17. TICK-BORNE RELAPSING FEVER: A FEVER SYNDROME MIMIC

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Introduction: Fever is a cardinal manifestation of both autoinflammatory disease and infection. Distinguishing the two is a familiar challenge to the rheumatologist. This case report describes a young female presenting with recurrent fevers, rash and inflammatory arthritis. The case illustrates the importance of a careful travel and social history in the diagnosis and management of a patient presenting with recurrent fevers, particularly in an era of globalisation and air travel.

Case description: A 19-year-old Caucasian female presented to her local district general hospital with episodic fevers, rash, arthralgia, and abdominal pain. Past medical history included autoimmune liver disease, treated with azathioprine. She had no relevant family history, took no medications other than azathioprine, was a non-smoker and had no allergies.

On presentation she was pyrexic with a temperature of 40 °C, and tachycardic (120bpm), with a BP of 108/59. She was synovitic in her wrists, knees and ankles. Pustular skin lesions were noted on the lower limbs, spreading to the groin, upper limbs and the face, and evolving into haemorrhagic bullae. Baseline bloods including cultures, and skin swabs were taken. Despite broad-spectrum antimicrobials and acyclovir, she continued to spike temperatures. Her symptoms briefly resolved on two occasions before recurring. Blood cultures and skin swabs were sterile and varicella PCR negative. She had high acute-phase reactants with a CRP of 238 and a ferritin of > 1000. Autimmune screen was positive for only anti-smooth muscle antibodies. The lack of response to anti-microbials and elevated ferritin raised suspicion of autoinflammatory pathology and prompted inpatient transfer to a tertiary rheumatology service.

After transfer further investigations included a PCTT which demonstrated splenomegaly (25cm) with multiple metabolically active lesions. Three pieces of further history were elicited: (1) Four weeks prior to symptom onset, the patient reported a new sexual partner; (2) The patient has a pet cat which frequently scratched her legs; and (3) She travelled to southern Spain four months prior to admission, and regularly walked her tick-infested grandfather’s dog through shrubland. She subsequently underwent screening for syphilis, HIV and gonococcus, molecular testing for Bartonella species, and serological assessment for tick-borne illnesses. She was positive for non-Lyme Borrelia species. A diagnosis of tick-borne relapsing fever (TBRF) was made, and treatment with doxycycline induced a rapid clinical response.

Discussion: Autoinflammatory diseases are characterised by recurrent episodes of inflammation due to defects in innate immunity. The absence of autoantibodies means recognition of clinical phenotype is crucial. In this patient, the presence of synovitis, high fevers, raised inflammatory markers and serum ferritin fit with adult-onset Still’s disease (AOSD). However, the rash was atypical. The rash in AOSD is salmon-pink, non-pruritic and typically occurs in the upper arms, abdomen and thighs. Additionally, although the spleen is often enlarged, focal lesions are rare. Infections were considered, particularly with background immunosuppression and liver disease. Negative cultures and failure to improve with antibiotics suggested a non-infectious cause. Detailed history identified risk factors for infections undetected by standard microbial tests. Disseminated gonococcal infection can present with pustular acral rash and asymmetric polyarthritis for which PCR is standard diagnosis. Bartonellosis or cat-scratch disease usually presents 3-12 days after a scratch with tender local unilateral lymphadenopathy, malaise and fever. Bacillary angiomatosis can occur in immunocompromised patients and can present with subcutaneous nodules which haemorrhage or ulcerate. Bartonella is a fastidious gram-negative rod that requires special conditions for culture so is not routinely performed. There is no commercial serology test, so the specimen was sent to Porton Down for PCR, which was negative.

A diagnosis of TBRF was reached due to exposure to ticks during travel to southern Spain and positive non-Lyme Borrelia serology. The species of tick found in this region are Ixodes Ricinus and Ornithodoros which are carriers of Borrelia and Babesia. TBRF’s incubation period is 3-18 days and presents with fever, arthritis, rash, abdominal pain and hepatosplenomegaly. Symptoms are episodic with periods of remission. The
patient’s symptomatology was consistent with non-Lyme Borrelia species, but the incubation period was significantly prolonged. Samples have been sent for molecular Borrelia testing and blood films.

**Key learning points:** Rheumatologists are often asked to review patients with recurrent fever. An awareness of atypical infectious differentials can be crucial to making the correct diagnosis. Relapsing fever is an umbrella term used to describe the characteristic pattern of infection caused by spirochetes of the genus Borrelia and can be transmitted by ticks or lice. Other infectious causes of recurrent fever include malaria and rat-bite fever. An important non-infectious cause is lymphoma. When trying to isolate the causative pathogen, it is important to note that standard microbial cultures are often insufficient for atypical pathogens. In the case of our patient, both spirochete and rickettsia are bacterial tick-borne illness which are undetected by standard cultures. Additionally, the lack of response to antibiotics does not exclude infection; rather it may reflect an inappropriate choice of antibiotics. Thus, an awareness of which pathogens respond to which antibiotics is crucial in the timely and effective treatment of infection.

This case illustrates the importance of a careful clinical history in diagnosis and treatment. Particularly in the context of a suspected infection, an extensive travel and social history is important in establishing risk of exposure to pathogens either directly or indirectly via vectors. In this case Bartonellosis was initially suspected before negative PCR made non-Lyme Borreliosis a more likely diagnosis. Fortunately doxycycline is the first-line treatment for both of these organisms.

Rheumatologists are familiar with the predisposition of immunocompromised patients to atypical pathogens. These atypical infections are frequently harder to detect, therefore a rheumatologist must keep these organisms in the back of their mind when considering sources of infection in immunocompromised patients.

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