

Case Report

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Therapeutic plasma exchange: A life-saving modality in Wegener's granulomatosis

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Abstract:

We report a case of Wegener's granulomatosis (WG) who very well responded to the combination strategy of therapeutic plasma exchange (TPE) and immunosuppression. The patient was a 38-year-old female, diagnosed with severe form of WG. A total of seven cycles was performed with 1.3 total plasma volumes (TPVs) on every alternate day. Standard induction therapy was also started that comprised of a combination of 500 mg intravenous (i.v.) cyclophosphamide and methylprednisolone 1 g slow i.v. daily for 3 days followed by oral prednisolone 60 mg daily for 4 weeks. After seven cycles of TPE, the patient improved and hence TPE was stopped.

Keywords:

Antineutrophil cytoplasmic antibodies, immunosuppression, therapeutic plasma exchange, Wegener's granulomatosis

Introduction

Granulomatosis with polyangiitis (GPA, formerly known as Wegener's granulomatosis [WG]) is an autoimmune small-vessel vasculitis, which is highly associated with anti-neutrophil cytoplasmic antibodies (ANCA) and has hallmarks which include systemic necrotizing vasculitis, necrotizing granulomatous inflammation, and necrotizing glomerulonephritis. It was first reported in the literature as a case report in the late 19th century and was previously known as WG who described this disease in 1936.^[1] Since 2011, WG has been renamed as GPA.^[2] The incidence of GPA is 5–10 cases per million populations per year with equal frequency in males and females.^[3] GPA requires prompt, effective management of acute and chronic manifestations of disease. Although most patients, even with serious renal involvement, respond well to the standard treatment of combination

therapy with cyclophosphamide and corticosteroid, a substantial fraction of the patients will develop end-stage renal disease (ESRD).^[4,5] Therapeutic plasma exchange (TPE) in combination with immunosuppression has dramatically improved the outcome in patients with WG.^[6]

Case Report

A 38-year-old female was admitted to the emergency ward with altered sensorium and anuria. She had off and on constitutional symptoms of disease such as general malaise, myalgia, polyarthralgia (mainly involved knee, elbow, and ankle joints), anorexia, weight loss, headache, and pyrexia from the last 4 years. She also had a history of recurrent blood-stained nasal discharge, epistaxis, nasal crusting, nasal ulceration, cough, breathlessness, stridor, and wheeze from the last 3 years. She had a history of pedal edema 3 months back. She also complained of diminution of vision with redness of eyes from 3 months. The patient

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had a history of ulcers on lips and tongue from the past 4 days and decreased frequency of urination from 3 days. There is no history of hematuria, hemoptysis, or cardiovascular manifestations. On examination, her vitals were deranged; she had tachycardia (120/bpm) and hypotension (100/60 mm of Hg). She also had pallor and bilateral pedal edema. There was high suspicion of GPA with acute renal failure or rapidly progressive glomerulonephritis associated with systemic small-vessel vasculitis. Keeping these two main diagnoses in mind, the investigations were ordered accordingly.

Diagnosis

It is based on a combination of clinical manifestations of systemic disease, positive ANCA serology, and histological evidence of necrotizing vasculitis, necrotizing glomerulonephritis, or granulomatous inflammation of affected organs such as skin, lung, or kidney.

A trucut biopsy was taken from the right kidney of the patient and detailed analysis was done. On light microscopy, there was focal segmental necrotizing glomerulonephritis involving more than 60% glomeruli associated with extracapillary proliferation with pauci-immune crescent formation. Electron microscopic examination showed fibrinoid deposition in the glomerular basement membrane. In biochemistry, serum sodium (159 mmol/L) and serum potassium levels (17 mmol/L) were deranged. In kidney panel, serum urea (155.8 mg/dL) and serum creatinine levels (8.9 mg/dL) were highly increased suggesting severe form of disease.

On performing ANCA serology, her serum showed a predominantly diffuse, granular cytoplasmic ANCA (c-ANCA) staining pattern on indirect immunofluorescence. By direct enzyme-linked immunosorbent assay, there were high titers of ANCA directed against proteinase-3 (PR-3). PR-3 (1:100 with 1+ intensity) was highly raised and confirmed the diagnosis of granulomatosis with polyangiitis associated with c-ANCA positivity.

Treatment

The patient underwent two sessions of hemodialysis with a 2-day interval with packed red cell transfusion. Following that, serum urea and creatinine levels were controlled. Due to high levels of circulating c-ANCA autoantibodies, TPE was planned in addition to the standard therapy. GPA comes under category I, Grade 1A; American Society for Apheresis guidelines 2016.^[7] TPE sessions were started on the 4th day of admission. A total of seven cycles was performed with 1.3 total plasma volumes exchanged on every alternate day. Fresh frozen plasma (FFP) and normal saline were used as replacement fluids. During the third cycle of TPE

after 5 units of FFP transfusion, the patient developed allergic reaction in the form of severe itching all over the body. To treat allergic reaction, oral pheniramine maleate 5 mg and injection hydrocortisone 100 mg intravenous (i.v.) were given, and after 20 min, procedure was restarted and completed successfully. Rest six cycles of TPE was done uneventfully. Simultaneously, standard induction therapy was also started that comprised of combination of cyclophosphamide (500 mg, i.v.) and methylprednisolone 1000 mg, i.v. daily for 3 days followed by oral prednisolone 60 mg daily for at least 4 weeks. Mesna 200 mg slow i.v. over 2 h was also given to prevent cyclophosphamide-induced hemorrhagic cystitis. Regular monitoring of full blood count, serum proteins, renal function, liver function, urine cytology, and clinical symptoms were done. After seven cycles of TPE, the patient was improved clinically as indicated by her renal function tests and ANCA serology and hence TPE was stopped. The patient's recovery was faster due to the timely intervention of TPE along with standard immunosuppression therapy. The total hospital stay of patient was 18 days which was lesser in comparison to the patient who were treated with standard therapy alone. After that, the patient was on maintenance therapy with azathioprine (2 mg/kg/body weight) at least for 12 months and advised for monthly follow-up.

Discussion

TPE is proposed to work by eliminating c-ANCA from peripheral circulation. The speed of response was more rapid in TPE plus immunosuppression group. The serum creatinine decreased also somewhat more in the TPE-treated patients.^[8] TPE in conjunction with cyclophosphamide and prednisolone can be used in patients with rapidly progressive life-threatening renal vasculitis, as it may prolong dialysis-free survival in these patients. Further, TPE reduces progression to ESRD.^[9,10]

Conclusion

GPA is a multifocal vasculitis characterized by frequent involvement of the upper and lower respiratory tract and kidneys. The presence of c-ANCA with anti-PR-3 specificity is observed in more than 90% of patients with GPA. It is a serious disease, with a nearly always fatal outcome in the absence of treatment. It responds well to prompt and aggressive treatment with TPE and immunosuppressive drugs.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in

the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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