Diagnosis and Management of Imported Chikungunya Fever in Taiwan: A Case Report

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Chikungunya virus, a mosquito-borne alphavirus, is endemic in Africa and Southeast Asia but is rarely reported in Taiwan. We report the case of a Taiwanese woman who developed Chikungunya fever, which was first diagnosed by a clinician rather than by fever screening at an airport. The woman presented with fever, maculopapular rash, and arthralgia, the triad for the disease, on the day she returned home after a trip to Malaysia. These symptoms are very similar to those of dengue fever, which is endemic in Southern Taiwan. Chikungunya infection was confirmed by reverse transcriptase-polymerase chain reaction and seroconversion on paired serum specimens. For approximately 40 years until 2006, no cases of Chikungunya fever had been found in Taiwan. Clinicians in Taiwan should consider Chikungunya fever as a possible diagnosis for a febrile patient with arthralgia, rash, and a history of travel to an endemic area, such as Africa or Southeast Asia.

Key Words: chikungunya fever, dengue fever, Taiwan
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Chikungunya fever, caused by the mosquito-borne alphavirus Chikungunya virus, is endemic to Africa and Southeast Asia. A seroprevalence study conducted in Taiwan approximately 40 years ago found a prevalence rate of 90% among people aged over 40 years [1]. Subsequently, however, the disease was not diagnosed in Taiwan until 2006, when all imported cases of Chikungunya virus infection were detected at airports in Taiwan [2]. Thus clinicians in Taiwan are unlikely to have experience of this infectious disease, which will probably lead to misdiagnosis and outbreak. Therefore, there is a concern that Chikungunya fever may reemerge as a public health threat in Taiwan.

Aedes albopictus is found throughout Taiwan while *Aedes aegypti* is mainly found in Southern Taiwan. Both vectors can transmit dengue and Chikungunya viruses. According to the Taiwan Centers for Disease Control data, the first two imported cases of Chikungunya fever were identified by fever screening sentinel systems at Taiwan airports [2]. Because of the increasing prevalence of international travel, the wide distribution of the competent vectors *A. albopictus* and *A. aegypti*, and recent climate changes, it is possible that concurrent increases in dengue and Chikungunya may be seen in Taiwan, as is the case in many African and Southeast Asian countries [3]. Here, we report the clinical manifestations of a patient with Chikungunya fever that developed immediately on return from Malaysia. To the best of our knowledge,

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this is the first report of a case with Chikungunya fever to be diagnosed by a physician in Taiwan, rather than by airport screening, for almost 40 years. This report should raise awareness of this disease among clinicians without experience of imported or indigenous Chikungunya fever.

Case Presentation

A 40-year-old woman was well before traveling to Malaysia between January 22 and January 30, 2009. Fever was noticed on the day she returned. Associated symptoms were chills, cough with whitish sputum, dyspnea, sore throat, headache, neck soreness, and bilateral arthralgia over her knees, wrists, and ankles. She had difficulty in walking, a rash appeared on the skin of her back and she had bilateral conjunctivitis. She denied any recent history of an insect bite or animal contact. She was admitted after presentation at the hospital emergency room.

On admission, her blood pressure was 110/55 mmHg with a heart rate of 97 beats/min, a respiratory rate of 20 breaths/min and a temperature of 38.2°C. Physical examination revealed a rash over the back of her torso, bilateral conjunctivitis, and bilateral tenderness over her ankles and knees. Her laboratory tests revealed mild anemia with a hemoglobin level of 13 g/dL and a hematocrit of 39.3%. Her platelet count was 139×10^9/L, and her white blood cell count was 4.07×10^9/L, with 85.5% neutrophils, 9.6% lymphocytes, 4.7% monocytes and 0.2% basophils. The prothrombin time was 10.9 seconds (control, 10.8 seconds) and the activated partial thrombin time was prolonged at 31.7 seconds (control, 28.3 seconds). Blood biochemistry showed normal renal function and normal levels of aspartate aminotransferase 20 U/L (normal, 5–40 U/L), and alanine aminotransferase 12 U/L (normal, 5–55 U/L). Her electrolytes were within normal limits (sodium, 135 mmol/L; potassium, 3.6 mmol/L). Chest X-ray showed no abnormal finding. Blood bacterial culture results were negative.

Bronchitis, influenza, dengue fever, and Chikungunya fever were the initial suspects. Doxycycline was used as an empirical antibiotic. The high fever persisted for 3 days. Follow-up laboratory data showed a white blood cell count of 1.38×10^9/L and a platelet count of 111×10^9/L. She had persistent joint pain. She was discharged without fever after a 4-day hospitalization. A Chikungunya serological survey obtained at initial presentation for fever revealed no detectable immunoglobulin (Ig) G or IgM antibodies to Chikungunya antigens based on enzyme-linked immunosorbent assay methods, but a positive result was obtained with reverse transcriptase-polymerase chain reaction by the reference laboratory of the Taiwan Centers for Disease Control [2]. A second serological survey obtained 14 days later was positive for IgG and IgM. After discharge, the mild bilateral ankle pain persisted for 30 days.

Discussion

Here, we have reported a case of imported Chikungunya fever in Southern Taiwan, a tropical area, to document the possibility of Chikungunya virus being introduced by international travel into an area where there are competent mosquito vectors. There was a high prevalence rate (90%) for Chikungunya virus among people aged over 40 years old in Taiwan 40 years ago. However, the low prevalence rate (< 5%) among people < 40 years old at that time suggested a positive effect associated with mosquito control as part of malaria eradication, although there was no evidence for a cause-effect relationship [1]. No indigenous cases of Chikungunya fever have since been reported, and there were no reports of imported cases until fever surveillance at airports detected some cases in 2006 [2]. Using the epidemiology of dengue and Chikungunya in Singapore as an example, dengue fever has been endemic in Singapore since the 1960s, but the first Chikungunya case was only reported in 2006 [4]. In Taiwan, there was a 37-year period without an endogenous case of dengue until the dengue-2 virus outbreak in 1987 [5]. Dengue fever, which is transmitted by the same vectors as Chikungunya (*A. albopictus* and *A. aegypti*), has reemerged in the last decade and has become endemic in Southern Taiwan. Collectively, these findings suggest there is a high risk for reemergence of Chikungunya fever in Taiwan because of the existence of suitable vectors. The Italian experience of an endemic outbreak of Chikungunya fever provides another example of how developed or developing countries with suitable weather for vectors may experience outbreaks once the disease has been imported unnoticed [6].

Table. Comparison of clinical characteristics between dengue fever and Chikungunya fever

	Dengue fever	Chikungunya fever
Etiology	Dengue virus	Chikungunya virus
Main vectors	*Aedes aegypti* *Aedes albopictus*	*Aedes aegypti* *Aedes albopictus*
Incubation period (d)	3–14	2–12
Endemic area	Southeast Asia, endogenous cases reported in Southern Taiwan	Southeast Asia, Africa, only imported cases in Taiwan
Clinical symptoms	Fever, severe bone pain, retrobulbar pain, headache, muscle pain, joint pain;	Fever, headache, muscle pain, joint pain at the finger/toe/wrist/ankle, with arthralgia persisting for weeks or months [7,8,10];
	Common hemorrhagic manifestations; Rash onset after 3–5 days of fever; Fever for 7 days [9]	Rare hemorrhagic manifestations (6.4%) [10]; Early rash onset early; Fevers usually resolve within 3–7 days
Laboratory data	AST and ALT usually increase by 2–5-fold; marked thrombocytopenia and leukopenia, initial neutrophilia	AST and ALT usually increase by 1.5–2-fold; mild thrombocytopenia and leukopenia with initial lymphopenia, and hypocalcemia [10]

AST = Aspartate aminotransferase; ALT = alanine aminotransferase.

Early diagnosis of Chikungunya fever is difficult because its manifestations resemble those of other tropical diseases, particularly dengue fever (Table) [7–10]. Thus Chikungunya might be under diagnosed or misdiagnosed as dengue in Taiwan. Arthritis and arthralgia associated with Chikungunya can be quite painful and usually involve small and large joints. Intense pain elicited by pressure on the wrist is considered to be strongly suggestive of Chikungunya [6,7]. Fever usually resolves within 3–7 days, but arthralgia can persist for weeks after onset [8]. A generalized maculopapular skin rash and conjunctivitis occur in approximately half of all cases on Day 2–5 of illness [11]. Another characteristic laboratory finding at admission is lymphopenia (79%). Thrombocytopenia, a typical finding for dengue fever, is not prominent in Chikungunya infection. In contrast, classic dengue fever is an acute febrile illness that is accompanied by headache, retro-orbital pain, and marked muscle and joint pains, the source of the term "break-bone fever" [12]. Dengue fever typically lasts for 5–7 days [9]. Hemorrhagic manifestations are common in patients with dengue fever, but are only present in 6.4% of cases with Chikungunya [13]. Dengue fever and dengue hemorrhagic fever typically result in marked leukopenia and thrombocytopenia, in contrast to Chikungunya fever. In addition, dengue fever is associated with prolonged suppression of leukocyte and platelet counts, and plasma activated partial thrombin time. Serum aspartate aminotransferase and alanine aminotransferase levels are also frequently elevated in patients with dengue fever [10]. In Chikungunya fever, normal aspartate aminotransferase and alanine aminotransferase levels are often found with mild prolongation of activated partial thrombin time. Our patient had bilateral tenderness over the ankles and fever; notably, she also had recently travelled to Malaysia. Her fever subsided in 3 days and only mild thrombocytopenia was found during admission. A rash was detected on the first day after the onset of fever. Therefore, dengue fever was considered less likely and our tentative diagnosis was Chikungunya fever, which was later confirmed by serologic and molecular tests.

After approximately 40 years without a confirmed Chikungunya case, the first imported case of Chikungunya fever was detected at Taiwan Taoyuan International Airport in November 2006 [2]. Between October 2007 and May 2009, 14 imported cases were confirmed in Taiwan. The Chikungunya cases in 2007 and 2008 originated from Indonesia, Malaysia, Singapore, India and Bangladesh [2,14]. The distribution of imported Chikungunya cases was island-wide. A limited awareness of Chikungunya fever by Taiwan clinicians is anticipated because there have been no endogenous cases for approximately 40 years, and no imported cases were found until 2006. Therefore, further education and experience sharing about the diagnosis and treatment of Chikungunya fever should be performed for clinicians throughout Taiwan.

The differential diagnosis of many tropical diseases by clinical characteristics can be difficult because they share common features, including fever, rash and arthralgia, with different degrees of severity. Clinicians should be vigilant for febrile patients who are recent travelers from Chikungunya endemic areas and who present with the triad of fever, rash and arthralgia. In addition, public health officials should watch for local transmission of Chikungunya virus because it may be introduced into Taiwan by travelers with viremia and then transmitted by local mosquito vectors.

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境外移入台灣之屈公熱的診斷與治療：病例報告

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屈公熱病毒是一種以蚊子為媒介的病毒，在非洲與東南亞有地區性的流行但在台灣很少見。我們報告一台灣女病患在馬來西亞旅遊後回國當天有發燒、皮疹與多發性關節炎之典型屈公熱症狀，這些症狀和南台灣地區性流行之登革熱症狀相似。經反轉錄聚合酶反應與血清學檢驗證實為屈公熱。這是非經機場發燒篩檢而由醫師診斷之病例。台灣在經過約 40 年沒有屈公熱病例報告後，於 2006 年在機場發燒篩檢開始陸續發現少數境外移入個案。本報告之個案是台灣 40 年來第一位通過機場發燒篩檢而由臨床醫師主動發現，也因此台灣醫師對於發燒病患合 關節痛、皮疹，並曾至屈公熱病毒流行區旅遊者，需將屈公熱列入鑑別診斷。

關鍵詞：屈公熱，登革熱，台灣

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