

Bilateral Brachial Plexopathy Associated with Dengue Infection: The First Case Report

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ABSTRACT

Brachial plexopathy is a rare neurologic manifestation that can be caused by a variety of etiology, Either infectious or non-infectious processes. Most infectious-related processes are caused by viral infections presenting as post-viral infection neuropathy. Viruses frequently reported in the literature included herpes zoster virus, poliovirus, cytomegalovirus, West-Nile virus. We described a 62-year-old who presented with a sudden onset of orthopnea and bilateral wing scapular. Acute b ilateral brachial plexopathy caused by dengue virus infection was diagnosed. This case was the first case of brachial plexopathy associated with dengue infection reported in the literature. (*J Infect Dis Antimicrob Agents* 2010;27:95-101.)

Note: This case had been presented and discussed in the Interhospital Case Conference on Infectious Diseases (ICCID), 26 March 2010, Bangkok, Thailand

INTRODUCTION

The term brachial plexopathy was similar to neuralgic amyotrophy, local neuritis of shoulder girdle, paralytic neuritis and Parsonage-Turner syndrome.¹ Neuralgic amyotrophy, which was first described as a distinct clinical syndrome in the late 1900s, is characterized by attacks of neuropathic pain and subsequent patchy paresis in the upper extremities.² It is a rare condition that usually develops abruptly in any age. Severe constant pain is classically located around

the shoulder girdle, and is usually resistant to common analgesics.³ Neuralgic amyotrophy represents a heterogenous clinical syndrome, illustrates by Van Alfen and Van Engelen in their case-series analysis of 246 cases.¹ Most presenting symptoms were pain (90%), paresis (5.8%), sensory loss (2.9%) and muscle atrophy (1.2%).

Dengue virus, a member of flavivirus group in the family Flaviviridae, has four antigenic distinct serotypes (DEN1, DEN2, DEN3, and DEN4). Dengue

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infection is an arboviral disease transmitted globally. The incubation period ranges from 2 to 7 days after mosquito(es) bite. The clinical syndromes range from asymptomatic, undifferentiated fever, dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS).⁴

Mild dengue disease is characterized by fever, skin rash, headache, retro-orbital pain, vomiting, myalgia, arthralgia, leukopenia, thrombocytopenia, and lymphadenopathy, while DHF is an often fatal disease characterized by hemorrhages and shock syndrome.⁴

Classical dengue fever is rare among indigenous people as most of the adults are immuned. DHF is usually associated with secondary dengue infection but can appear during a primary infection, especially in infants who possess maternal IgG dengue antibody.⁴

Recently, unusual manifestations of dengue infection have been reported including encephalopathy, encephalitis, aseptic meningitis, transverse myelitis, intracranial hemorrhage, thrombosis, mononeuropathy, polyneuropathy, and Guillain-Barré syndrome.⁵⁻⁸ To our knowledge, no case report of dengue infection associated with brachial plexopathy.

CASE REPORT

In November 2009, a 62-year-old Thai woman with a well-controlled hypertension and dyslipidemia who lived in Bangkok, presented with sudden onset of orthopnea. Three days prior to admission, she developed pain at her interscapular region and her neck. The pain was aggravated by movement. She also had low-graded fever. On the following day, the pain became more severe so that she went to see a physician at a private hospital.

At the private hospital, the physician noticed two vesicles on her right shoulder. Varicella-Zoster infection was diagnosed and she received valacyclovir, orphenadrine and acetaminophen for her treatment.

Eight hours prior to admission, she experienced a sudden onset of orthopnea. The symptoms disappeared when she was in upright position. She did not report any other respiratory symptoms or chest pain. She went back to the same private hospital. At the hospital, she was found to be hypertensive (blood pressure 180/110 mmHg), tachypneic (respiratory rate 26/minutes), and hypoxemic (oxygen saturation was 89 percent at the room air). The widening mediastinum was noted on the chest X-ray. Either aortic dissection or acute pulmonary embolism was suspected, so that she was transferred to the King Chulalongkorn Memorial Hospital.

On physical examination at the King Chulalongkorn Memorial Hospital, her vital signs were recorded as follows; the body temperature 36.3°C, the pulse rate 102/minute, and the blood pressure 160/100 mmHg. In upright and supine position, the respiratory rates were 20 and 28/minute and oxygen saturations were 97 and 98 percent at room air. Decrease breath sounds at both basal lungs with dullness of percussion were noted.

Neurological examination showed that she had wing scapular bilaterally (right more than left, Figure 1). She also had weakness of the following muscles; right biceps (Medical Research Council scale for muscle strength (MRC) 4/5), right serratus anterior (MRC 3/5), and bilateral infraspinatus (MRC 3/5). There was no atrophic muscle. Bilateral biceps and radial tendon reflexes were decreased. Babinski's signs were absent. Other examinations were within normal limits.

Complete blood count revealed a hemoglobin level of 12.6 g/dL, total white cell blood count of $10.6 \times 10^9/L$ with normal differentiation, and platelet count of $342 \times 10^9/L$. Other blood chemistry results were within normal ranges. Arterial blood gas at room air showed pH 7.391, PaO₂ 60 mmHg, PaCO₂ 32.3 mmHg, HCO₃ 19.6 mEq/L. A screening test

for HIV antibody was negative. Chest X-rays performed at emergency room are shown in Figure 2 and 3.

With prior available findings, acute bilateral diaphragmatic hernia due to Guillain-Barre syndrome (variant type) was diagnosed and intravenous Immunoglobulin (IVIg) was prescribed. A lumbar puncture was subsequently performed and the cerebrospinal fluid was normal. Electromyography (EMG) and Nerve Conduction Velocity (NCV) test which were done on the fifth day of illness shows neurogenic process affecting bilateral C4, 5 myotomes, given the absence of phrenic motor responses and non abundant degree of denervation potential; brachial plexopathy are preferred.

Infectious Diseases service was asked on the following day to evaluate the possibility of Herpes Zoster brachial plexopathy, based on the presence of the vesicles on her right shoulder. Intravenous immunoglobulin (IVIg) was discontinued and intravenous acyclovir was started.

Tzanck smear and indirect fluorescent antibody (IFA) from the lesion were both negative. Polymerase

chain reaction (PCR) for Varicella-zoster viruses, Herpes simplex viruses type 1, 2 and Pan-enteroviruses RNA (Coxsackie viruses A&B, Echoviruses, Polioviruses and Enteroviruses) from cerebrospinal fluid and serum were performed and were all negative. Cerebrospinal fluid was reevaluated at the 10th day of illness. (Table 1) Again, PCR for the same viruses mentioned above were repeated and still had the negative results.



Figure 2. Chest radiograph on upright position.



Figure 1. Wing scapular both sides (Right>Left).

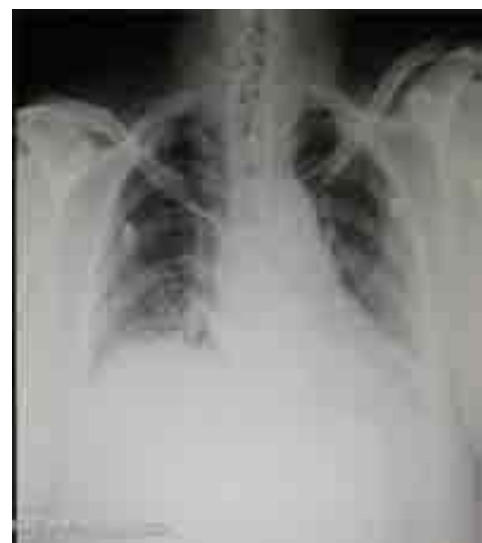


Figure 3. Chest radiograph on supine position showed bilateral elevation of diaphragm.

Table 1. Results of ELISA on serum and cerebrospinal fluid (CSF) and Hemagglutination-inhibition test (HI) on serum during acute phase and convalescence phase.

Serology	Day of illness (date)	17 th (04/12/09)	35 th (22/12/09)	90 th (17/02/10)
ELISA test				
CSF for DEN-IgM (ELISA unit)		0	Not done	Not done
CSF for DEN-IgG (ELISA unit)		15	Not done	Not done
CSF for JE-IgM (ELISA unit)		0	Not done	Not done
Serum for DEN-IgM (ELISA unit)		115	132	127
Serum for DEN-IgG (ELISA unit)		3	0	2
Serum for JE-IgM (ELISA unit)		94	88	>100
HI test				
DEN-1		1:80	1:80	1:160
DEN-2		1:80	1:160	1:40
DEN-3		1:80	1:80	1:80
DEN-4		1:80	1:80	1:160

By that time, with the unknown etiology of brachial plexopathy, we then investigated other possible viruses which could cause the similar manifestation such as Flaviviruses, especially Japanese encephalitis virus and dengue virus. Hence, serum and CSF from the 17th day of illness were reevaluated (Table 1). Serology from serum was compatible with primary dengue infection (serum dengue IgM \geq 40 U and IgG titer was not rising).⁹

MAC-ELISA from the other laboratory for the same specimen was done and showed the same results.

Follow-up ELISA and Hemagglutination-Inhibition test (HI)¹⁰ from serum during the acute and convalescence phases were shown below with unexpected findings of persistently elevation of dengue IgM antibody and negativity of dengue IgG antibody. (Table 1)

Three reverse-transcription-nested polymerase chain reaction (PCR) protocols for dengue virus were performed on plasma and CSF samples on day 17th, 35th and 90th of illness. The samples from day 17th of illness in one protocol (RT-nested PCR using 3'URT 102bp) were positive in CSF, plasma and peripheral

blood mononuclear cell (PBMC). In the repeated PCR testing from the same specimen, only plasma and PBMC remained positive.

Test for other infectious causes, such as Japanese encephalitis viruses and West-Nile viruses were negative.

In summary, her diagnosis was acute brachial plexopathy from dengue virus infection. She was hospitalized for one month for diagnosis and supportive treatment. At the time of discharge, the muscle power improved gradually; right biceps (MRC 5/5), right serratus anterior (MRC 3/5), and bilateral infraspinatus (MRC 4/5). However, she still required Bi-level positive airway pressure (BiPAP) during sleep overnight. Three months after discharge, she could sleep without BiPAP for about 30-60 minutes overnight.

DISCUSSION

Neurological manifestations of dengue infection reported previously included encephalopathy, encephalitis or aseptic meningitis, transverse myelitis, intracranial haemorrhages or thrombosis, mono-neuropathies, polyneuropathies, and Guillain-Barre syndrome.⁶⁻⁸ The study from Vietnam found that 4.2 percent of 378 patients with suspected CNS infections were infected with dengue viruses. Most of symptoms were reduced consciousness and convulsion.⁷ The other study, also from Vietnam, reported that dengue-associated encephalopathy was found in 0.5 percent of 5,400 patients admitted with DHF.¹¹

Pathophysiology of neurologic involvement may include 1) direct tissue invasion by the virus due to its neurotropicity, 2) capillary haemorrhage, 3) disseminated intravascular coagulation, and 4) metabolic disorders.¹²

In this case, the clinical and EMG findings were compatible with the diagnosis of bilateral brachial plexitis or plexopathy that affected phrenic, long

thoracic, suprascapular and musculocutaneous nerves. These nerves arise from the brachial plexus.

The etiology of brachial plexopathy or neuralgic amyotrophy can be generally categorized into hereditary and acquired forms. Of the acquired form, various precipitants have been classified into infectious and non-infectious etiologies. Reported infectious precipitants include viral infection (25%) such as flaviviruses, Epstein-Barr virus (EBV),^{1,13-14} Cytomegalovirus (CMV),¹⁵⁻¹⁶ Herpes zoster virus,¹⁷⁻¹⁸ Human immunodeficiency virus (HIV),¹⁹ parvovirus,²⁰ hepatitis E virus,²¹ West Nile virus,²² poliovirus²³ and influenza virus.²⁴ Other infectious precipitants are *Mycoplasma pneumoniae*,²⁵ *Borrelia burgdorferi*,²⁶ and atypical mycobacteria. Non-infectious precipitants which have been identified included trauma, heavy exercise, surgery, immunization (influenza vaccine, tetanus toxoid,²⁷ diphtheria-pertussis-tetanus (DPT) vaccine, human papillomavirus (HPV) vaccine) and autoimmune mechanisms (serotherapy, foreign serum injection, subcutaneous injections of allergens, immunogenic substances, pregnancy).²⁸

To our knowledge, we described the first case of brachial plexopathy from dengue virus infection. The diagnosis of dengue infection in this case was made by the detection of dengue antibodies (serology) in which MAC-ELISA IgM for dengue virus ≥ 40 U from a single specimen (with dengue IgM was greater than JE virus IgM). A dengue IgM-IgG ratio of $\geq 1:8$ defined a primary dengue infection with surprised us. The patient was 62 years old and lived in endemic area, which should have immunity to dengue virus. Dengue-specific IgG was not rising even after three months. The diagnosis was confirmed by the positive PCR for dengue virus.

Concerning cross-reactivity to other viruses, especially Japanese encephalitis virus, the PCR for dengue virus and other viruses was performed.

Eventually, reverse-transcription-nested PCR for dengue virus was positive and PCR for other viruses were negative. We concluded that our patient had acute brachial plexopathy from dengue virus infection.

CONCLUSIONS

Our patient presented with acute dyspnea from bilateral diaphragmatic paralysis and acute pure motor weakness without other features of dengue viral infection. Initial diagnosis was Guillain-Barré syndrome, however, her clinical and investigations did not support this diagnosis. Finally, acute brachial plexopathy was diagnosed and further investigations were performed to find the etiology. Post-viral infections are more common and primary dengue virus infection was diagnosed in this case.

By reporting this case, we hope to raise the awareness of unusual manifestations and interpretation of serologic laboratory diagnosis of dengue virus infection.

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