Guillain-Barre's Syndrome Associated with Plasmodium Falciparum Malaria: Role of Plasma Exchange

PASIRI SITHINAMSUWAN, M.D.*,
SUWANNA SINSAWAIWONG, M.D.*,
KITTI LIMAPICHART, M.D.*

Abstract

Guillain-Barre's syndrome (GBS) associated with malarial infection is a rare condition reported in the literature. We report a case of Plasmodium falciparum (PF) malarial infection with Guillain-Barre's syndrome complicated by respiratory failure and review of the literature. Our patient gradually improved after treatment with plasma exchange. Review of the literature showed 11 cases of GBS associated with malaria. Four of 8 patients with GBS associated with PF had respiratory failure, whereas, none of the patients with GBS associated with Plasmodium vivax (PV) developed respiratory failure. Three of four patients with respiratory failure died and one who survived was treated with intravenous immunoglobulin. Our patient was the second case to survive after treatment with plasma exchange. The role of plasma exchange, the pathogenesis of malaria in GBS and the mechanism that induced more severe GBS in PF than in PV were discussed.

Key word : Guillain-Barre's Syndrome, Plasmodium Falciparum Malaria, Plasma Exchange

**SITHINAMSUWAN P,
SINSAWAIWONG S, LIMAPICHART K
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Neurologic complications of malaria can be categorized as 1) self-limiting post malaria neurological syndrome consisting of acute confusional state, acute psychosis, generalized convulsion, tremor or cerebellar ataxia with the reported prevalence of 0.12 per cent in patients infected by Plasmodium falciparum malaria[1] and 2) neurologic sequelae that include confusion, convulsion, cranial nerve palsies, tremor and persisting coma[2]. Guillain-Barre's syndrome (GBS) is a rare neurological complication of malaria and has been described in both Plasmodium vivax (PV) and Plasmodium falciparum (PF) infec-

* Department of Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla 90110, Thailand.

tion particularly in uncomplicated cases[3-8]. A case of GBS complicated by respiratory failure as a consequence of uncomplicated PF infection improved by plasma exchange treatment was described and a review of the literature regarding GBS and malaria was presented.

CASE REPORT

A 28-year old woman was referred to Songklanagarind Hospital in November 1998 because of quadriplegia and respiratory failure. Ten days before admission, she had fever with chills without any upper respiratory tract symptoms or diarrhea and went to a local hospital for medical attention. Ring form trophozoites of PF malaria were found in the blood smear so she was treated with quinine and tetracycline. Numbness and weakness first of both lower extremities then of both upper extremities developed two days later and eventually quadriplegia, urinary retention and respiratory failure, which required ventilator support, supervened within 10 days. Physical examination at this stage revealed a body temperature of 38°C, a pulse rate of 100 beats/min and blood pressure of 140/80 mmHg. Neurological examination revealed bilateral facial paresis, quadriplegia, areflexia of all extremities, decreased sensation to both pin-prick as well as proprioception below both knees and wrists, and loose anal sphincter tone. The rest of the examination was unremarkable. Ring form trophozoites of PF malaria were still found in the blood smear. Cerebrospinal fluid (CSF) was clear and the fluid analysis showed lymphocyte count of 5/mm^3, protein concentration of 240 mg/dl and normal sugar value. CSF virologic study for cytomegalovirus IgM antibody, viral capsid antigen IgM and IgG antibody for Epstein-Barr virus were negative so were the serologic studies for anti-HIV antibody, HbsAg and anti-HCV antibody. Motor nerve conduction studies of median, ulnar, tibial and peroneal nerves showed markedly prolonged distal and F-wave latency, markedly reduced velocity, and moderate decrease in amplitudes. Sensory nerve conduction studies of median and ulnar showed no response. The findings were compatible with demyelinating polyneuropathy. Treatment by plasma exchange on every other day was started and five sessions were required till her recovery from respiratory failure. The neurological deficits gradually improved with bladder dysfunction recovering within 5 days, the ventilator support was weaned off within 10 days and the muscle strength improved from MRC grade I to grade IV in upper extremities and grade III in lower extremities within 14 days.

Literature review

The literature was searched in Medline database by using the keyword "malaria" and "Guillain-Barre" and all the references in the articles retrieved from the Medline search were scanned manually for other reports regarding GBS and malaria. The cases from the literature and the case reported herein are shown in Table 1.

There were 11 cases of GBS following malarial infection in the literature and eight of these cases were infected by PF, whereas, three were infected by PV[3-8]. The time from the onset of fever to the development of GBS varied from 5-21 days with a mean of 15 days. All of the patients reported but one were uncomplicated malarial infection. The only one complicated patient had cerebral malaria. Six patients were treated with chloroquine, two with chloroquine and primaquine, one with quinine and there was no information available in two. Respiratory failure due to GBS occurred in four patients, all of these cases were infected by PF and three of them died. The one who survived and recovered completely was treated with intravenous immunoglobulin. All patients with GBS associated with PV infection had an uneventful clinical course with complete recovery.

DISCUSSION

Guillain-Barre's syndrome is acute demyelinating polyneuropathy that develops as a consequence of many exogenous stimuli particularly antecedent infectious processes[9]. The organisms frequently implicated as the culprits are viruses especially Herpes virus, hepatitis virus and HIV, bacteria such as Campylobacter jejuni and Mycoplasma pneumoniae[9]. Parasitic infections including toxoplasmosis and malaria are rare associations[9].

Our patient suffered from GBS with respiratory failure 10 days following PF infection. She had no clinical symptoms of antecedent viral illness, some other potential viruses were excluded by serological studies and no exposure to other known chemical substances that can induce GBS was obtained by careful inquiry. She was treated with quinine and tetracycline, however, there is no data pertaining to peripheral neuropathy induced by quinine and tetra-

Table 1. Clinical features of twelve patients with Guillain-Barre's syndrome associated with malaria.

No	Age (years)	Sex	Interval of fever and GBS (days)	Type of malaria	Severity of malaria	Drug treatments before GBS	Respiratory failure	Treatment of GBS	Outcome	Reference
1	15	Male	14	*P. vivax*	Not severe	Chloroquine, primaquine	No	Steroids	Complete recovery	3
2	28	Male	11	*P. vivax*	Not severe	Chloroquine	No	None	Complete recovery	3
3	24	Male	12	*P. vivax*	Not severe	Chloroquine	No	None	Complete recovery	3
4	47	Male	15	*P. falciparum*	Not severe	Chloroquine	Yes	IV Ig	Complete recovery	3
5	30	Female	16	*P. falciparum*	Cerebral malaria	Quinine	No	None	Complete recovery	3
6	32	Male	15	*P. falciparum*	Not severe	Chloroquine	No	None	Complete recovery	4
7	NA	NA	21	*P. falciparum*	Not severe	NA	Yes	NA	Died	5
8	38	Female	21	*P. falciparum*	Not severe	Chloroquine	Yes	Steroids	Died on day 5	6
9	48	Male	13	*P. falciparum*	Not severe	NA	Yes	Steroids	Died on day 3	6
10	35	Female	8	*P. falciparum*	Not severe	Chloroquine	No	None	Mild weakness	7
11	45	Male	5	*P. falciparum*	Not severe	Chloroquine, primaquine	No	None	Complete recovery	8
12	28	Female	5	*P. falciparum*	Not severe	Quinine, Tetracycline	Yes	Plasma exchange	Mild weakness	Present case

Note : NA = Information not available

cycline reported in the literature. The chronological sequence of malarial infection and the development of GBS in our patient highly suggested a causal link between them. The fever detected at the onset of weakness in GBS is an unusual finding in GBS per se, but this may be explained by the ongoing malarial infection in our case.

The pathology of GBS is characterized by infiltration of inflammatory lymphocytes and macrophages surrounding endoneural vessels leading to the adjacent demyelination. However, there is no vascular occlusion by these inflammatory cells[10]. The pathogenesis is an immune mediated mechanism *via* cell-mediated and humeral response triggered by exogenous stimuli[10]. The pathogenesis of GBS following malaria may be an immune mediated mechanism triggered by cytokines that were released by the asexual stage of malarial infection[11]. No patient with GBS associated with PV had respiratory failure compared with 50 per cent found in GBS associated with PF. However, the difference may be due to the small number of cases of GBS in PV or the microcirculatory disturbance associated with PF infection may be an important factor that induced more severe GBS. PF is the only human parasite that can produce cytoadherence of red blood cells leading to vascular occlusion or stagnation of red blood cells in capillary and post capillary venule of vasa-nervorum of peripheral nerve[1,11]. This may lead to microcirculatory disturbance with subsequent ischemia and end up finally with demyelination. Pathological studies have confirmed that the ischemic process is capable of inducing neuropathy of both the axonopathy and demyelination type[12].

The current treatment of GBS is supportive treatment to maintain vital function until the time of recovery[9,10]. Intravenous immunoglobulin or plasma exchange is recommended in patients with a disability scale of grade II or greater[9,10]. Three of four patients with GBS and respiratory failure associated with PF died and two of these were treated with steroid. Corticosteroid has no benefit in shortening the course of GBS or reducing the residual neurological deficit in GBS[9,10]. One patient with GBS and respiratory failure was treated with intravenous immunoglobulin and survived. Our patient is the second case of GBS with respiratory failure associated with PF that survived with plasma exchange treatment. Plasma exchange removes circulating agents, malarial parasites and antibodies from

the patient and is of benefit in severe malaria per se[9,11]. The role of plasma exchange contributing to the outcome in our patient is unclear. Further study to assess the role of plasma exchange in patients with GBS associated with PF is required before any conclusion can be drawn.

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พาสิริ สิทธินามสุวรรณ, พ.บ.,*
สุวรรณา สินไสววงศ์, พ.บ., กิตติ ลิ่มอภิชาต, พ.บ.**

กลุ่มอาการกีแลง บาเร ร่วมกับการติดเชื้อมาเลเรียพบน้อยมากจากรายงานในอดีต ผู้ศึกษาเสนอรายงานผู้ป่วยติดเชื้อมาเลเรียชนิดพลาสโมเดียม ฟาลซิพารัม ร่วมกับกลุ่มอาการกีแลง บาเร ที่มีภาวะแทรกซ้อนคือ การหายใจล้มเหลว ผู้ป่วยอาการดีขึ้นหลังจากรักษาด้วยการฟอกเลือดร่วมกับยาต้านมาเลเรีย การทบทวนวารสารในอดีตพบผู้ป่วยกีแลง บาเร ร่วมกับมาเลเรีย 11 ราย สี่ในแปดรายของผู้ป่วยกีแลง บาเร ร่วมกับพลาสโมเดียม ฟาลซิพารัมมีการหายใจล้มเหลวร่วมด้วย ขณะที่ผู้ป่วยกีแลง บาเร ร่วมกับพลาสโมเดียม ไวแวกซ์ จำนวน 3 ราย ไม่พบการหายใจล้มเหลว สามในสี่รายของผู้ป่วยที่มีการหายใจล้มเหลวเสียชีวิต ผู้ป่วยหนึ่งรายที่รอดชีวิตได้รับการรักษาด้วยอิมูโนโกลบูลินทางหลอดเลือด ผู้ป่วยที่รายงานนี้เป็นรายที่สอง ซึ่งรอดชีวิตภายหลังรักษาด้วยการฟอกเลือด

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* ภาควิชาอายุรศาสตร์, คณะแพทยศาสตร์ มหาวิทยาลัยสงขลานครินทร์, สงขลา 90110