



## Sadfly fever: two case reports

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### Abstract

Sadfly fever, also known as 'three-day fever' or 'pappataci fever' or 'Phlebotomus fever' is a viral infection that causes self-limited influenza-like symptoms and characterized by a rapid onset. The disease occurs commonly in endemic areas in summer months and especially in August during which sandflies are active. In this article, two siblings who presented with high fever, redness in the eyes, headache, weakness, malaise and inability to walk, who were found to have increased liver function tests and creatine kinase levels and who were diagnosed with sadfly fever with positive sadfly IgM and IgG antibodies are reported because of the rarity of this disease. (Turk Pediatri Ars 2016; 51: 110-3)

**Keywords:** Child, lower respiratory tract infection, vitamin D

### Introduction

Sadfly fever is a self-limiting infectious disease which occurs only in humans as a result of sandfly (phlebotomus spp.) bite. It leads to different symptoms including fever, rash, diffuse muscle pain, headache, loss of appetite, nausea and vomiting. The laboratory findings include leukopenia, lymphopenia, monocytosis, thrombocytopenia, increased liver enzymes and increased creatinine kinase (CK). The agent of sandfly fever 'Sandfly fever virus (SFV)' is classified in the phlebovirus species which is an enveloped RNA virus belonging to the bunyavirus group from the arbovirus family. Immunologically it has four serotypes including 'Sandfly Sicilian' virus (SFSV; Sicilian serotype), 'Sandfly Cyprus' virus (SFCV; Cyprus serotype), 'Sandfly Naples' virus (SFNV; Naples serotype) and 'Toscana' virus (TOSV; Toscana serotype) (1). The chain of infection in sandfly fever is human-phlebotom-human. The disease is observed commonly in the Mediterranean region surrounded by the Middle East, Europe, Africa and Asia continents. In our country, cases of sandfly fever were reported in 2007 and 2008 in the Kozan district of Adana, in the Ödemiş district of İzmir and in the Mamak

district of Ankara. These two cases have been presented to emphasize that sandfly fever should be considered in the differential diagnosis together with the other infectious diseases in children who present with a complaint of fever.

### Cases

A twelve-year old girl and her six-year old brother presented to our clinic with complaints of fever, pain in the legs, weakness and inability to walk. In the history it was learned that both patients had resistant fever reaching up to 40°C which started three days ago, leg pain started one day after the onset of fever, they received amoxicillin-clavulanic acid and antipyretic treatment regularly which was recommended in another healthcare institution where they presented with these complaints, were referred to our hospital, because fever did not subside despite treatment and redness in the eyes, headache, fatigue, weakness and inability to walk were added to the picture and cases with similar complaints were present in the area they lived. The physical examination findings of the patients were similar. Their general status were

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moderate, their consciousnesses were open, but they appeared faint. The axillary body temperature was found to be 39.5°C in the female patient and 38.9°C in the male patient. The blood pressure and apical heart beat among vital findings were within the normal limits in both patients. Their physical examination findings were found to be normal except for muscle tenderness which was prominent in the lower extremities. The laboratory findings of the female patient were as follows: hemoglobin 14.1 g/dL, WBC 4 460/mm<sup>3</sup>, platelet count 173 000/mm<sup>3</sup>, AST 318 IU/L, ALT 105 IU/L, CK 4267 IU/L. Erythrocyte sedimentation rate was found to be 7 mm/h. CRP, PT, aPTT and the other biochemical variables were found to be normal. Predominance of lymphocytes was found on peripheral blood smear. The human Parvovirus IgM and IgG antibodies measured to elucidate the etiology were found to be negative. The other possible causes of infection considered in the differential diagnosis including brucellosis, salmonellosis, viral hepatitis, toxoplasma, Epstein Barr virus, cytomegalovirus, herpes virus and leptospirosis were excluded with serologic tests. Growth did not occur in the blood and urine cultures. Fever subsided on the day after hospitalization and sandfly IgM and IgG antibodies were found to be positive. In the follow-up, muscle pain and weakness improved. On the third day, the laboratory findings were as follows: WBC 8 400/mm<sup>3</sup>, CK 51 IU/L, AST 19 IU/L, ALT 36 IU/L. The laboratory findings of the male patient who had similar findings at the time of hospitalization were as follows: hemoglobin 14.3 g/dL, WBC 5 340/mm<sup>3</sup>, platelet count 172 000/mm<sup>3</sup>, AST 444 IU/L, ALT 143 IU/L, CK 5184 IU/L. The sandfly IgM and IgG antibodies were found to be positive also in the male patient. On the next day after hospitalization, fever subsided. His general status improved and complaints regressed. The laboratory findings become normal (WBC 11 400/mm<sup>3</sup>, AST 28 IU/L, ALT 41 IU/L, CK 153 IU/L). The patients were discharged with recommendations and included in outpatient follow-up. Written informed consent was obtained from the family of the patients included in this study.

## Discussion

Sandfly fever is an infectious disease which is characterized with formation of a papule on the site of sandfly bite, high fever, rash and diffuse muscle and joint pain and with epidemics. It was noted with epidemics observed among soldiers during the Second World War for the first time and SFSV was isolated in the patients (2). In the later years, SFSV was isolated in 37 Swedish tourists who had a holiday in Cyprus between 1986 and 1989

and SFNV was isolated in one subject. In 2002, SFSV was isolated in 256 of the patients during the epidemic which occurred in 581 Greek soldiers who were doing military service in the same region (3, 4). Sandfly Sicilian virus was found to be positive in 13 of 14 American soldiers who were serving and tested because of fever in 2007 in Irak. In the study of Çarhan et al. (2) from our country which was performed in recent years, a total of 106 subjects with sandfly fever reported from Adana (4 patients), İzmir (47 patients) and Ankara (55 patients) were examined serologically and SFSV was found in 38% of the patients, SFSV/SFCV was found in 12% and SFCV was found in 4%; they described 'Sandfly fever Turkey virus (SFTV)' for the first time. In 2010, Torun et al. (5) reported eight patients (5 SFNV, 3 SFSV) from the region of Kırıkale and Güler et al. (6) reported nine patients (7 SFSV, 2 SFCV) from the region of Kahramanmaraş in 2012.

Sandfly which is the vector of leishmaniasis is also the vector for sandfly fever. *Phlebotomus* and *Sergentomyia* which are among the species of sandfly are found commonly in Turkey. While sandflies feed at night, they are found in dark places and in low-slung places during the day. Sandflies become infective 6-10 days after they suck blood and remain infective for a life time. The virus is transferred from one generation to another with egg (2-4). The person who is bitten does not feel any pain. When contact with vector was questioned during detailed history taking, it was learned that there was no contact with any tick, but patients presented with similar complaints as a result of fly bite in the area where our patients lived. It was found that the houses where our patients lived were in yards and surrounded by plenty of trees and on the first floor. There were stream beds nearby and they were exposed to excessive infestation with flies.

A papule may be observed at the site of sandfly bite and the body temperature rises with shivering after an incubation period of 3-6 days. The temperature is measured between 39 and 40°C and lasts averagely three days (1-9 days). The virus can be identified in the blood in the period 24 hours before and after the onset of fever. The most common accompanying symptoms include loss of appetite, muscle pain, joint pain, headache, pain behind the eyeball, diarrhea, nausea, vomiting and abdominal pain. Rarely, maculopapular rash may be observed and hyperemia in the conjunctivae and photosensitivity may be present. It was reported that the common symptoms observed in the patients in Adana and Ankara included high fever, headache, muscle pain and vomiting (2). In another study, fever and muscle pain were found in all of

the eight patients, vomiting and diarrhea were found in seven, headache was found in five and hyperemia in the eyes was found in one (5). Fever was found in all of the fifty patients reported by Koçak et al. (7) in 2011 from Ankara, weakness was found in 96%, muscle pain and/or joint pain was found in 80%, headache was found in 66% and photosensitivity and hyperemia in the eyes were found in 56%. Our patients presented with the complaints of high fever, hyperemia in the eyes, headache, malaise, weakness, diffuse muscle pain and inability to walk. Hepatomegaly, splenomegaly and conjunctivitis may be observed during the course of the disease. Organomegaly or conjunctivitis was not found in our patients.

The most remarkable laboratory findings related with sandfly fever include leukopenia, lymphopenia, monocytosis, thrombocytopenia, increased liver function tests and increased CK level (5, 6). Studies have reported up to five-fold increases in liver enzymes and up to 10-fold increases in CK level. The white blood cell count generally returns to normal with improvement of infection. The white blood cell counts of our patients were found to be about 5 000/mm<sup>3</sup> and the liver enzyme and CK levels were found to be markedly increased. A marked improvement was observed in the clinical and laboratory findings on the third day of hospitalization in our patients who were given only supportive treatment. In the differential diagnosis, infections which lead to fever and leukopenia, especially viral infections, Crimean-Congo hemorrhagic fever, hepatitis, salmonella and brucella should be considered. In our patients, other viral infections, salmonella, brucella and viral hepatitis were excluded with serologic tests. Crimean-Congo hemorrhagic fever was not considered in our patients who had no history of contact with ticks and were not found to have any finding related with ticks on physical examination and whose hemorrhagic diathesis tests were found to be normal.

The diagnosis is made with clinical findings, epidemiological information and serologic tests. Since sandfly fever is characterized with short-term viremia, sandfly fever IgM positivity alone is a reliable variable in identifying acute infection in addition to demonstration of seroconversion (5). In the diagnosis, immunofluorescence antibody test and plaque reduction neutralization tests which is used to confirm this test result are used commonly (8). The serum samples of our patients were sent to Refik Saydam Sanitation Center Headship, Virology Reference and Research laboratory in accordance with

cold-chain rules by way of the Local Health Authority for the objective of investigating SFV antibodies. A diagnosis of sandfly fever was made in our patients who had positive sandfly fever IgM and IgG antibodies.

As in other arbovirus infections, sandfly fever may also be associated with aseptic meningitis. Becker et al. (9) reported a 15-year old German patient who was diagnosed with severe meningitis related with SFSV following vacation in Turkey. It is known that especially Toscana viruses have neuropathic effects. Meningitis and meningo-encephalitis epidemics related with this disease have been reported from Italy, France, Spain and Portugal. Ergünay et al. (10) found TOSV in 16 of 102 patients with fever of unknown origin who were diagnosed with central nervous system infection. Therefore, TOSV should be kept in mind in cases of aseptic meningitis and meningoencephalitis especially in summer months.

Treatment of sandfly fever is symptomatic and the disease resolves spontaneously. No mortality has been reported in patients who have been followed up. Fluid treatment, bed rest and analgesics were given to our patients who were hospitalized and no sequela or complication was observed.

In conclusion, sandfly fever should be included in the differential diagnosis in patients who present with fever lasting longer than three days, muscle pain and headache, who have accompanying laboratory findings including increased CK, increased liver enzymes and leukopenia in summer months during which mosquitos are found extensively and serologic tests directed to the disease should be performed.

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