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Central Retinal Venous Occlusion Following Intravenous Immunoglobulin Therapy-A Case Report

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Abstract
IV immunoglobulins has been widely used in a variety of diseases, including primary and secondary immunodeficiency diseases, neuromuscular diseases, Guillain-Barré syndrome and Kawasaki disease. Although a large number of clinical trials have demonstrated that immunoglobulin is effective and well tolerated, various adverse effects have been reported. The majority of these events, such as flushing, headache, malaise, fever, chills, fatigue and lethargy, are transient and mild. However, some rare side effects, including renal impairment, thrombosis, arrhythmia, aseptic meningitis, hemolyticanemia, and transfusion-related acute lung injury (TRALI), are serious. IVIg treatment can cause thrombotic complications. Five cases of stroke, two cases of deep vein thrombosis, seven myocardial infarctions, one case each of RVO and pulmonary embolism have so far been described with IVIg. The rate of thrombotic complications following IVIg may be as high as 3-5% though underreported and can involve both arterial and venous circulation. In this case we describe a patient with Guillain Barré syndrome (GBS) who experienced retinal vein occlusion (RVO) following IVIg therapy.
Keywords: *Guillian barre syndrome, central retinal vein occlusion, IVIG Intravenous immunoglobulins.*

Introduction

Intravenous immunoglobulin (IVIg) is concentrated human immunoglobulins made from pooled donor plasma. Commercial preparations were used for clinical administration since early 1980s. It modulates the immune response in a variety of inflammatory and autoimmune disorders. These conditions include primary immunodeficiency, immune thrombocytopenic purpura, chronic inflammatory demyelinating polyneuropathy, Kawasaki disease, certain cases of HIV/AIDS and measles, Guillain-Barré syndrome, and in certain other infections when a more specific immunoglobulin is not available. Depending on the formulation it can be given by injection into muscle, a vein, or under the skin. The effects last a few weeks. Although high-dose IVIg generally is considered safe, it is not without side effects and may promote life-threatening thrombosis. We describe a patient with Guillain Barré syndrome (GBS) who experienced retinal vein occlusion (RVO) following IVIg therapy.

Case Report

A 75 yr old female presented with chief complaints of Fever which is intermittent, low grade and relieved with medication. Loose stools since 10days followed by weakness in both lower limbs since 1 week gradually progressive to involve low back and upper limbs. She is known diabetic and

hypertensive. General condition fair. Vitals stable. Pallor present.CNS examination: reduced power (2/ 5), hypotonia and absent reflexes in b/l lower limbs.

Investigations:

Hb: 7.3gm/dl, TLC:5600, Platelets:3.8lakhs/cumm, ESR:20mm/hr, RBS:142gm/dl,

Blood urea34, sr.creatinine1.1, Na137meq/l, k3.5meq/l, sr.albumin:1.9mg/dl, T3:0.78nmol/l, T4:90nmol/l, TSH: 8.78ul/ml, CT Brain: no significant abnormality detected, USG abdomen: NAD,

CSF Analysis:

Glucose: 52mg/dl, Protein: 98mg/dl, TC:1cell/cumm, DC:1cell/cumm S/O (Albuminocytological dissociation).

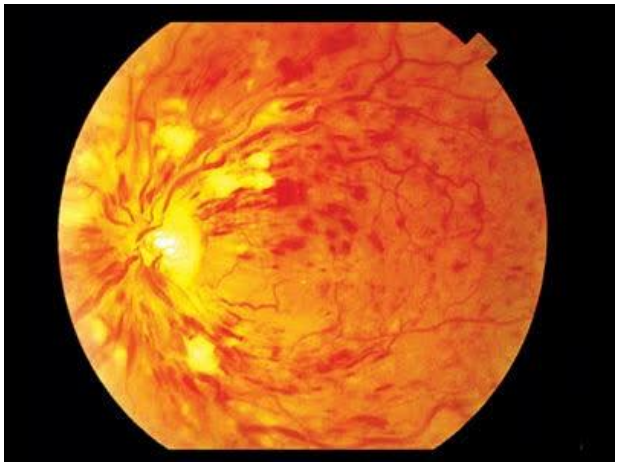
Nerve conduction studies:

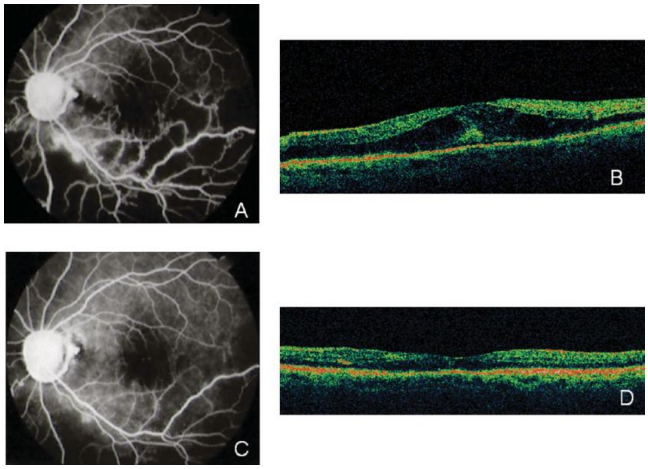
Acute demyelinating Neuropathy involving Motor Nerves.

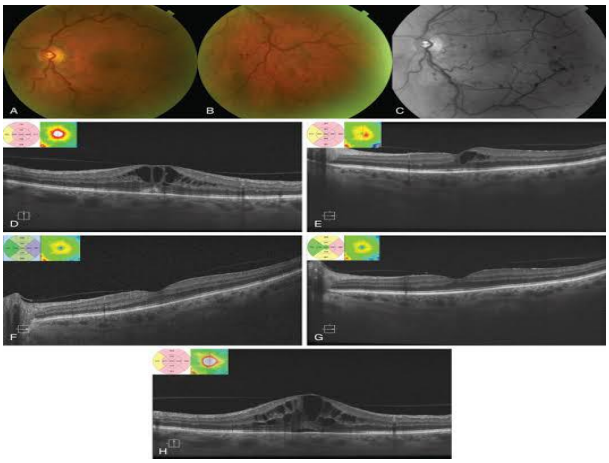
Fundus examination: showed retinal hemorrhages, dilated tortuous retinal veins, cotton-wool spots, macular edema, and optic disc edema

Clotting screen and thrombophilia screen including protein C, protein S, antithrombin 3, factor V Leiden and APC resistance were all normal. Anticardiolipin antibody was not detected. Intraocular pressure was normal

Patient has been diagnosed as Guillian barre syndrome and started on IVIG therapy. She complained of visual loss in right eye on 5th day of IV immunoglobulin therapy.







Discussion

A 75yr old female has been treated with IV immunoglobulins with the diagnosis of Guillian Barre syndrome. When she applied to receive fifth session of IVIG therapy, she complained about visual loss. On ophthalmologic examination, right central retinal venousocclusion was determined. There was no other detectable cause for CRVO and it was thought that central retinal vein thrombosis might be due to IVIG therapy. Guillian barre syndrome (GBS) is an acute, immune-mediated polyneuropathy that often leads to severe weakness. GBS is a post infectious disorder. The most frequently identified preceding infection is Campylobacter jejuni. Others are cytomegalovirus, Epstein–Barr virus, Mycoplasma pneumoniae, and Haemophilus influenzae.

Many reports have documented the occurrence of GBS shortly after vaccinations, operations, or stressful events, but the causality and pathophysiology are still debated.

The main features of GBS are rapid progressive bilateral and relative symmetrical weakness of the limbs with or without involvement of respiratory or cranial nerve-innervated muscles or sensory disturbances. Cerebrospinal fluid examination typically shows an increased protein level with a normal white cell count.Intravenous immunoglobulin (IVIG) is a proven effective treatment for GBS.

Hyperviscosity syndromes have well-recognised associations with CRVO. In vitro studies have confirmed a dose-related increase in viscosity with IVIg products and there are a number of documented cases of thrombotic complications associated with the therapeutic use of IVIg. There has been one case in the literature of bilateral CRVO occurring in a 17-year-old man requiring immune replacement therapy following treatment for acute lymphoblasticleukemia. Raised cholesterol greater than 6.2 gm/has also been reported as an independent risk factor for CRVo.

We propose that in this case the therapeutic use of lVIg, possibly combined with the raised cholesterol, may have precipitated the episode of visual loss, although we do acknowledge that it may have been coincidental as a significant percentage of cases of CRVO have no detectable systemic cause. Hyperviscosity does not appear to be the direct cause. Nitric oxide plays a critical role in vascular homeostasis through the inhibition of platelet aggregation and promoting vasodilatation, and in vitro studies have shown that human immunoglobulins are able to downregulate the production of thrombin- induced nitric oxide production in a dose-dependent fashion. In vivo studies have shown a correlation between adverse reactions and elevated levels of the proinflammatory cytokine interleukin 6 and the vasoactive substance thromboxane (TXB2). It is possible that IVIg-induced alterations in the profile of cytokines and vasoactive substances may have precipitated a localised thrombotic occlusion. This case emphasises the importance of screening for vascular risk factors in patients requiring treatment with IVIg.

Conclusion

High dose IV immunoglobulins or Plasmapheresis are equally effective for treatment of GBS. IV immunoglobulins are chosen as initial therapy due to its ease of administration. However it can rarely cause serious side effects like thrombosis. In literature there are a few cases of central retinal vein occlusion due to IVIG therapy. Patients having emerging eye symptoms must be evaluated for the possibility of CRVO. Therefore thromboembolic complications must be kept in mind during IVIg treatment and risk factors that trigger thrombosis must be ruled out and more attention is required in such patients also benefits of IVIg therapy should be weighed against risks in individualized patients.

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