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SHORT REPORT

# Treatment of brucellosis in a young child with trimethoprim/sulfamethoxazole anaphylaxis



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## KEYWORDS

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**Summary** Brucellosis is a common zoonotic disease throughout the world. *Brucella* spp. transmit to humans through contact with fluids of infected animals, especially sheep, cattle, and goats. It is also transmitted by ingestion of fluid-derived products of infected animals, such as unpasteurized milk and cheese. *Brucella* spp. changes pH level of intracellular environment, so the first treatment approach is to administer antibiotics that have activity in acidic conditions. Anti-brucellosis treatment regimens include doxycycline for children older than eight years old and rifampicin and trimethoprim/sulfamethoxazole (TMP-SMX) combination therapy for children under eight years old, which may be able to act intracellularly under acidic conditions. A TMP-SMX allergy causing anaphylaxis has been reported previously. No alternative anti-brucellosis treatments have been reported in the literature for patients under eight years old with a TMP-SMX allergy. Here, we report a case of a child with brucellosis and a TMP-SMX allergy who was under eight years old at the time of diagnosis and was successfully treated with rifampicin, ciprofloxacin, and gentamicin.

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## Introduction

Brucellosis is a common zoonotic disease throughout the world. Treatment options for childhood brucellosis are limited. A trimethoprim/sulfamethoxazole (TMP-SMX) allergy causing anaphylaxis has been reported [1,2] previously. However, an alternative anti-brucellosis treatment for children under the age of eight with a TMP-SMX allergy has not been reported in the literature. Here, we present a case of a child under eight years of age with brucellosis and a TMP-SMX allergy who was successfully treated with rifampicin, ciprofloxacin, and gentamicin.

## Case report

A previously healthy 2.5-year-old girl had been admitted to a hospital with a high-grade fever (39.5°C). She had a history of consumption of unpasteurized cheese and a family history of brucellosis. A diagnosis of brucellosis was confirmed by a positive serum agglutination test (SAT) and Coombs test at a titer of 1/160. Thereafter gentamicin (5 mg/kg/day, twice daily i.v) plus TMP-SMX (10 mg/kg/day, twice daily p.o) was prescribed to the patient. Because of the occurrence of a generalized rash 10 h after the last TMP-SMX dose on the 13th day of treatment, the patient was referred to our hospital. A physical examination at admission revealed a maculopapular skin rash on her cheeks, upper arms and legs (Fig. 1). The results of laboratory investigations were as follows: hemoglobin 12.6 mg/dL, white blood cell count (WBC) 7100/mm<sup>3</sup>, platelets 253,000/mm<sup>3</sup>, aspartate aminotransferase 165 U/L (normal <48 U/L), alanine aminotransferase 167 U/L (normal <48 U/L), and total immunoglobulin (Ig) E 23.4 IU/mL (normal range 0–5 IU/mL). Serological tests for hepatitis A virus, hepatitis B virus, hepatitis C virus, human immunodeficiency virus, Epstein–Barr virus and cytomegalovirus were negative. Tests for *Brucella* ELISA IgG and IgM were positive. A serum agglutination test and Coombs test were positive at titers of 1/800 and 1/640, respectively. A blood culture yielded *Brucella* spp. We consulted with the pediatric allergy clinic to determine whether TMP-SMX could be used for her treatment. Because the patient's skin prick test for TMP-SMX was negative, the application of a challenge with 10 mg/kg/day TMP-SMX was performed. Although the patient did not display symptoms of an allergic reaction immediately after the first TMP-SMX dose of 5 mg/kg, 3.5 h later, the

patient experienced restlessness, a generalized maculopapular rash, uvular edema and significant tachycardia (pulse rate 200/min). After adrenaline, prednisolone and H<sub>1</sub>-antihistamine injections, the patient was clinically stabilized. The patient was diagnosed as having experienced TMP-SMX anaphylaxis, and the patient's family was informed of this diagnosis and the desensitization protocol for TMP-SMX. Her family rejected the desensitization protocol; therefore, we searched for alternative treatment protocols. Rifampicin (20 mg/kg/day), ciprofloxacin (20 mg/kg/day), and gentamicin (for the first five days) were prescribed to the patient as an alternative treatment. On the 5th day of the treatment regimen, she became asymptomatic, and on the 10th day of the treatment, a blood culture was negative for *Brucella* spp. She was discharged with a good clinical condition and was followed as an outpatient for and relapses or recurrences of brucellosis. Her blood culture, SAT, *Brucella* ELISA IgM, IgG and Coombs test results were negative. The treatment regimen of rifampicin and ciprofloxacin was stopped after six weeks.

## Discussion

Brucellosis is a major public health problem in Turkey. Risk factors that have been reported for 654 (63.6%) of 1028 Turkish brucellosis patients include a history of consumption of raw milk and dairy products. Brucellosis has a wide clinical spectrum, from asymptomatic cases who were diagnosed during family screening life-threatening cases. A family history of brucellosis has been reported for 17.8% of brucellosis cases in Turkey [3]. The present case had a history of a three-day fever, but the patient's epidemiological history was strong in regard to brucellosis. In the present case, the diagnosis of brucellosis was confirmed both bacteriologically and serologically.

*Brucella* spp. are intracellular pathogens that reside and proliferate in *Brucella* containing vacuoles in phagocytic cells; thus, they avoid immune system recognition. The optimal antimicrobial treatment for brucellosis includes agents that act intracellularly and have a low risk of generating *Brucella* resistance in order to prevent relapses. For this reason, combination treatment regimens that include TMP-SMX, doxycycline and rifampicin are recommended for brucellosis. There are two effective traditional treatment regimens for different age groups: for children over 8 years old, oral doxycycline (4 mg/kg/day) and rifampicin



**Figure 1** Maculopapular skin rash of the patient.

(20 mg/kg/day) are typically prescribed, and for children under 8 years old, oral co-trimoxazole (8 mg/kg/day), trimethoprim (40 mg/kg/day) and rifampicin (20 mg/kg/day) are typically prescribed. Both are prescribed for 6 weeks [4].

The present 2.5-year-old brucellosis patient had a TMP-SMX allergy. To our knowledge, no alternative anti-brucellosis therapy for the children under eight years old has been reported in the English literature. Tigecyclin, meropenem, liposome-encapsulated aminoglycoside, azithromycin and gentamicin have been reported as alternative drugs for the treatment of brucellosis in adults and children over 8 years old [5–8]. It is well known that brucellosis treatment with a single agent or treatment for less than 4–6 weeks can result in relapses and complications [9]. Relapses are identified by a new positive blood culture or the appearance of signs or symptoms of brucellosis. The rate of relapse following treatment is approximately 5–15% with the traditional treatment regimen [10].

It has been reported that ciprofloxacin may be useful for brucellosis cases of drug resistance, antimicrobial toxicity and relapse. These studies showed that although ciprofloxacin is not the first choice for brucellosis treatment, due to its good in vitro activity, it can be used in combination with rifampicin [10,11]. According to the literature,

follow-up visits take place each month during the first three months after the initiation of brucellosis treatment. In this case, after the first three months, follow-up visits also took place every three months for the rest of the first year after the initiation of treatment. In this case, the clinical and serological findings at the follow-up visits were negative. According to the reported treatment success criteria, the ciprofloxacin + rifampicin + gentamicin regimen was successful in our patient [4].

In conclusion, alternative treatment regimens for children under eight years old with a TMP-SMX allergy that have been reported in the literature are not sufficient. Using the best approach in such cases is important because unsuccessful treatment of brucellosis can cause significant complications and the risk of relapse. Therefore, it is necessary to search for alternative treatments for this patient population and to provide new treatment suggestions.

### Conflict of interest

*Funding:* No funding Sources.

*Competing interests:* None declared.

*Ethical approval:* Not required.

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