

Acute Brucellosis Following Accidental Exposure to *Brucella melitensis* Rev 1 Vaccine

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ABSTRACT

Brucellosis is mainly transmitted to humans by direct contact with infected animals, consumption of non-pasteurized dairy products or through inhalation of aerosols. However, the disease may also be transmitted by exposure to Brucella vaccination that is used in veterinary medicine. In the literature, there were a few case reports of persons who developed brucellosis after unintentional inoculation or conjunctival exposure to the live Brucella vaccine. Here, we describe a sheep farmer with acute brucellosis that occurred as a result of unintentional percutaneous exposure to Brucella melitensis Rev 1 animal vaccine while vaccinating lambs.

Keywords: *Brucella* vaccine, brucellosis, percutaneous exposure

Brucelosis Aguda tras la Exposición Accidental a la Vacuna *Brucella melitensis* Rev-1

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RESUMEN

La brucelosis es principalmente transmitida a los seres humanos por contacto directo con animales infectados, consumo de productos lácteos sin pasteurizar, o por inhalación de aerosoles. Sin embargo, la enfermedad también puede transmitirse por la exposición a la vacuna de Brucella que se utiliza en medicina veterinaria. En la literatura, se encuentran algunos reportes de casos de personas que desarrollaron brucelosis tras la inoculación accidental o exposición conjuntival a la vacuna de Brucella viva. Aquí describimos el caso de un ganadero de ovinos que desarrolló brucelosis aguda, producida a consecuencia de la exposición percutánea accidental a la vacuna animal Brucella melitensis Rev-1 mientras vacunaba corderos.

Palabras claves: Vacuna Brucella, brucelosis, exposición percutánea

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INTRODUCTION

Brucellosis is a zoonotic disease caused by *Brucella* species which are Gram-negative coccobacilli. It is a progressive disease which starts with nonspecific symptoms such as fever, night sweating, muscle and joint pain (1). The disease is endemic in Turkey and other Mediterranean countries and may cause many systemic complications. Basically, brucellosis is transmitted by direct contact with infected animals and consumption of unpasteurized contaminated dairy products. In addition, it has also been reported that the disease may be

acquired by inhalation, sexual intercourse and exposure to animal *Brucella* vaccinations that are used in veterinary medicine (2, 3). In this article, a case with acute brucellosis that occurred after accidental percutaneous exposure with *Brucella* Rev 1 animal vaccine during vaccination of lambs is presented.

CASE REPORT

A 49-year old female was accidentally inoculated with *Brucella melitensis* Rev 1 animal vaccine on the upper one-third of her left arm by the veterinary surgeon during vaccination of her lambs. On the 13th day after the incident, she presented with complaints of painful swelling at the inoculation site as well as fever, fatigue and arthralgia. She had no documented medical illness at admission.

On physical examination, fever was 39.4 °C and a painful induration with a diameter of 2 cm was detected on the upper part of her left arm. There was no hepatosplenomegaly. Other physical examination findings were normal. Laboratory

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findings were as follows: white blood cell (WBC) count $7800/\text{mm}^3$ (65% polymorphonuclear cells, 25% lymphocytes, 10% monocytes), haemoglobin 12.7 g/dL, platelet count $168\,000/\text{mm}^3$, C-reactive protein (CRP) 15.55 mg/dL, erythrocyte sedimentation rate 52 mm/hour (Westergren). Other biochemical tests were within normal levels. *Brucella* Rose Bengal slide agglutination test was positive and standard tube agglutination test was positive with a titre of 1/1280 for antibodies to *Brucella* spp. *Brucella melitensis* was isolated from two blood cultures at the same time. The patient was initiated on an oral combination of rifampicin 600 mg daily and doxycycline 100 mg twice daily. Fever resolved on day four of treatment. After 14 days of treatment, there was an improvement in the clinical symptoms including the painful induration on her left arm. The treatment was given for six weeks and she made a complete recovery. There was no relapse during the 12-month follow-up period after the treatment.

DISCUSSION

Brucellosis is the commonest zoonotic disease in endemic areas including Turkey. Brucellosis is transmitted to humans by direct contact with infected animals, consumption of non-pasteurized dairy products or through inhalation of aerosols (2). In order to control human brucellosis, the disease should be eradicated from animals such as cattle, goats and sheep. For this purpose, primarily, animals should be vaccinated with approved *Brucella* animal vaccines. The live *Brucella* animal vaccine also can cause brucellosis in humans.

In Turkey, the National Brucellosis Control and Eradication Programme was implemented in 1986 by the Ministry of Food, Agriculture and Livestock.

In the literature, there are few case reports of patients that developed brucellosis as a result of exposure to animal *Brucella* vaccinations with a live bacterial strain (4). In the series by Ashford *et al*, 26 individuals with accidental exposure to *Brucella abortus* strain RB51 vaccine were stratified according to the type of exposure (5). The exposures were needlestick injury in 21 cases (81%), conjunctival splash in 4 (15%) and splash on an open wound in 1 (4%) case. Although 18 (69%) of the individuals had received post-exposure prophylaxis (PEP), at least one systemic symptom consistent with brucellosis appeared in 19 (73%) persons during the follow-up period.

According to the Centers for Disease Control and Prevention recommendations (6), PEP is recommended for person with high-risk exposure (*eg* sniffing bacteriologic cultures, direct skin contact, pipetting by mouth, inoculation or spraying into the eyes, nose or mouth). Post-exposure prophylaxis includes doxycycline 100 mg twice daily and rifampin 600 mg once daily for three weeks. Local wound care and tetanus vaccination are also recommended after accidental exposure to *Brucella* spp. When a person is exposed to *B abortus* RB51 vaccine strain accidentally, rifampin should not be used for PEP due to *in vitro* rifampicin resistance. Furthermore, serological tests should be performed at the time of exposure and

also on the 2nd, 4th, 6th and 24th week of exposure for serological follow-up of *Brucella* infections (6, 7).

We described a patient with acute brucellosis due to unintentional injection of *B melitensis* Rev 1 animal vaccine. Post-exposure prophylaxis could not be given to our patient because she did not appear in hospital until the symptoms occurred. Similar to our patient, Blasco *et al* reported two veterinarians with acute brucellosis due to unintentional needlestick injury of animal vaccine who had taken no antibacterial prophylaxis after exposure to Rev 1 vaccination (8). However, Karakaş *et al* described a case of acute brucellosis associated with unintentional inoculation of *B abortus* S19 animal vaccine, despite the use of antibacterial prophylaxis (9). Several new studies reported that the development rate of active brucellosis was very low (0 to 2%) in laboratory staff members exposed to *B melitensis*; similarly, none of them received PEP (10, 11). Therefore, further research is needed to re-evaluate the potential efficacy of PEP.

Brucellosis is a chronic granulomatous infection and may present with various clinical manifestations. Granulomas are aggregation of macrophages, often admixed with other inflammatory cells, which usually result from a chronic presence of antigens. Granulomas are a unique inflammatory response. The induration at the inoculation site also occurred in our patient. In the literature, the inflammation at the inoculation site was reported in three of 32 persons who developed brucellosis after unintentional inoculation of the *Brucella* vaccine (12).

In the literature, the majority of cases who were injured by unintentional autoinoculation of animal vaccine are veterinarians or employees of vaccine manufacturing plants. But our case was a sheep farmer. In our country, generally, the breeders help the veterinarians during vaccinating. Moreover, both breeders and veterinarians do not use protective equipment (*eg* goggles, gloves). The use of protective equipment by trained veterinarians seems to be the most effective way to minimize the risk of unintentional inoculation while giving animal vaccines.

In conclusion, the control of brucellosis in humans is possible by eradicating the disease in animals. Performing animal vaccinations using protective equipment by experienced staff will reduce accidental exposure. Also, implementing PEP after high-risk exposure can reduce active brucellosis in humans.

CONFLICTS OF INTEREST

All authors report no commercial relationship or funding and conflicts of interest related to this study.

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