

Drug Induced Aseptic Meningitis due to IV Immunoglobulins

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Abstract

Drug induced aseptic meningitis (DIAM) is an uncommon condition that can mimic infectious process. DIAM constitutes a diagnostic and management challenge. We report a case of a 23-year-old female presenting with aseptic meningitis, two days after commencing a course of intravenous immunoglobulins (IVIG) treatment.

Keywords: Management; Treatment; Vomiting; Therapy

Introduction

Drug induced aseptic meningitis (DIAM) is an uncommon condition that can mimic infectious process. DIAM constitutes a diagnostic and management challenge. We report a case of 23-year-old female with a history of acetylcholine receptor (ACHR), antibody positive Myasthenia Gravis was commenced on two-day course of Intravenous Immunoglobulins (IVIG), for worsening myasthenia gravis symptoms at a dose of 1 g/Kg/day. It is important that clinicians be aware of and be vigilant for aseptic meningitis as a drug induced complication of IVIG.

Case Report

A 23-year-old female with a history of acetylcholine receptor (ACHR), antibody positive Myasthenia Gravis was commenced on 2-day course of IVIG, for worsening myasthenic symptoms at a dose of 1 g/Kg/day for 2 days. Two days after IVIG infusion, she presented to emergency department with severe headache, which was worse on sitting up and coughing, associated with photophobia. She also had one episode of vomiting. She did not have fever and no recent use of analgesia.

She had been diagnosed as Myasthenia Gravis in 2010 and had a myasthenia exacerbation in 2012, requiring IVIG and Rituximab. For maintenance therapy she was on Pyridostigmine, Prednisone and Azathioprine. She did not have past history of migraine.

On examination she was afebrile and irritable and had features of meningism, like positive neck stiffness and positive head jolt test. Physical examination revealed signs consistent with myasthenia gravis but no new focal neurological signs and no skin rash. Full blood count, urea and electrolytes and inflammatory markers were normal.

CT scan of the head was normal. Lumbar Puncture was performed cerebrospinal fluid (CSF) results (Table 1) showed white cell count 241/cm³, higher proportion of polymorphs and mildly elevated proteins and normal glucose 2.7 mmol/L, Gram stain and culture were negative. Viral PCR for herpes simplex, enterovirus and Cryptococcus were negative (Table 1).

Patient was diagnosed with aseptic meningitis secondary to IVIG. Her headache has improved on the second day of admission, with IV fluids and analgesia.

Discussion

The common causes of drug-induced aseptic meningitis (DIAM) are nonsteroidal anti-inflammatory drugs (NSAIDs), antimicrobials, intravenous immunoglobulin (IVIG) treatment, and monoclonal antibodies [1]. DIAM is a diagnosis of exclusion and depends on the establishment of a causal relationship with a certain drug, as well as clinical features compatible with cerebrospinal fluid (CSF) findings.

CSF Constituent/Test	Result
Appearance	Clear
White cell count	241/cm ³
White cell differential (%)	Polymorphs 54% Mononucleated 46%
Red cell count	3/cm ³
Protein	0.62 g/L
Glucose	2.7 mmol/L
Paired serum glucose	4.6 mmol/L
Gram Stain	Negative
Culture	Negative
Viral PCR for Herpes simplex, Enterovirus	Negative
Cryptococcus neoformans antigen	Negative

Table 1: Patients cerebrospinal fluid results.

IVIGs are commonly used as replacement therapy for immunodeficient conditions and immunomodulatory therapy for immune-mediated neurology and haematological conditions.

Patients receiving IVIG therapy can have minor side effects, such as headache, nausea, vomiting, and flushing in 1 to 15% of them. In a retrospective analysis, this could be as high as 81% [2]. Aseptic meningitis (AM) is an uncommon complication of IVIG treatment. Reports in the literature demonstrate a prevalence of approximately 1% [3-5]. One retrospective analysis of 54 patients found clinical evidence of AM in 11% of patients following IVIG [6]. Factors which may predispose to its development include high-dose IVIG (2 g/kg of body weight), history of migraine [6], and underlying connective tissue disorders, which might include systemic lupus erythematosus (SLE) [7].

Symptoms of AM generally occur within 48 hours of starting IVIG and can remain for up to 7 days following the last infusion [6]. CSF findings in DIAM vary considerably, however; there can be a pleocytosis of one hundred to several thousand cells per microliter (µl). Polymorphonuclear predominance is typical, but lymphocytic and eosinophilic findings are also frequently reported [6].

The cause of AM with IVIG is unknown. Theories include an allergic hypersensitivity reaction, serum immunoglobulin crossing the blood brain barrier, or sensitivity to stabilising agents like polyethylene glycol, maltose, sucrose, and glycine- all of which can cause AM [6].

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Our patient did not have any risk factors, except for high-dose IVIG. In fact, she had a course of high-dose IVIG in the past for myasthenia exacerbation with no complications.

The management of DIAM is withdrawal of the medication, supportive fluids and analgesia for symptom relief. If there is no evidence of infection, antibiotics are not required. Patients usually make an excellent recovery with no long-term sequelae. There are several measures that should be done to prevent DIAM if high-dose IVIG might be administered in the future: measures are good fluid intake, co administered with antihistamine, and a slower IVIG infusion rate. Corticosteroids have not been of significant benefit in the management of IVIG-induced AM. Sometimes, changing IVIG preparations can prevent its recurrence [6].

Conclusion

It is important that clinicians be aware of AM as a drug-induced complication of IVIG.

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