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Case report

Aseptic meningitis complicating immunoglobulin therapy in AIDP

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ABSTRACT

Introduction: A case of aseptic meningitis due to intravenous immunoglobulin is being reported.
Aim: To learn rare side effect of intravenous immunoglobulin.
Case report: Intravenous immunoglobulin is a safe therapy in many diseases. Side effects due to IVIG therapy usually are mild. Rarely can it lead to meningitis. We encountered aseptic meningitis in patient with acute inflammatory demyelinating polyneuropathy following IVIG.
Results and discussion: The incidence of drug-induced aseptic meningitis (DIAM) is unknown. Other drugs that have been associated with DIAM include NSAIDs, ranitidine, carbamazepine, vaccines against hepatitis B and mumps, immunoglobulin, and radiographic agents. Most of the reported cases had ITP as the primary disease or received high dose IVIG therapy. It has rarely been reported in patient with AIDP.
Conclusions: Recognition of aseptic meningitis as an adverse reaction following IVIG therapy is important as it may be treated effectively.

1. Introduction

Intravenous immunoglobulin (IVIG) therapy is usually associated with mild, transient and often self-limiting adverse effects with potentially serious complications occurring in less than 5% of patients. IVIG-associated transient aseptic meningitis is one such rare adverse effect.

2. Aim

To learn that IVIG can lead to serious but self-limiting aseptic meningitis.

3. Case report

A 33-years-old male presented with acute onset weakness of all four limbs which gradually progressed to peak within 4 days. It was associated with pain in the limbs for last 10 days. He was non diabetic and not a hypertensive. Past history was not suggestive of tuberculosis. There was no such illness in past. Family history was not significant. He was not an alcoholic and was not addicted to anything. On examination power in all muscles was 4/5 with no sensory or autonomic involvement. Other systemic examinations were normal. A provisional diagnosis of acute inflammatory demyelinating

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polyneuropathy (AIDP) was made. Cerebrospinal fluid (CSF) analysis showed protein of 60 mg/dL, sugar of 77 mg/dL and white blood cell count of 4 cells/mm^3. Nerve conduction velocities study (NCV) was suggestive of Guillain–Barre syndrome. Thus after the diagnosis was established the patient was started on IVIG at a dose of 0.4 g/kg per day. It was administered at rate of 0.5 mL/kg per minute. After first dose he complained of anxiety and was hypotensive. IVIG was withhold following suspicion of acute reaction due to IVIG infusion and was started on IV inotropic support following that blood pressure improved. On the next day he complained of headache, vomiting and neck stiffness. On examination, his temperature was 37°C and other vital signs were stable. He had signs of meningeal irritation in the form of marked neck stiffness, photophobia, positive Kernig's and Brudzinski's signs. Fundus examination was normal. There was no focal neurological deficit.

Acute meningitis was suspected and the patient was investigated accordingly. Investigations at this point revealed peripheral blood smear showed hemoglobin of 10 g/dL, white blood cell count 15,400 cells/mm^3 and platelet count of 160,000 cells/mm^3. CT scan of brain showed no abnormalities.

CSF was clear and showed leukocyte pleocytosis (225 cells/mm^3) with lymphocytic predominance (87%). CSF glucose was normal but proteins were elevated (105 mg/dL). CSF gram-stain showed no organisms. In the meantime an intravenous antibiotic (ceftrixone) was administered. Bacterial and fungal cultures of CSF and blood cultures remained sterile. Polymerized chain reaction of CSF was also negative for herpes simplex virus and tuberculosis. He improved gradually and a repeat CSF analysis on the fifth day of hospitalization showed white blood cell count 65 cells/mm^3 with persistent lymphocytosis (97%). CSF glucose and protein levels were normal. A diagnosis of aseptic meningitis possibly due to immune reaction of IVIG therapy was made and antibiotics were stopped. His symptoms and signs of meningitis completely regressed within next week of hospitalization. His weakness of limbs also was improving.

4. Results and discussion

The incidence of drug-induced aseptic meningitis (DIAM) is unknown. Many antimicrobials can cause this entity (e.g. trimethoprim sulfamethoxazole, ciprofloxacin, cephalexin, metronidazole, amoxicillin, penicillin, and isoniazid). Other drugs that have been associated with DIAM include non-steroidal anti-inflammatory drugs, ranitidine, carbamazepine, vaccines against hepatitis B and mumps, immunoglobulin, and radiographic agents.

The pathogenic mechanisms of DIAM are not well understood but presumably differ from drug to drug. It is probably due to direct meningeal irritation following intrathecal drugs and hypersensitivity reactions to the drug (type III and IV). In type III hypersensitivity reactions, the drug or its metabolite forms a complex with antibodies in the serum, in turn activating the complement cascade. In type IV reactions T helper cells, after previous sensitization, are recruited to the site of inflammation.[1] Aseptic meningitis along with cerebral vasospasm or ischemic encephalopathy has been reported with IVIG therapy.[2] Activation of TNF-α primed neutrophils by atypical antineutrophil cytoplasmic antibodies of IVIG can contribute to these side effects.[3] The effectiveness of IVIG is well documented and generally considered a safe therapy in many immunological and inflammatory diseases.

Most frequent adverse effects are mild and transient occurring in less than 5% of patients.[4] It includes flu-like symptoms i.e., headache, fever, chills, myalgia, and fatigue. Other symptoms being dyspnea, back pain, nausea, vomiting, diarrhea, blood pressure changes, and tachycardia. Most resolve within an hour of stoppage, slowing of infusion and respond to symptomatic treatment. More serious effects are rare and include anaphylaxis, hemolysis, hepatitis, thrombosis, arthritis, and renal failure. Though aseptic meningitis has also been reported as a serious complication following IVIG therapy, it is a self-limiting condition and easily manageable.[5]

In most of the reported cases, signs and symptoms occurred within 48 h of IVIG infusion, but some cases presented as late as 7 days after the therapy.[6]

The side effects including aseptic meningitis are particularly frequent in patients treated with high-dose IVIGs (2.0 g per kilogram of body mass), e.g. in individuals with neuromuscular disorders.

Most of the reported cases had idiopathic thrombocytopic purpura as the primary disease or received high dose IVIG therapy.[5] It has rarely been reported in patient with AIDP. The CSF analysis revealed white blood cells count ranging 200–6670 × 10 cells/L (pleocytosis) and in most cases, mildly to moderately elevated CSF protein with normal CSF glucose concentration. No long term sequelae are reported so far. Slow infusion of low concentration IVIG products and hydration, especially in high-risk patients can help to prevent aseptic meningitis. In addition prehydration, paracetamol and use of antihistamines can be helpful.

5. Conclusions

Recognition of aseptic meningitis as an adverse reaction following IVIG therapy is important as it may be treated effectively.

Conflict of interest

None declared.

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