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RESEARCH ARTICLE

CASE REPORT ON CRYOGLOBULINAEMIA

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ABSTRACT

Cryoglobulinemia refers to the serum presence of cryoglobulins, which are immunoglobulins that reversibly precipitate and form a gel when the temperature is <37 degree Celsius and re-dissolve if the temperature rises to >37degree Celsius. The disease mainly involves small to medium sized blood vessels and mainly causes vasculitis due to cryoglobulin containing immune complexes. The cryoglobulins maybe composed only of a monoclonal Ig (type 1), of a monoclonal Ig bound to the constant domain of polyclonal Ig heavy chains(type 2) or only of polyclonal Ig (type 3).The prevalence of cryoglobulinemia remains unknown.5.About 10-30% of the cases of mixed cryoglobulinemia are not related to HCV. The many causes include other infections, autoimmune diseases and b-cell lymphoid malignancies. The development of vasculitis with cutaneous and peripheral nervous system involvement should prompt an evaluation for lymphoma.For most patients cryoglobulinemia disease is diagnosed by the presence of typical organ involvement (mainly skin, kidney or peripheral nerve) and circulating cryoglobulins.The directed therapy for different types of cryoglobulinemia is based on expert opinion due to disease rarity.Cryoglobulinemic vasculitis unrelated to HCV: Infection should be managed with appropriate anti-infectious agents. Rituximab combined with glucocorticoid therapy is the first line treatment in the event of the autoimmune diseases.Conventional therapy is of high-dose corticosteroids, intravenous cyclophosphamide, rituximab, bortezomib, and plasma exchange. Prognosis in patients with grave manifestations is often poor. Plasma exchange therapy may deserve consideration in patients at the severe end of clinical spectrum.

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INTRODUCTION

Cryoglobulins are immunoglobulins that precipitate at low temperature and disappear when incubated at 37degreeCelsius**.** This phenomenon was first recognized by Wintrobeand Buell (Roccatello, 2018). Cryoglobulin derived clinical symptoms differ by pathogenesis, which is represented eitherby hyper-viscosity syndrome or by manifestations related to immune complex deposition (Tocut et al., 2019). Among the Clinical and immunological classification of the Cryoglobulinemias, Brouet's classification is the most widely distinguished. The chemical and immunological features of the cryoglobulins are used to define 3 types of the cryoglobulinemia. Type I cryoglobulinemia (simple cryoglobulinemia is characterized by a single monoclonal Ig, which is usually an IgM or IgG.

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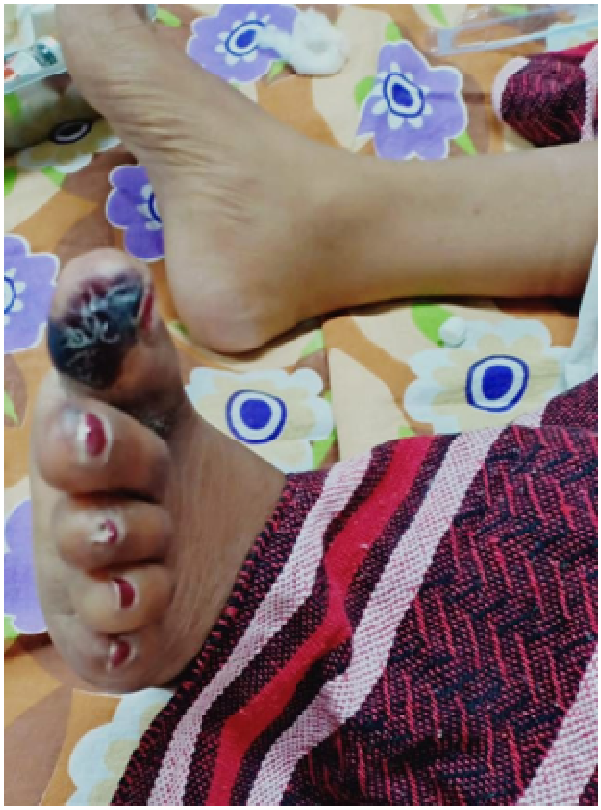
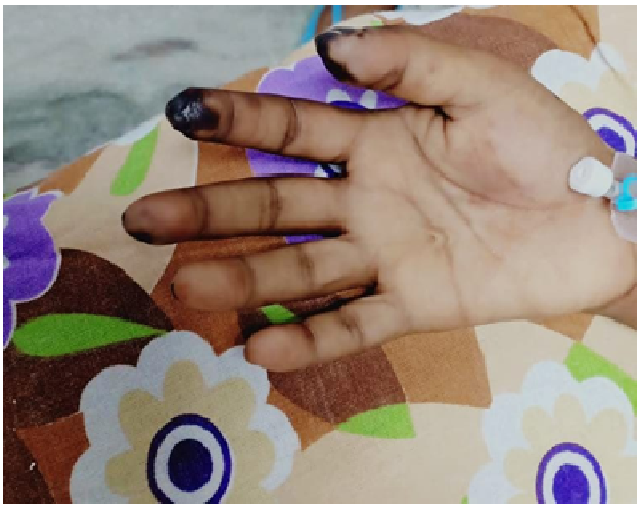
In Type 2 Cryoglobulinemia, polyclonal Ig's form immune complexes with one or more monoclonal Ig's. The most common form combines a monoclonal IgM and polyclonal IgG's (mixed monoclonal cryoglobulinemia) (Desbois, 2019). The immunosuppressive approaches used in cryoglobulinemic vasculitis, based on high dose glucocorticoids and cyclophosphamide, where derived mainly from strategies used in other systemic vasculitis.

Before it was understood that most cases result from HCV infection. Both plasma exchange and plasmapheresis remove cryoglobulins from the circulation, thereby interrupting the immune complex mediated pathogenesis. Most robust anti-viral approach to the treatment of HCV related Cryoglobulinemia involves the use of both pegylated interferon –alpha and Ribavirin (Ramos-Casals, 2012).





PATIENT DESCRIPTION

39year lady was transferred from the local hospital with known complaints of chronic kidney disease and Coronary artery disease. On presentation, she had sub conjunctival hemorrhage and blackish discoloration of right and left toes, and right hand. She also had the complaints of severe pain over upper and lower limbs. A low-grade fever was also observed. Investigation revealed creatinine value of 200mmol/L.Negative reportsof tumor markers were collected. Hepatitis B and C were negative. Elevated ESR of 150 mm/hr was reported.The dark color skin showed leukocytoclastic vasculitis. Immunological investigation showed lowC4 and C3,and apositive rheumatoid factor. As per the results of immunology, cryoglobulin was sent.

Cryoglobulin Type 2 was identified. One day later, the patient developed fluffy shadows in chest and then the x-ray revealed pulmonary hemorrhage. She was started on plasma exchange and then when the oxygen saturation declined, mechanical ventilation was provided and shifted to Intensive Care Unit. She was treated with cyclophosphamide and steroids. Antipyretics were given for raised temperature and antibiotics for the treatment of infections. The symptoms resolved after about one week and were discharged with immunosuppressants and other supportive drugs.

DISCUSSION

Cryoglobulinemia is considered to be a rare disorderand epidemiological studies on its prevalence are inadequate. Clinical manifestations of the disease and its management varies substantially due to wide variation in underlying diseases.We present a case of pulmonary hemorrhage associated with cryoglobulinemia. Here, pulmonary hemorrhage was diagnosed based on clinical findings and CXR findings. Treatment is often determined on the basis of the underlying diseases intense immunosuppressive or immunomodulatory therapy including steroids, plasmapheresis or cytotoxic agents is reserved for organ-threatening or recalcitrant disease.

Conflicts of interest: The authors have declared no conflicts of interest.

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