Case Report

Guillain-Barre Syndrome Following Combined Chikungunya and Dengue Infection: Critical Care Management and Future Research

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Abstract

Guillain-Barre Syndrome (GBS) is an autoimmune inflammatory polyneuropathy, which usually develops following infectious diseases. It is a known complication of dengue fever, in particular; however, GBS following combined Dengue and Chikungunya infection is extremely rare. We hereby report a patient with combined Dengue and Chikungunya fever, without associated thrombocytopenia. The main concern in this case was the sudden development of GBS, which was responsive to double immunoglobulin therapy and required a percutaneous dilatational tracheostomy (PCT) to facilitate weaning from ventilation.

Introduction

Combined Chikungunya and Dengue infections can occur in endemic areas, especially during epidemics.[1] Both of the viruses are transmitted by the same *Aedes* mosquito, and both are acute febrile illnesses characterised by fever, myalgia, lethargy, headache and rash.[2] They could occur as either coinfections or superinfections. Chikungunya virus is an RNA alphavirus belonging to the *Togaviridae* family (group A arbovirus). Dengue virus is a single-strand RNA virus, belonging to the *Flaviviridae* family, with four antigenic serotypes (DENV 1–4). The presentation of such combined infections can be quite fascinating and unpredictable, possibly due to viral interactions at the cellular level. The resultant clinical picture could be either devastating, with high mortality, or of a relatively milder nature, with good recovery.

Guillain-Barre syndrome (GBS) is a known complication of any viral illness, and is a known sequelae of Dengue infection.[3] It is a rare, but cases of Chikungunya infection have been reported. GBS with bulbar and respiratory involvement can be life-threatening and requires immediate airway management. Tracheostomy may be done to assist in weaning from ventilation and tracheobronchial toilette. Percutaneous tracheostomy (PCT) has several advantages over the traditional surgical tracheostomy and can be performed as an elective procedure by intensivists.[4]

Herein, we discuss the management of GBS in a patient with combined Dengue and Chikungunya infection by percutaneous tracheostomy. Destruction of platelets, which is an over-riding feature of Dengue fever and its complications, was conspicuous by its absence in this case scenario. Another highlighting point was the requirement of double dose of intravenous immune globulin (Ig) for clinical improvement in muscle power.[5]

Case Report

A 48-year-old male patient (American Society of Anesthesiologists grade 1) was admitted to our tertiary care centre with complaints of fever along with weakness of bilateral upper and lower limbs. The patient was apparently well 3 days previous, when he started developing numbness and weakness of lower limbs below the knees, which was progressive, symmetric and ascending in nature. After 3 days, the patient also developed similar weakness of both the upper limbs. The patient also reported a history of febrile illness 7 days prior to the onset of limb weakness, which was accompanied by mild generalised joint pains. There was no previous history of chronic illnesses or any other co-morbidities or allergies.

At the time of presentation, all vital parameters were within normal limits. On systemic examination, no abnormality was detected on cardiovascular, respiratory and abdominal examinations. On central nervous system examination, the Glasgow coma scale score was 14/15, with normal pupils and muscle power grading of 3/5 in the upper limbs and 2/5 in the lower limbs. There was loss of deep tendon reflexes. Sensory examination did not reveal any sensorineural deficit. Serologic tests were positive for both Chikungunya and Dengue viruses. Widal test and other viral markers were negative. Standard supportive therapy, along with empirical antibiotics and intensive monitoring, were instituted. The next day, the patient developed an inability to swallow and difficulty in breathing. Bulbar involvement was suspected.

Keywords: Dengue fever; Chikungunya; Guillain-Barre syndrome; Polyneuropathy; Percutaneous dilatational tracheostomy; Immunoglobulin therapy; Thrombocytopenia.

Abbreviations: GBS, Guillain-Barre syndrome; ICU, Intensive Care Unit; PCT, percutaneous tracheostomy; IVIG, intravenous immune-globulin; DENV, Dengue virus.

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The patient was intubated with an oral, cuffed endotracheal tube and put on mechanical ventilation (synchronised intermittent mandatory ventilation mode). Hemodynamic parameters were maintained within normal limits. Invasive monitoring (via arterial and central venous pressure lines) was also instituted. Findings from nerve conduction studies were suggestive of inflammatory polyradiculopathy, indicating a diagnosis of post-viral GBS. Computed tomography of the brain was unremarkable. All biochemistry investigations were within normal limits, except for an elevated total leucocyte count. Surprisingly, there was no thrombocytopenia.

Treatment with intravenous (IV)-Ig was started (daily dose of 0.4 g/kg for 4 days). In view of the prolonged ventilation due to bulbar involvement, an elective percutaneous dilatational tracheostomy was performed under complete aseptic conditions, with local anaesthesia and intravenous sedation. An 8-mm cuffed tracheostomy tube was inserted and the endotracheal tube was withdrawn after verifying adequate bilateral air entry. The tracheostomy tube was connected to the ventilator and weaning was initiated slowly.

The patient started showing dramatic improvement after the second round of IV-Ig therapy (0.4 g/kg for another 5 days) and intensive physiotherapy. The patient was maintaining oxygen saturation and vital parameters consistently well on continuous positive airway pressure mode, and was finally put on T-piece with humidified oxygen. After observation in the Intensive Care Unit for 72 hours on T-piece, the patient was shifted to the High Dependency Care Unit, and showed a motor power of 4/5 in both the upper and lower limbs. All other supportive measures were continued and the patient was finally shifted to the ward after 2 weeks in stable condition.

Discussion

GBS is named after French neurologists Georges Guillain and Jean Alexandre Barré, who identified the syndrome along with Andre Strohl in 1916.[6] It develops following an autoimmune reaction of the body's immune system against its own peripheral nervous system by damaging the myelin sheaths (acute immune-mediated polyneuropathy). Nearly a quarter of these patients may require definitive airway and artificial ventilation. This form of immune dysfunction is triggered by any stressful situation, in the form of infection (viral or bacterial), surgery or vaccination.

GBS following dengue infection is a known, though rare complication. GBS following Chikungunya is a rarer complication. Another important observation in the patient described herein is the absence of thrombocytopenia following the combined Dengue and Chikungunya infection. In one study by Caron *et al*, it was found that coinfection with Dengue and Chikungunya reduces the overall viral load in the affected patients.[7] More evidence-based research is required, however, to explain absence of thrombocytopenia in our patient. Since the effects of each of the viruses at the cellular level can be either complementary, additive and/or opposite, their presentation can be varied and unpredictable.

Three important insights arise from our case. One is the possibility of prevention of platelet destruction by the presence of Chikungunya virus on the platelets infected with the Dengue virus. The second is a hypothesis for the development of inflammatory polyneuropathy as a presenting feature in combined Dengue and Chikungunya infection. The third is the possible administration of a second course of IV-Ig in severe GBS with partial clinical response to the first dose.

Both of the viruses are transmitted by the Aedes mosquitoes (mainly *Aedes aegypti* and less commonly *Aedes albopictus*).[8] Hence, their infections are related epidemiologically. Both the viruses can also co-circulate in endemic areas, so that combined Chikungunya and Dengue virus infections can occur during an epidemic or in travellers to endemic regions. Neurological complications of Dengue virus infection occur in 0.5–0.7% of symptomatic cases.[9] Moreover, several immune-mediated neurological syndromes can occur following Dengue infection.

The clinical presentation of GBS following either Dengue or Chikungunya infection is similar and comprises acute, progressive and ascending (distal to proximal) weakness of lower and upper limbs, generalised hypo- or areflexia and autonomic symptoms (in one-third of cases). Involvement of cranial nerves is seen in nearly 45–75% of patients, presenting with any of the following features: facial drop, diplopia, dysarthria, dysphagia, ophthalmoplegia and pupillary abnormalities.[10]

Our patient presented with fever and sudden onset neurological weakness, which is a rare mode of presentation of either viral illness in isolation. Further, there was no evidence of thrombocytopenia or platelet destruction in our patient, which is the hallmark of Dengue infection. GBS with bulbar involvement and progressive weakness with respiratory difficulty was responsible for the institution of ventilatory support in our patient. IV-Ig has been shown to have efficacy in early, severe GBS patients, who cannot walk unaided. There are several reports in the literature citing the efficacy of a repeat, second course of IV-Ig in some selected patients.[11–14] A low increase in serum IgG levels after a standard dose of IV-Ig has been associated with slower recovery and unfavourable prognosis. The Erasmus GBS outcome score can be used to predict the prognosis of patients with GBS and may be used to guide therapy.[15] Our patient showed only partial improvement with the first course of IV-Ig and hence a second course was given, which resulted in good improvement in muscle power.

In the initial part of the illness, reverse transcriptase-polymerase chain reaction was used to directly detect the Chikungunya virus nucleic acids (CHIKV) and the Dengue virus nucleic acids (DENV) in serum, as recommended for suspected cases. After 5 or more days, serum should be evaluated for anti-CHIKV and anti-DENV IgM antibodies by immunoassay.[16] Anti-DENV IgG antibodies have little utility in the diagnosis of acute Dengue, however, due to false positivity and cross-reactivity. Both viruses should be suspected in people returning from the tropics who present with acute febrile illness.

Apart from standard supportive therapy for acute febrile illnesses and GBS, appropriate ventilatory management is a major influencing factor for the outcome of these patients. PCT is a promising technique carried out in the Intensive Care Unit as a semi-elective procedure under sedation and local anaesthesia, with numerous advantages as compared to surgical tracheostomy.

Clinical perspectives

Combined Dengue and Chikungunya infections are becoming more common in endemic areas and during epidemics. More rigorous control of the vector (*Aedes* mosquito) is the need of the hour. Such clinical scenarios pose several important perspectives, which need to be addressed by large-scale epidemiologic studies. The clinical presentation of these combined infections is generally unpredictable. Microbiologic studies at the cellular level may answer a few of the unanswered questions.

The important observations from this case are the occurrence of severe GBS, which required double-dose IV-Ig therapy for clinical improvement, and the absence of thrombocytopenia. Viral inter-

actions at the cellular level may confer both a deleterious and a protective effect. High-dose or double-dose IV-Ig therapy has been recently investigated to produce improvement in muscle power in resistant or severe cases of GBS. IV-Ig is preferable to plasmapheresis in most situations, as it is more likely to be completed and is non-invasive. Tracheostomy as an option for intubated GBS patients requiring prolonged ventilation, and has been advocated since time-immemorial. PCT is an attractive option for these patients, according to its advantages over the conventional technique. It facilitates early weaning from the ventilator, thereby preventing ventilator-associated complications.[17]

Conclusions

Combined Dengue and Chikungunya infections can occur in travellers to endemic regions and in epidemic areas. GBS can be the presenting feature in either of the two infections. Viral co-infection or superinfection and interactions at the cellular level are responsible for the varied and unpredictable presentations of combined Dengue and Chikungunya infection. There is a definite role of a double dose of IV-Ig in severe GBS cases that are unresponsive or partially responsive to the first dose. In patients with bulbar or respiratory involvement, securing of the airway and artificial, mechanical ventilation is required as a life-saving measure. PCT is an advantageous technique performed in such patients by intensivists, which assists in early weaning of the patient from the ventilator as well as in trachea-bronchial toilette.

Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Conceived, wrote, edited & finalized the entire manuscript in all stages (UH), edited & guided the final draft of manuscript (LC), collected, compliled and wrote the case details (NB).

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