

GUILLAIN-BARRÉ SYNDROME AFTER A SNAKEBITE: CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

The Guillain-Barré syndrome is an autoimmune disorder of the peripheral nervous system and an important medical emergency. It is commonly a post-infectious disorder but there are cases occurring after vaccinations or other events. Snakebite is a rare cause of GBS with only a few reports in medical literature. This article reports a case of a 62-year-old man with acute flaccid tetraparesis and areflexia following a *Crotalus* snakebite occurred in the Northern Brazilian Amazonian region. The CSF study showed albuminocytological dissociation and the patient had improvement after treatment with intravenous human immunoglobulin. The development of GBS occurred due to snakebite, administration of tetanus toxoid or antivenom. The purpose of this article is to report a case of GBS following a snakebite event, and to review the literature on this peculiar association.

Keywords: Guillain-Barré syndrome; Snake bites; *Crotalus*; Tetanus toxoid.

SÍNDROME DE GUILLAIN-BARRÉ PÓS-ACIDENTE OFÍDICO: RELATO DE CASO E REVISÃO DE LITERATURA

RESUMO

A síndrome de Guillain-Barré (SGB) é uma desordem autoimune do sistema nervoso periférico e constitui uma emergência neurológica grave. É comumente um distúrbio pós-infeccioso, existindo casos de ocorrência após vacinações ou outros eventos. O acidente ofídico é uma causa rara da SGB havendo apenas poucos relatos na literatura mundial. Apresentamos o caso de um paciente de 62 anos com quadro de tetraparesia flácida aguda e arreflexia após uma semana de um acidente ofídico do tipo crotálico ocorrido no extremo setentrional brasileiro. O estudo do líquido evidenciou dissociação albumino-citológica e o paciente obteve melhora do quadro após tratamento com imunoglobulina humana intravenosa. O desenvolvimento da SGB ocorreu devido à picada de cobra, à administração da vacina antitetânica ou do soro antiofídico. O objetivo deste artigo é relatar um caso de desenvolvimento de Síndrome de Guillain-Barré após picada de cobra e realizar uma revisão da literatura sobre essa associação peculiar.

Palavras-chave: Síndrome de Guillain-Barré; Acidente Ofídico; *Crotalus*; Vacina antitetânica.

INTRODUCTION

Guillain-Barré syndrome (GBS) is an autoimmune disorder of the peripheral nervous system.⁽¹⁻²⁾ The first authors to describe the SGB were three French neurologists in 1916 – Georges Guillain, Jean-Alexandre Barré and Andrew Strohl. They described two soldiers with acute paralysis and areflexia followed by recovery.⁽²⁻³⁾ Nowadays it represents an important medical emergency and it is the most common cause of acute neuromuscular paralysis since the control of poliomyelitis.⁽¹⁻²⁾ The disease is characterized by progressive flaccid paralysis associated with areflexia, sensory and autonomic alterations.⁽⁴⁾

Usually GBS is a post-infectious disorder. Approximately two thirds of patients have a history of acute infection within three weeks preceding the onset of symptoms.⁽¹⁻⁵⁾ Although some studies have reported the occurrence of GBS following other acute events, like immunization and surgery, few cases have been reported associating snakebite and SGB.⁽⁵⁻⁶⁻⁷⁻⁸⁻⁹⁾ The aim of this study is to report a case of GBS following a snakebite event, and to review the literature on this peculiar association.

CASE REPORT

A 62 year-old man from the indigenous village of Guariba (Roraima State, Northern Brazilian Amazonian region – ethnic group Macuxi) was admitted to the Hospital Geral de Roraima on August 2013, due to acute motor deficit (paresis of upper and lower limbs). There was no history of either loss of consciousness or convulsions. No recent respiratory or gastrointestinal infections was reported, and no medication was in use before admission. However, he had been hospitalized in the same health unit about two weeks earlier due to snakebite involving a *Rattlesnake* species (*Crotalus sp.*). During the previous hospitalization, specific antivenom and tetanus vaccine were administered uneventfully and he had been discharged three days after, with a satisfactory wound healing. The onset of neurologic symptoms was paresthesia of extremities and paresis of lower limbs about a week after the first hospital discharge. The paresis had a progressive and ascending pattern. During physical examination, the patient was awake and complained of numbness in the upper and lower limbs, mainly in hands and feet. A tetraparesis with crural predominance was observed, with muscle strength grade 2/5 in the lower limbs and grade 4/5 in the upper limbs (Medical Research Council scale). It was also observed generalized areflexia, dysphagia, dysphonia and bilateral peripheral facial palsy. Examination of the other cranial nerves were normal. At the

time of our evaluation, a CT scan had already been performed and it showed no alterations. The cerebral spinal fluid (CSF) analysis revealed albuminocytologic dissociation: protein concentration of 147 mg/dL (RV: 10 - 45 mg/dL) and cell counts of 2 leukocytes/mm³ (RV: 0 to 5/mm³). Blood count and biochemistry routine were unremarkable. The patient was diagnosed with GBS and was transferred to Intensive Care Unit (ICU). Therapy with intravenous human immunoglobulin was instituted in addition to rehabilitative support. Improvement of muscle strength was gradually noted. The patient remained hospitalized for 40 days and then he was discharged with muscle strength grade 4/5 in upper and grade 3/5 in lower limbs. He was referred to outpatient follow-up. An electromyography was performed on the 60th day and it was consistent with sensory and motor axonal polyradiculoneuropathy, associated with fibrillations in distal muscles. After this exam, the patient returned to his indigenous village and never returned to follow-up.

DISCUSSION

GBS is usually preceded by a viral infection of the upper respiratory tract or gastrointestinal infection and the most frequently identified agent is the *Campylobacter jejuni*.⁽¹⁻²⁻⁴⁾ There are only three reports on medical literature about the development of GBS after snakebite. Chuang et al., in 1996, were the first authors to report a case of GBS following a snakebite. The authors reported a case of a 36-year-old man who developed the syndrome and presented, as only relevant precedent, a prior admission for snakebite involving the Formosan krait (*Bungarus multicinctus*) – an elapid snake restricted to the island of Taiwan. The patient presented with symmetric paresis and sensory signs in the upper and lower limbs, autonomic dysfunction, facial nerve involvement, and mild elevated cerebrospinal fluid protein at about 4 weeks after the bite.⁽⁹⁾ Similar to our case, the patient reported by Chuang et al. presented profound sensory and motor polyneuropathy in electrodiagnostic studies. The patient reached satisfactory functional outcome after a short-term intensive rehabilitation program despite severe axonal degeneration.⁽⁹⁾

In 2010, Srivastava et al. reported a case of a man who developed GBS after a snakebite in India. The snake species was not identified. After about 2 weeks, he experienced tingling and numbness distally in all four extremities, followed by the development of weakness in all four limbs over the next week. Cranial nerves examination was normal except

for bilateral facial weakness. CSF revealed albuminocytological dissociation. The patient was treated with plasmapheresis and resumed working in the fields 6 months later⁽⁷⁾

In the present case, as in the cases described above, the lack of molecular evidences causally linking the exposure to snake venom with GBS leads us to consider other possible etiologic associations. For example, the victims of snakebite were vaccinated for tetanus, received antivenom therapy, they are commonly affected by secondary infections – factors that could also be implicated in the pathogenesis of GBS in these patients. Indeed, the association between vaccination with tetanus toxoid and GBS has been reported worldwide¹⁻⁽¹⁰⁻¹¹⁾, although this relationship has not been confirmed by large surveys.⁽⁵⁻¹²⁾

On this subject, Neil et al., in 2012, made an important contribution on the etiologic basis of the relationship between GBS and snake venom. They reported a case of a patient that presented GBS after a snakebite of *Vipera aspis* species. The authors have investigated the cross-reactivity between venom proteins and GM2 gangliosides (by Western blot assay) after immunoabsorption of patient's serum with increasing amounts of purified GM2. They demonstrated that the patient's serum presented specific cross-reactions with several glycosylated venom proteins.⁽⁶⁾ Then, Neil et al. proved the auto-immunological etiology of GBS based on molecular mimicry mechanisms between venom proteins and GM2 ganglioside. Although still not fully understood, evidences suggest that the pathogenesis of GBS is related to the presence of molecular mimicry and cross-reactivity between components of peripheral nerves (GM2 gangliosides) and epitopes from infectious agents or exogenous substances.

Indeed, antibodies against various gangliosides can be found in about half of patients with GBS.⁽¹³⁻¹⁴⁾ Serologic and biochemical studies have demonstrated that the fraction of lipooligosaccharides from the outer cell wall of *C. jejuni* contains structures that mimic gangliosides.⁽¹⁵⁾ The bacterial lipooligosaccharides GM1-like or GD1a-like induce the production of anti-GM1 and anti-GD1a in some patients.⁽²⁾

CONCLUSIONS

To the best of our knowledge, this is the fourth case of GBS to be reported in the English literature following a snakebite event. Recognition of this unusual complication following snakebite has considerable epidemiological and therapeutic significance

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