discrepancy regarding the smoking status of the subjects results from inadequate expression of the data of the study subjects, that is to say, some ex-smokers included in the study have not been mentioned in the study population segment. Although there is nothing to get excited about the presentation, we might be excused for the same. The subject numbers are relatively small; however, statistically adequate.

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Reference

1 Caliskan M, Erdogan D, Gullu H, Tok D, Bilgi M, Muderrisoglu H. Low serum bilirubin concentrations are associated with impaired aortic elastic properties, but not impaired left ventricular diastolic function. *Int J Clin Pract* 2007; **61**: 218–24.

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LETTER

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Brucella melitensis in the aetiology of febrile neutropenia: report of two cases brucellosis and febrile neutropenia

To the Editor:

Brucellosis is a zoonotic infection caused by *Brucella* species. It is an important disease and still causes significant morbidity (1–4). *Brucella* spp. is a very rare cause of febrile neutropenia. Sari et al. (5) and Ozcay et al. (6) reported a total of four cases of febrile neutropenia in whom brucellosis was shown to be responsible in the aetiology of fever. In this report, it is aimed to present two cases of febrile neutropenia due to *Brucella* spp.

A 56-year-old male patient with non-Hodgkin lymphoma (NHL) developed fever (38.6°C) 5 days after receiving a chemotherapy regimen with doxorubicin, cyclophosphamide, cytosine arabinozide and methotrexate (89C41A chemotherapy protocol). He had received several chemotherapeutic and radiotherapeutic regimens for the last 4 years. He was neutropenic (neutrophil count, 90/mm^3). There was no remarkable finding in the physical examination. After blood and urine culture sampling, meropenem and neutromycin were initiated empirically. As fever did not resolve, teicoplanin was added on the third day and liposomal amphotericin B was added on the sixth day of fever. On the ninth day of the antibacterial therapy, he still had fever; blood cultures (in two different sets) obtained in the first day yielded *Brucella melitensis*. He did not have a history of animal feeding or eating fresh cheese. Abdominal ultrasonography did not reveal any specific focus. Other antimicrobials were stopped; doxycycline (100 mg × 2), rifampin (300 mg, 1 × 2) and ciprofloxacin (500 mg, 2 × 1) were started empirically. His fever resolved on the fourth day of this regimen. There was no bacterial growth in the control cultures. After 45 days, *Brucella*-related antibacterial therapy was stopped. Unfortunately, patient died 15 days later probably due to NHL. Autopsy was not performed.

A 59-year-old male patient who received chemotherapy with vincristin, l-asparaginase, daunorubicin, prednisolone due to acute lymphocytic leukaemia 8 days before, developed fever (39°C). He was neutropenic (neutrophil count, 167/mm^3). There was no remarkable finding in physical examination. Other laboratory findings were as follows: haemoglobin, 6.7 g/dl; thrombocyte, 22,000/mm^3; aspartate aminotransferase, 40 U/l and alanine aminotransferase, 50 U/l. After blood and urine culture sampling, cefepime and ciprofloxacin were initiated empirically. Two days later, his general status deteriorated and he developed hypotension. Therapy was switched to imipenem/cilastatin and teicoplanin. Despite this regimen, his general status continued deteriorating, he developed respiratory failure, chest pain and cough, and was referred to Anaesthesiology and Reanimation Intensive Care Unit. On the day he was referred, it was learnt that his blood cultures yielded *B. melitensis*. Unfortunately he died on the same day because of probable pulmonary embolism (diagnosis not confirmed). Autopsy was not performed.

Despite several developments in the quality of care and antimicrobial therapy, febrile neutropenia is still a morbid and mortal syndrome. In spite of extended spectrum antibacterial and antifungal agents, fever may persist in several situations (4). Aetiological cause of fever can be demonstrated in only 15–30% of neutropenic patients (4). *Brucella* is a very rare cause of febrile neutropenia. To our knowledge, there are four published cases of febrile neutropenia due to *Brucella* spp. (5,6) and all are reported from Turkey. The fact that all cases are reported from Turkey is of interest. Brucellosis is prevalent in Middle East (7–9). Al Sekait (9) from Saudi Arabia reported seroprevalance of brucellosis as 15% in 23,613 subjects. Brucellosis seroprevalance in Turkey (Standard Wright test positivity ≥ 1/40 titre) is reported between 0.3% and 3.3% (7,8). In a recent study performed in Odemis-Izmir, where domestic animal feeding is prevalent, *Brucella* seroprevalance (Standard Wright test positivity ≥ 1/160 titre) was found as 7% (18/257) (C. Buke, Izmir, personal communication).

Brucellosis has a wide range of signs and symptoms mimicking many other diseases and causing problems in diagnosis. The clinical picture of brucellosis is often non-specific, with swings in fever, malaise and myalgia (1,2). Fever was the main presentation in both cases.

Brucellosis may be associated with a variety of haematological abnormalities (2); one study of 104 cases reported that 6.7% had anaemia, 4.8% had leucopenia, 2.8% had pancytopenia and 3.8% had thrombocytopenia (2). Whether brucellosis further complicated the haematological presentation of the cases is unknown.

Although blood cultures are highly specific for the diagnosis of brucellosis, it is often difficult to isolate *B. melitensis* from blood cultures (10,11). In a study from Turkey, blood cultures yielded *B. melitensis* in only 15 of 124 patients (10). In both cases, blood culture was positive. Consumption of unpasteurised milk and products, animal breeding, accidental infection during veterinary processes are associated with brucellosis (1). Both patients did not have such a risk factor. Wright agglutination and Rose Bengal test were negative three months before the positive blood culture in the first case. Tests could not be repeated after the positive culture.

Both cases died. Whether brucellosis played a role in the mortality is unclear. The subsequent blood cultures were sterile after doxycycline–rifampin and ciprofloxacin in the first case. Treatment could not be started in the second case. Autopsy could not be performed in both cases.

Rarely *Brucella* spp. may be the aetiological agent in febrile neutropenia especially in countries with endemic brucellosis. Whether these cases are sporadic or *Brucella* spp. is a major agent in patients with neutropenic fever in Turkey needs to be analysed in larger cohorts.

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References

1 Tasbakan MI, Yamazhan T, Gokengin D et al. Brucellosis: a retrospective evaluation. *Trop Doct* 2003; **33**: 151–3.
2 Cesur S, Capar Y, Demir P et al. A retrospective evaluation of 104 cases of Brucellosis. *Turk J Infect* 2004; **18**: 169–75.
3 Bosilkovski M, Krteva L, Caparoska S, Dimzova M. Hip arthritis in brucellosis: a study of 33 cases in the Republic of Macedonia (FYROM). *Int J Clin Pract* 2004; **58**: 1023–27.
4 Akan H, Akan OA, Akova M et al. Guidelines for diagnosis and treatment of neutropenic patients. *Flora* 2004; **9**: 5–28.
5 Sari R, Buyukberber N, Sevinc A, Bayindir Y, Buyukberber S. Brucellosis in the etiology of febrile neutropenia: case report. *J Chemother* 2002; **14**: 88–91.
6 Ozcay F, Derbent M, Ergin F, Duru F, Ozbek N. Febrile neutropenia caused by *Brucella melitensis* in a child with hypoplastic acute lymphoblastic leukemia. *Med Pediatr Oncol* 2000; **35**: 496–7.
7 Bozkurt S, Aytac N. The prevalence of Brucellosis in adults over 20 years of age in the Doğankent Health Education Research Center's service area. *Ankara Üniversitesi* Tıp Fakültesi Mecmuası, 2001; **54**: 23–30.
8 Buke AC, Ciceklioglu M, Erdem I et al. Brucellosis prevalence and knowledge on Brucellosis in individuals working with milk products. *Turk J Infect* 2000; **14**: 321–5.
9 Al Sekait MA. Seroepidemiological survey of brucellosis antibodies in Saudi Arabia. *Ann Saudi Med* 1999; **19**: 219–22.
10 Tasova Y, Saltoglu N, Yilmaz G, İnal S, Aksu HSZ. Brucellosis: an evaluation of clinical, laboratory and treatment features of 238 adult cases. *Turk J Infect* 1998; **12**: 307–12.
11 Al-Attas RA, Al-Khalifa M, Al-Qurashi AR, et al. Evaluation of PCR, culture and serology for the diagnosis of acute human brucellosis. *Ann Saudi Med* 2000; **20**: 224–8.

