Case Report

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Brugada syndrome following febrile episode caused by malarial infection: a case report

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Background: Brugada syndrome (BrS) is a rare genetic disorder with specific electrocardiographic (ECG) patterns carrying an increased risk of sudden cardiac death.

Case presentation: The authors present a 36-year-old gentleman who had a travel history to the Central African Republic and came to the hospital with a fever and chest pain. The lab investigation revealed Falciparum Malaria infection and the ECG pattern revealed the type 1 Brugada pattern, which was normalized with anti-malarial medication and symptomatic treatment of fever.

Discussion: BrS is a disorder with high prevalence in males and people of the Asian continent. Patients can present with symptoms like syncope, seizure, and nocturnal agonal respiration or may be asymptomatic. The ECG pattern of BrS could be seen in the febrile phase and normalized when non-febrile, like in our patient. Prompt treatment of fever and follow-up with cardiologists would be an effective treatment of asymptomatic patients, whereas ICD is a management of choice for symptomatic patients.

Conclusion: For a patient with chest pain, fever, and an ECG pattern of ST elevation, a clinician should think BrS one of the differential diagnoses.

Keywords: Brugada syndrome, fever, malaria

Introduction

Brugada syndrome (BrS) is an autosomal dominant inherited disease that can cause fainting and sudden cardiac death in young people who have a healthy heart and is characterized by a specific electrocardiogram pattern of complete or incomplete right bundle branch block and elevated ST-segment in leads V1–V3[1]. Three Brugada electrocardiographic (ECG) (Br-ECG) patterns have been described: type 1, or "coved type" (coved ST-segment elevation greater than or equal to 2 mm in leads V1–V3, followed by a negative T-wave), and type 2/3, or "saddleback" (J point elevation greater than or equal to 2 mm, ST-segment elevation greater than 1 mm in type 2; less than or equal to 1 mm in type 3, followed by a positive or biphasic T-wave) and the BrS diagnosis is made when a type 1 Br-ECG is observed[2]. Patients with BrS are highly susceptible to fatal arrhythmias, which could be caused by various factors like pyrexia, electrolyte imbalance, alcohol, and drugs, and thus, we should monitor and regulate these factors to prevent fatal outcomes[3].

We present a case of a 36-year-old gentleman with BrS unmasked by a febrile episode of malaria.

HIGHLIGHTS

- Brugada syndrome (BrS) is a rare genetic cardiac disorder characterized by specific electrocardiographic (ECG) abnormalities and an increased risk of sudden cardiac death.
- We present a case of a young gentleman who presented with fever and chest pain. His symptoms and lab investigation suggested malarial infection and characteristic ECG changes consistent with BrS, which resolved with a febrile state.
- We should consider BrS as a differential diagnosis in febrile patients with chest pain and provide early referral to a cardiologist.

Case presentation

A 36-year-old previously healthy army man presented to the emergency department with fever and chest pain following his return from a UN Mission in the Central African Republic. His fever was intermittent, with a maximum recorded temperature of 103°F, associated with body aches for three days. The chest pain had been occurring for 2 months, described as intermittent, non-radiating, and unaffected by activity or breathing. He denied respiratory symptoms, palpitations, bladder and bowel symptoms, as well as substance abuse. He is non-smoker. No family history of similar illness and cardiac disease.

When asked about a similar illness, he remembered feeling dizzy multiple times in the past, which he thought to be associated

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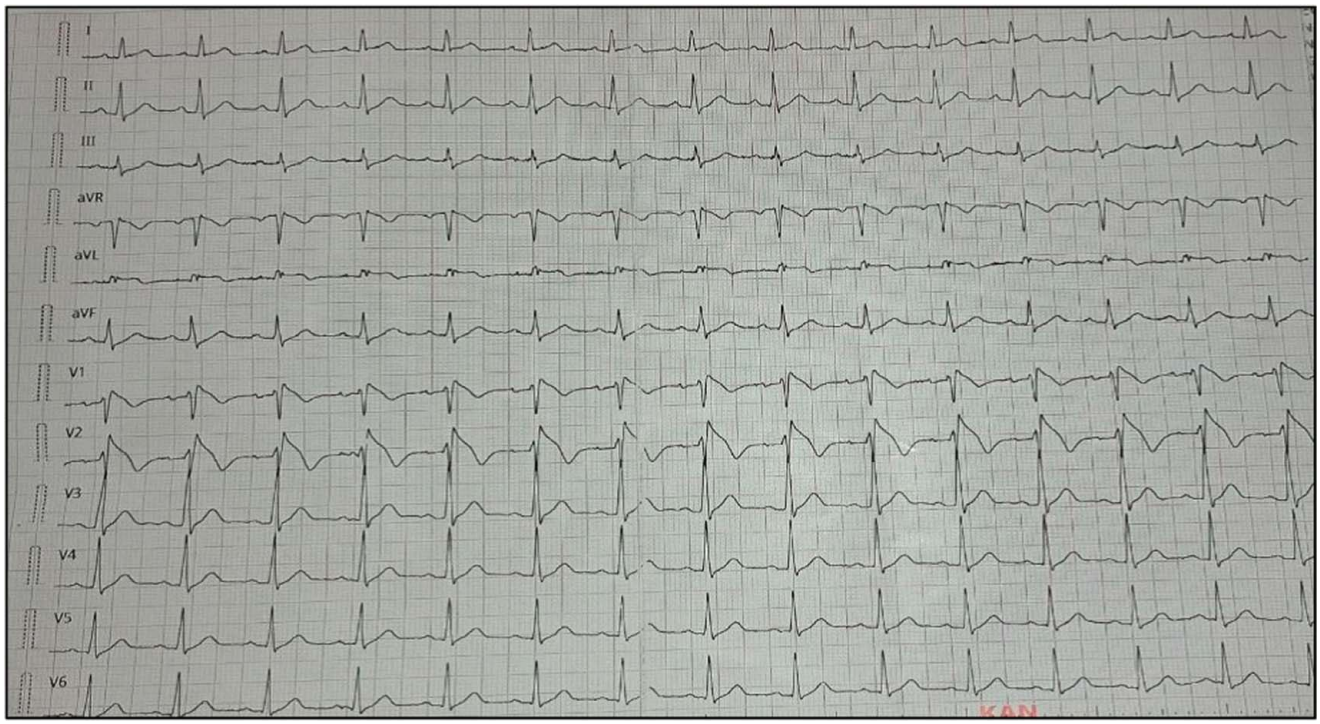

Figure 1. Coved ST-segment elevation more than 2 mm in lead V1 and V2 followed by T-wave inversion.

with strenuous training sessions as army personnel. He denied using anti-malarial drugs as a preventive measure against infectious disease as guidelines during travel. Physical examination findings were insignificant, but laboratory tests, which included baseline investigation with complete blood panel [hemoglobin : 14.4 mg/dl, platelets: 176 000 cumm, total leukocyte count (TLC) : 3200 cumm, neutrophils: 77%, lymphocytes: 17%, monocytes: 04%, eosinophils 02%], liver function test (total bilirubin: 1.3, direct bilirubin : 0.3, amylase : 23), renal function test (urea: 32 mg/dl, creatinine: 0.82, sodium: 138, potassium: 3.74), urine analysis (yellow, acidic, albumin: nil, sugar: nil, pus cells: 1–2/hpf, epithelial cells: 1–2/hpf, red blood cells: nil, and fever tropical panel including test for dengue and malaria, revealed *Plasmodium falciparum* malaria infection and suggested leukopenia (TLC: 3200). Chest X-ray was normal. An ECG showed coved ST-segment elevation (>2 mm), followed by T-wave inversion in leads V1 and V2.(Fig. 1) Cardiac markers were within normal limits, and serial cardiac markers were within normal limits.(Table 1) Echocardiography showed no structural abnormality or ventricular dysfunction, ruling out any myocardial disease. Subsequent ECGs continued to demonstrate characteristic Brugada patterns. Renal function test on the second day of admission revealed urea: 14.2 mg/dl, creatinine: 0.82 mg/dl, sodium: 142 mg/dl , potassium: 4.06 mg/dl.

The clinical findings and investigation ruled out pneumonia, pericarditis, myocarditis, pulmonary embolism, infective endocarditis, esophagitis, cellulitis, herpes zoster, hematologic malignancy, electrolyte abnormalities, substance abuse, etc.

Based on history, clinical examination, lab investigation, and ECG, the patient was diagnosed with Uncomplicated Falciparum Malaria infection with BrS.

The patient was initiated on anti-malarial therapy as per the National guideline (20/120 mg Artemether and lumefantrine 4 tablets BD for three days, and Primaquine 0.25 mg/kg on the first day) and supportive treatment with Tab acetaminophen (1g IV tds) along with IV fluid (1l over 24 h), which resolved the fever and normalized the ECG finding (Fig. 2) on the third day of hospital stay. The patient was advised against strenuous activities, promptly treating fever, and regular follow-up.

Discussion

BrS has an estimated incidence of 1 in 5000 to 1 in 2000 in different populations, the highest being in male and Southeast Asian countries[4].

Various literature describes the association between febrile illnesses and BrS with fever-triggering arrhythmias in susceptible individuals[2–7]. In this case, the febrile malaria episode unmasked BrS, leading to characteristic ECG changes consistent with the syndrome.

Our patient had a history of travel to Central Africa, where malaria was the predominant disease[8], and based on the presentation and history of travel, we sent a baseline investigation and test to look for dengue and malaria, which are common in

Table 1

Cardiac markers on different date.

	22/5/11	22/5/11	22/5/12	22/5/13	22/5/14
Troponin I	Negative	Negative	Negative	Negative	Negative
CPK MB	14	10.3	10.7	11.2	8
CPK nac	128	85	73	64	63

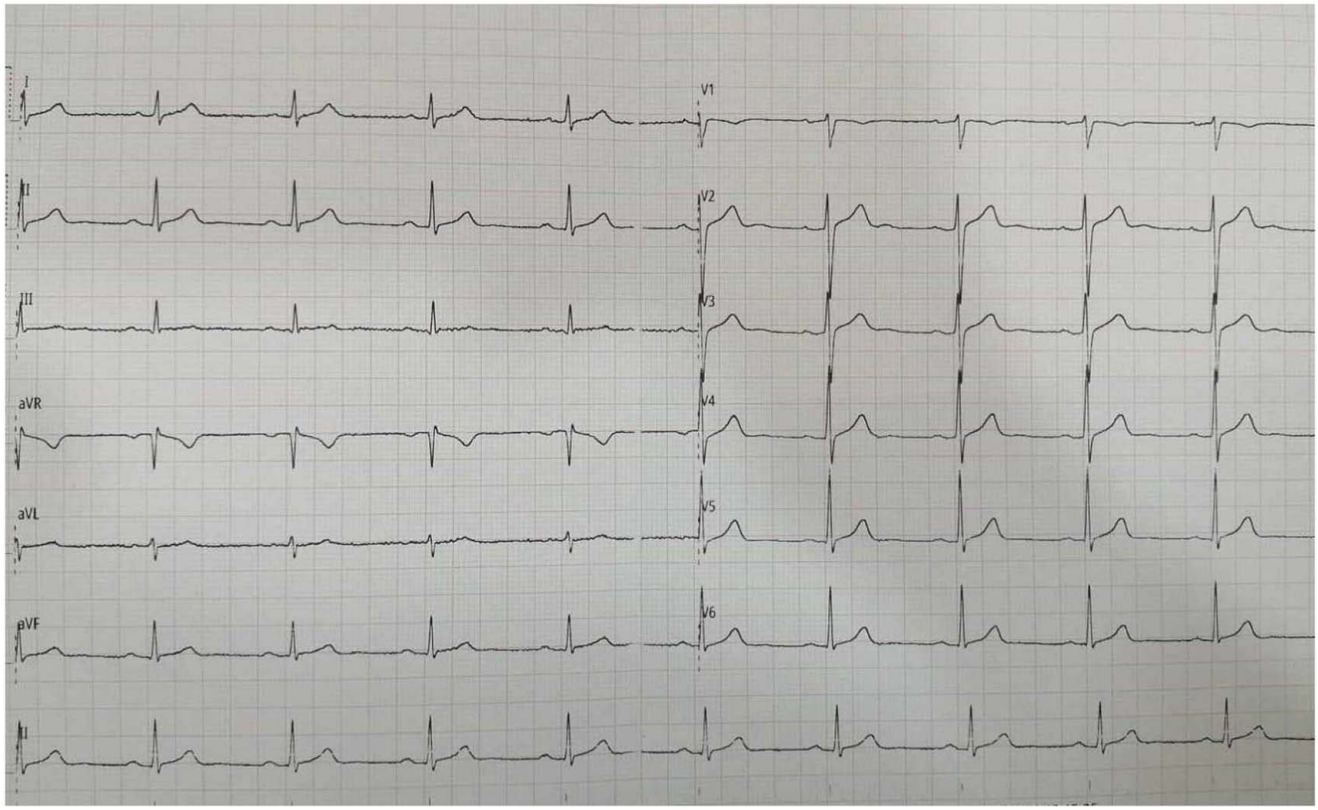

Figure 2. Normal electrograph.

our country and the country where the patient had traveled. The CDC recommends that travelers take chemoprophylaxis before traveling to the Central African Republic[9]. However, our patient had not taken chemoprophylaxis against Malaria.

As the patient had chest pain, we opted for an ECG, which revealed a Brugada type 1 pattern. Repeat ECG and Serial cardiac markers were sent to rule out Myocardial Infarction. Studies have shown that BrS can mimic Myocardial infarction[10,11].

Various case reports and review have shown that patients with BrS can present with chest pain and fever[5,12]. We should consider differential diagnoses like pneumonia, pericarditis, myocarditis, pulmonary embolism, infective endocarditis, esophagitis, cellulitis, herpes zoster, hematologic malignancy, electrolyte abnormalities, substance abuse, and aortic dissection in a patient with fever and chest pain[12,13]. Ruling out these differentials with history, physical examination, and lab findings, and as ECG was suggestive of a Type 1 Brugada pattern, we made the diagnosis of BrS, which could be made from the ECG pattern alone[2,14]. A genetic test although recommended to support the clinical diagnosis; however, knowing about specific mutation does not provide guidance in formulating a diagnosis or determining the prognosis[14].

While the exact mechanism remains unclear, fever-induced alterations in ion channel function, particularly sodium channel dysfunction, are thought to contribute to arrhythmogenesis in BrS[6]. As with our report, other case reports also reported that the patient's ECG returned to normal with normalization of the febrile state[5,6]. Various studies also state that normalizing fever can control ventricular arrhythmia[5,6].

Seizures and nocturnal agonal respiration are other symptoms associated with BrS[14]. Our patient neither had symptomatic features like syncope, seizure, and nocturnal agonal respiration nor a family history. As with the consensus for the management of asymptomatic BrS[14], no specific treatment is needed for this type of patient, so we followed up with the patient with an explanation of his disease condition and advised him to follow up with a cardiologist.

The first therapy option for a symptomatic individual is an implantable cardioverter defibrillator (ICD), but radiofrequency catheter ablation can work for those who can't have an ICD[4,6].

The limitation of this study is that urine or serum examination for potential drug abuse was not performed. The patient lost to follow-up as he had to return to his regular work outside the country.

Conclusion

This case underscores the importance of considering asymptomatic BrS as a differential diagnosis in febrile patients with chest pain.

Ethical approval

This is a case report, therefore, it did not require ethical approval from ethics committee.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal on request.

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The study did not receive any grant from funding agencies in the public, commercial or not-for-profit sectors

Author contribution

E.A.: involved in conceptualization of the case report, literature review, writing the original draft, supervisor, visualization, writing—review and editing. A.M.: involved in conceptualization of the study, data collection, literature review, original draft preparation, data curation. S.A.: involved in conceptualization of the study, literature review, and writing the original draft, writing—review and editing. All the authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors declare no conflict of interest.

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Data availability statement

Not applicable.

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