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Laboratory acquired brucellosis: A case report

Laboratuvar kaynaklı bruselloz: Olgu sunumu

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ÖZET

Laboratuvar kaynaklı bir bruselloz olgusu, ülkemiz gibi brusellozun hala endemik olduğu ülkelerde önem taşır. Brusella türleri laboratuvarlarda oldukça bulaşıcıdır. Brusellozdan şüphelenildiğinde klinisyen, elde çalışılan örnekler bağlamında laboratuvar çalışanlarını uyarmalıdır. Ancak, biyolojik güvenlik kabinlerinin kullanılması gibi infeksiyon kontrol önlemlerine rağmen laboratuvar kaynaklı bruselloz, çalışanların enfekte materyallerle teması nedeniyle önemini korumaktadır.

Sonuç olarak; brusellozda laboratuvar kaynaklı bulaş riskinin azaltılabilmesi, enfekte hayvan sayısını ve insanlarda hastalığın endemisitesini azaltmayla ilişkilidir.

Anahtar kelimeler: *Bruselloz, laboratuvar çalışanı, güvenlik kabini.*

SUMMARY

Laboratory originated brucellosis, maintains its importance in areas like our country where brucellosis is still endemic. Brucella species are highly contagious when handled in the laboratory. Clinicians should alert the laboratory workers when brucellosis is suspected so that the specimens are handled by workers carefully. But despite the enforcement of infection control measures including the use of biological safety cabinet in the laboratory, laboratory acquired brucellosis still maintains its importance because of handling infected samples by the workers.

Consequently, laboratory transmission risk reduction depends on efforts to reduce number of infected animals and to lower the disease endemicity level in humans.

Key words: *Brucellosis, laboratory workers, safety cabinet.*

INTRODUCTION

Brucellosis is an infective disorder which is widely seen in Turkey, which can infect any organ and system, and which have a wide spectrum of clinical forms. Source of infection is mostly contaminated raw milk and fresh cheese. Farmers and veterinarians who are in contact with infected animals and laboratory workers are under the risk of infection. In this study we report one of our microbiology laboratory workers who had laboratory acquired brucellosis and we aim to go over what we should do to lessen laboratory sourced infection risks.

CASE REPORT

The patient is a 29 years old, married woman. She has felt herself weak and tired for the last month but she did not care. She had back pain and myalgia in her legs increasing for the last 15 days. She did not have any other complaints. Her general state was good in physical examination. All system examinations were normal. We performed haemogram test, routine biochemical tests, Rose-Bengal (RB) test, standard tube agglutination test (STA) for brucellosis, since the growth rate of Brucella bacteria in the laboratory for last 4 months was high in blood cultu-

res (20 % of total positive blood cultures) and since we had experience of laboratory sourced brucellosis in another personnel before. White blood cell count was 4.820/mm^3, haemoglobin 12 g/dl, ESR 24 mm per hour. Routine biochemical tests were in the normal limits. Dorsal and lumbosacral radiographs were applied since osteoarticular complications are generally seen in brucellosis and the patient suffered from pain in her back and legs. There were no abnormal radiographic findings. STA test was found positive in 1/160 titres. Although she did not have fever, blood cultures were taken and the classical treatment as rifampicin (RIF) with doxycycline (DOX) was started. As sexual transmission is possible, we performed RB and STA tests for her husband and found negative.

On the fourth day of the treatment, growth was determined in blood culture by Bactec 9050 (Bio Merieux, France). Passage was made onto chocolate agar medium from the blood culture bottle. Grown bacteria was identified as Brucella spp. by means of colony morphology, Gram staining and conventional biochemical tests. MIC values for RIF, streptomycin (SM), tetracycline (TS) were investigated by E test method and determined as 0.75, 0.50, and 0.032 µg/ml, respectively.

On the 12th day liver function tests were elevated (ALT 83 mg/dl, AST 58 mg/dl). We continued to follow the treatment. However, the levels of the enzymes were 3 times the normal values after 3 days. Considering RIF might have caused hepatocellular damage, the treatment was stopped for a while. In the following days, repeated tests showed that liver enzyme levels started to decrease. On the 3rd day of the period when the treatment was interrupted, a blood culture was again taken from the patient and it had growth. The MIC points for this grown bacteria was 0.75, 0.50, and 0.016 µg/ml for RIF, SM, and TS, respectively. Treatment was restarted with ciprofloxacin (CIP) and DOX and on the 33rd day when liver enzyme levels decreased to normal values. During the following 3 weeks the liver enzymes were not elevated and then RIF was added to the treatment again. The following repeated blood cultures of our patient did not have growth. Her complaints vanished. Her treatment was completed on the 45th day.

CONCLUSION

Brucellosis is the most widely seen zoonosis in the world. It is still endemic in our country. Transmission of Brucella species to human mostly occurs by direct contact with infected animals and by consuming raw milk and milk products. It is also transmitted by inhalation of the infectious aerosols. The laboratory workers get infected by either inhalation or by direct contact through the injured skin. In fact 2% of all cases are laboratory workers and brucella species are the most contagious pathogens in laboratories (1, 2). The laboratory worker who is the subject of this study, have been studying on blood cultures for the last 4 months. In our laboratory, blood cultures have been studied by Bactec 9050 (Bio Merieux) since 1998. In order to protect laboratory workers from infections like tuberculosis or brucellosis which have high reported laboratory transmissions, the studies concerning these microorganisms are performed in safety cabinets. In the previous month before the patient got sick, Brucella spp. was grown among 20 % of all positive blood cultures. In a recent study of ours concerning 46 brucellosis cases, the growth rate in blood cultures was 70 % and this ratio is pretty high compared to similar studies (3). Hence, the risk of contact and transmission of the pathogen to the laboratory workers is high in our country, being an endemic region for brucellosis. Laboratory acquired infections are rarely diagnosed or reported. Mazuelos et al. (4) observed a high brucellosis growth rate in their laboratory in 4 months of a summer season in Spain, which is an endemic country like ours, and observed brucellosis in 4 laboratory workers. Memish et al. from Saudi Arabia reported that brucellosis risk is still high among laboratory workers in spite of taking precautions like using safety cabinets. They related this result to the large number of brucellosis suspected materials sent to the laboratory (5).

What attracts our attention is the occurrence of the transmission although safety cabinet was used. Ho-

wever, the area where passages from blood culture bottles to plates are done, is the common usage area. When Brucella genus is suspected to grow on a plate, the continuing studies are held in safety cabinets. We guess this short period might be the transmission time considering the high potential transmission rate of this bacteria. For this reason, RB and STA tests were applied for all the personnel working in the laboratory and the results were negative. Staszkiewicz et al. (6) mentioned about an outbreak which occurred in 1988 concerning 8 people working at a microbiology laboratory. They determined the outbreak had occurred during the identification of the microorganism stored in the deep freeze in a tube on which the bacteria name was not mentioned. Brucella bacteria had infected people probably by inhalation because of not using a safety cabinet. The transmission route is still speculative for laboratory workers. But inhalation looks like the most probable way.

The diagnosis of brucellosis was based on serological tests because of the late growth of the bacteria on blood cultures. Recently, the isolation of the bacteria from the blood cultures is essential in the diagnosis of the disease because of the advanced technology. Blood culture of our patient had growth on the fourth day. In a previous study of ours, the mean growth period for Brucella bacteria in blood cultures was found to be 3.3 days by BACTEC 9050 system. This is a very pleasing result for a microorganism which grows hardly and slowly (7).

In the therapy of brucellosis, a combination of doxycycline and rifampicin is administered for 6 weeks according to the recommendations of WHO in 1986 (8). In a study of Ariza et al., 6 weeks therapy of doxycycline and rifampicin was found as efficient as doxycycline and streptomycin. And the side effects were much less than the latter (9). We also administered doxycycline and rifampicin for the therapy. But the therapy was interrupted by the hepatotoxicity which occurred on the twelfth day and lasted for 2 weeks. The elevation of liver function tests in brucellosis may be due to both the microorganism invasion of the liver and the medication. Brucella hepatitis is varied as granulomatous form, diffuse non-specific inflammation or abscess formation and it can be detected by USG. Because we did not detect any pathology in the abdominal USG of our patient, the elevation of the liver function tests was thought to be related to hepatotoxicity caused by the drugs. Both of the drugs administered for the patient were hepatotoxic. Rifampicin toxicity was major suspect in our patient. Although treatment with a combination of streptomycin and doxycycline is also recommended, we preferred to interrupt the therapy because doxycycline is also hepatotoxic (10, 11). At the end of two weeks of therapy interval which followed two weeks of combination therapy, there was still growth on the blood cultures of the patient. The grown bacteria in the latter blood culture had the same MIC points as for the first culture. Difference to make us think about resistance development was not determined. After the liver function tests decreased to normal levels, we started a combination therapy of ciprofloxacin and doxycycline. Studies about the efficacy of quinolones in brucellosis treatment have different results. It is stated that a combination of doxycycline with quinolones other than ofloxacin has higher relapse rates compared to the combination of doxycycline with rifampicin (11-14). By taking relapse probability into consideration, and seeing that the liver function tests were in normal ranges in the first 3 weeks, we added RIF to the therapy at the end of the third week. The medication was continued with the three drugs. There was no elevation in the liver function tests again. There was no growth in the repeated blood cultures and the clinical symptoms improved.

It is a fact that the personnel of the microbiology laboratories face some risks. Working manually with materials like blood culture and not using safety cabinets have a major role in transmission by inhalation. Although we have a safety cabinet in our laboratory, we have seen that during the short time when passages are done from the blood culture bottles to the plates and the first growth is evaluated, infections may occur by rapidly disseminating microorganisms

like brucella. Clinicians should alert the laboratory workers when brucellosis is suspected so that the specimens are handled under the most stringent safety measures. To avoid laboratory transmission, taking CDC recommendations into consideration, each laboratory personnel must work cautiously and with responsibility against laboratory risks and handling of bio safety level 3 microorganisms, such as Brucella spp. must be conducted under bio safety hoods and the plates should be sealed for safety when they are not in use (15). We believe these precautions will definitely lower the risks of working in a microbiology laboratory.

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