

CANDIDAL SEPTICEMIA FOLLOWING INTRAVENOUS IMMUNOGLOBULIN

A Case Study by Karnik ND¹, Kannan S², Gupta V¹, India
(Departments of Medicine ¹ & Clinical Pharmacology ², Seth GS Medical College & KEM
Hospital, Parel, Mumbai)
Email: drndkarnik@hotmail.com

ABSTRACT

Intravenous immunoglobulin (IVIG) is used in various autoimmune disorders and is the agent of choice in the management of Guillain Barre Syndrome. Review of literature shows association of viral and bacterial infections with the use of IVIG and in this paper we describe a case of fungal septicemia that occurred after treatment with IVIG.

KEYWORDS: Fungal sepsis, Intravenous immunoglobulin

INTRODUCTION

Guillain-Barre syndrome (GBS) is an acute, demyelinating polyneuropathy involving the spinal roots, peripheral nerves, and often the cranial nerves due to segmental destruction from a lymphocyte-mediated autoimmune reaction. Intravenous immunoglobulin (IVIG) is the agent of choice along with other supportive measures. Adverse reactions to intravenous immune globulin occur in less than 5 percent of patients [1]. Some of the reported side effects of IVIG include fever, myalgia, headache, nausea, vomiting, aseptic meningitis, neutropenia, hypertension, numbness, tingling, dizziness, anaphylaxis, thrombosis, Parvovirus B19 and hepatitis C infections (transmitted through the immunoglobulin products), cutaneous vasculitis, aseptic meningitis, sepsis and viral infection [2]. We here describe a case of candidal sepsis in association with IVIG in a patient who developed GBS following malaria. This association, based on our literature review in MEDLINE, has not been reported previously.

DESCRIPTION OF THE CASE REPORT

A 42 year old male was admitted for malaria in another hospital and was being treated with antimalarials developed weakness of all the four limbs associated with giddiness and loss of balance. The weakness progressed, patient developed bulbar and respiratory muscle weakness requiring intubation and mechanical ventilation. On transfer to our hospital, he had a power of 2/5 and 3/5 in both the upper and lower limbs respectively, bifacial, bulbar and respiratory weakness and was afebrile. MRI brain was normal and nerve conduction study was suggestive of

severe demyelinating polyneuropathy. He was administered injection IVIG 25 grams IV daily (0.4 g/kg/day) for 5 days with injection artesunate 120 mg IV once a day and injection heparin 5000 units subcutaneous twice a day.

Injection piperacillin and tazobactam 4.5 grams IV thrice a day was added for purulent respiratory secretions and leucocytosis. On day 3 of admission the patient developed fever of 38.4 degree C and the antibiotic was changed to injection imipenem with cilastatin 1 g IV four times a day and vancomycin 1 gram IV twice a day. Bronchoalveolar lavage (BAL) had shown a mixed growth of *Acinetobacter* sensitive to imipenem and *Klebsiella* species sensitive to polymyxin B and colistin and resistant to imipenem. Patient's fever persisted (>38.4 degree C) and hence on day 7, imipenem and vancomycin were stopped and the patient was started on injection colistimethate sodium 2 MIU intravenously every 8 hourly.

However, fever continued and on day 13 of admission, his sample for BAL and two blood samples for fungal cultures that were sent on day 9 of admission revealed budding yeast cells and candidal species. He was started on injection amphotericin B 40 mg IV once a day after confirming the candidal growth with the repeat blood culture and after 48 hours of amphotericin B initiation, the patient became afebrile. He was given a total of 2 grams of amphotericin over 20 days and subsequent blood cultures were negative for candida.

DISCUSSION

In tropical countries, GBS has been described in literature as a very rare complication following falciparum malaria. The possible mechanism may be the damage of peripheral nerves due to the vascular occlusion by malarial parasite, causing anoxaemic stagnation in the vasa nervosum leading to temporary demyelination [3]. In recent years, IVIG has become standard treatment for GBS because of ease of administration and a comparatively better side-effect profile than plasmapheresis. The beneficial effects of IVIG in GBS are attributed to multiple, mutually nonexclusive mechanisms that include modulation of Fc receptor expression and function, interference with activation of complement and the cytokine network including chemokines, regulation of cell growth, and the effects on the activation and effector functions of dendritic cells, macrophages, natural killer (NK) cells, and T and B cells and suppression of immunoglobulin production of B lymphocytes [3-8].

Chemotactic factors produced by a variety of cells, including leukocytes, epithelial cells, endothelial cells, fibroblasts and smooth muscle cells following stimulation by cytokines or microbial products and phagocytic activity of neutrophils are the primary effector mechanism in preventing infection by *Candida albicans* and *Aspergillus fumigatus* [9]. Although intensive care unit (ICU) stay of more than 20 days, prolonged administration of broad spectrum antibiotics and immunosuppressive states are risk factors for candidal infection, our patient had a short stay of 8 days prior to the development of candidal infection, was otherwise immunocompetent, had no evidence of sepsis on admission (serum procalcitonin levels were normal) and was persistently febrile despite being administered antibiotics according to culture and sensitivity report. Hence candidaemia as a complication of ICU stay or broad spectrum antibiotics administration is unlikely.

Causality assessment for the likelihood of candidal septicemia with IVIG in this patient was performed with Naranjo scale [10] and a score was 3, suggestive of a possible association was obtained. The probable mechanism for the development of candidal septicemia in this patient may be the decrease in production of chemotactic factors by lymphocytes and reduced phagocytic function of neutrophils. Although WBC count may be within the normal range, their functions may be altered due to the possible immunosuppression by IVIG. Fungal sepsis should be considered (and ruled out by cultures) in the differential diagnosis of fever and sepsis post IVIG.

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