ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 11, pp.61533-61534, November, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ACUTE ASEPTIC MENINGITIS DUE TO INTRAVENOUS IMMUNOGLOBULIN: ABOUT A PEDIATRIC CASE

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ARTICLE INFO

Article History:
Received 28th August, 2017
Received in revised form
10th September, 2017
Accepted 07th October, 2017
Published online 30th November, 2017

Key words:
Aseptic meningitis, Child, Immunoglobulin.

ABSTRACT

The occurrence of aseptic meningitis as a result of intravenous infusion of immunoglobulin is a rare complication (Approximately 1% of patients treated). We report our first case of a girl aged 9 years followed for hyper Ig M syndrome, having developed a febrile meningeal syndrome 7 hours after its first intravenous immunoglobulin infusion, The lumbar puncture showed pleocytosis (total cell counts: 90 cells) with 70% neutrophiles, cerebrospinal fluid(CSF) Chemistry was normal. CSF gram stain, culture for bacteria were negative. The outcome was favorable with analgesics. The first observations of aseptic meningitis after intravenous immunoglobulin have been reported since 1968 in both adults and children. The exact pathophysiology is not clear. Although rare, the medicinal origin, especially intravenous immunoglobulin of aseptic meningitis in children should be evoked in the absence of any other cause.

Citation: Daoudi, A., Rada, N., Etalbi, C., Draiss, G. and Bouskraoui, M. 2017. "Acute aseptic meningitis due to intravenous immunoglobulin: About a pediatric case", *International Journal of Current Research*, 9, (11), 61533-61534.

INTRODUCTION

Immunoglobulin (IG) therapy is actually used for a broad range of diseases including primary and secondary immunodeficiency disorders, and autoimmune diseases (Patrick Cherin *et al*., 2015). Generally, IG infusions are well tolerated; however some well-known adverse reactions, ranging from mild to severe, are associated with the therapy. One of these severe events is aseptic meningitis who is rare but significant complication of intravenous immunoglobulin (IVIG) therapy. The true incidence and natural history of this adverse reaction are unknown; the majority of literature is limited to case reports, the literature suggests an incidence of 0% to 1 % (Vighnesh Bharath *et al*., 2015). We describe our first case of aseptic meningitis following IVIG therapy for hyper Ig M syndrome.

Case Report

A 9-year-old girl followed in our department for hyper Ig M syndrome revealed by repeated otitis and repiratory infections, presented with a history of worsening headache, neck pain and recurrent episodes of vomiting with fever, 7 hours after infusion of IVIG. On clinical examination, meningeal signs including neck rigidity, Kernig's and Brudzinski's signs were positive and Consciousness was preserved without focal neurological signs. The lumbar puncture showed pleocytosis (total cell counts: 90 cells) with 70% neutrophiles, cerebrospinal fluid (CSF) Chemistry was normal. CSF gram stain, culture for bacteria was negative. Haemogram revelated hemoglobin 11.6 g/dl, white blood cell count 7500 cells/mm3, and platelet count of 300,000/ mm3 and blood culture was sterile. The patient was managed symptomatically with semi-seated position and analgesics without any specific antibiotic. The outcome was favorable after 2 days with disappearance of the signs of meningeal irritation and fever. The Child was discharged after 3 days in normal conditions and without sequelae. The following administrations of IVIG were conducted monthly without incidents.

DISCUSSION

In recent years, human-driven intravenous immunoglobulins (IVIG) administered intravenously have been widely used in treatment of many diseases (Bülent Zülfikar and Basak Koç, 2014) used in the first time in USA in 1981 used in patients with immunodeficiency characterized hypogammaglobulinemia (Schwartz, 2000). Generally, immunoglobulin infusions are safe and well tolerated; however some well-known adverse reactions, ranging from mild to severe, are associated with the therapy. Most reactions are mild and reversible (Peter J. Späth *et al*., 2015). The most reported adverse reactions are related to the infusion rate. Others may be

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related to the dosage, the selected product (due to differences in manufacturing processes and final composition) or even to the pre-existing comorbidities (Patrick Cherin *et al*., 2015; Cherin and Cabane, 2010). Other more severe adverse effects may occur after intravenous infusion of immunoglobulin, including the occurrence of aseptic meningitis. This complication was rare and often described on a few cases and the literature suggests a 0% to 1% incidence. In a recent study including 1324 patients and 11,907 IGIV infusions, the incidence of aseptic meningitis was evaluated at 0.6% (Vighnesh Bharath *et al*., 2015). It occurred in both sexes and in al ages. Compared to our experience of about 9 years of care for about 100 patients treated with immunoglobulins in its multiple indications, this is our first case of aseptic meningitis served after IVIG. Most of the literature report appearance of symptoms within 48 h of initiation of IVIG therapy; however, in our case, aseptic meningitis developed only after 7 hours. The exact pathophysiology of IVIG-induced aseptic meningitis is unknown, but it is postulated that IgG crossing the blood-brain barrier may be responsible for the activation of local immune reaction and the inflammation of the meninges (Patrick Cherin *et al*., 2015). The risk factors for IVIG-associated aseptic meningitis include rapid, high-dose infusion of IVIG and previous history of migraine (Patrick Cherin *et al*., 2015). Most patients develop the condition during their first cycle of therapy, but the recidive of this condition is possible and described in the literature (Hamrock, 2006). The diagnosis of aseptic meningitis is not always easy, because it is first necessary to eliminate an infectious origin that will require urgent and specific care. Aseptic meningitis due to IVIG was frequently associated with polymorphic pleocytosis in the CSF examination. In our case the leukocytes in CSF were mainly neutrophils and the culture was sterile after 48 hours of incubation. Slow infusion of low-concentration IVIG products and hydration, especially in high-risk patients may help prevent aseptic meningitis (Kaarthigeyan and Vasu V. Burli, 2011). Pretreatment with analgesics, nonsteroidal anti-inflammatory drugs, antihistamines or intravenous glucocorticoids may also be beneficial. The outcome of aseptic meningitis after IVIG was favorable in the majority of cases (Vighnesh Bharath *et al*., 2015; Rajendra Singh Jain *et al*., 2014) and the treatment is essentially symptomatic.

Conclusion

The occurrence of aseptic meningitis after intravenous infusion of immunoglobulin is rare but considered a severe adverse reaction. The diagnosis should not be retained without elimination of an infectious origin. The prevention of this reaction is possible with simple measures based mainly on the slower infusion rate and good hydration.

Conflict of interest

The authors declare that they have no conflict of interests.

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