after detection of myeloma, as it is known to be associated with multiple primary neoplasms[4].

References

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