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Lumbar pain in a married couple who likes cheese: Brucella strikes again !

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ABSTRACT

A 69-year-old man living in Florence reported fever and acute lumbar pain one month after transurethral resection of a superficial transitional cell carcinoma of the bladder. The radionuclide bone scan suggested metastatic lesions of the L3-L4 vertebrae. However, cobalt treatment was ineffective. A bone biopsy of L4 showed an inflammatory pattern and antibiotic therapy was started which did not produce any clinical improvement. Six months after the onset of the back pain brucellar spondylitis was serologically diagnosed and treatment with doxycycline and streptomycin produced a significant clinical and radiological improvement.

After 2 months the patient's wife presented with fever and lumbar pain, and brucellar spondylitis was diagnosed as well. An extensive epidemiological examination revealed that 8 months earlier the family had eaten unpasteurized goat cheese and serological examination of the entire family showed that 3 out of 4 members had significant titres of brucellar antibodies. Finally it was discovered that 4 months after consuming the cheese the third infected subject experienced an episode of epidydimo-orchitis for which no diagnosis and effective treatment was found.

This family cluster of brucellar infection indicates that a high degree of suspicion in the diagnosis of brucellosis is necessary even in non-endemic areas, to reduce the delay in the diagnosis and treatment of the disease and to prevent the occurrence of complications that may prove difficult to treat.

Introduction

Human brucellosis is an important disease of man which is largely underdiagnosed or misdiagnosed due to absence of characteristic clinical symptoms, chronic nature of the infection and difficulty in isolation of the causal agent from the patients.

Early recognition and management of this systemic disease in its acute or chronic form is vital to avoid development of severe complications like bone and joint involvement, neurobrucellosis and endocarditis.

Case report

A 69-year old man living in Florence was admitted to our Department in March 1999 with lumbar pain and stiffness of 6 months duration. He reported undergoing in August 1998 transurethral resection for a superficial transitional cell carcinoma of the bladder. One month later fever and acute, progressively worsening lumbar pain developed. In November 1998, T1 weighted magnetic resonance image (MRI) showed a decreased intensity signal from the L3-L4 vertebral bodies and from the relative intervertebral disc space that was associated with an increased signal intensity from the L3-L4 vertebral bodies on T2 weighted images (Fig. 1). A radionuclide bone scan with ^{99m}technetium methylene diphosphonate showed a significant hypocaptating signal involving the vertebral bodies, which was considered highly suggestive of metastatic lesions.

Cobalt treatment was started (300 mRad thrice in week), which was followed by a slight improvement in the pain. However, a bone biopsy of L4 showed a picture of inflammation; therefore cobalt treatment was withdrawn and antibiotic treatment with teicoplanin 200 mg/day and levofloxacin 500 mg/day was started. Peripheral radiculopathy and neurological deficit of the lower limbs occurred concomitantly with a significant worsening of the back pain for which the patient neither stand nor lie in bed and had difficulty in walking. An orthopedic corset was applied.

Since the pain did not subside and the neurological signs were worsening, the patient presented to our Department in March 1999. On admission, reduced lower limb strength, and muscle hypotrophy of the left leg were found. Mild hypocromic anemia (Hb 9.5 g/dl) and an increased erythrocyte sedimentation rate (ESR 84 mm/h) were found; fibrinogen (593 mg/dl), C reactive protein (CRP: 5.5 mg/dl) and total IgA (748 mg/dl) levels were abnormal. Aerobic and anaerobic blood coltures were negative. On x-rays destruction of the upper L4 and lower L3 anterior vertebral end plates was found, with a significant reduction in the L3-L4 intervertebral space (Fig. 2).

Fig. 1. T2 weighted image from the L3-L4 vertebral bodies and the relative intervertebral disc space obtained in November 1998 from the 69-year-old male patient with brucellar spondylitis.

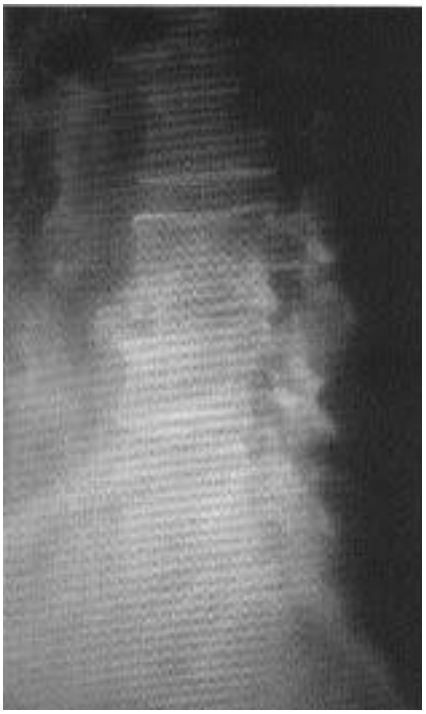

Fig. 2. X-ray showing upper L4 and lower L3 anterior vertebral end plate destruction with a significant reduction in the L3-L4 intervertebral space in the same patient.

A second bone biopsy was performed, and although a culture of the specimen was negative, brucellar spondylitis was diagnosed on the basis of a highly positive Wright's seroagglutination test (titre 1:1600). Treatment with doxycycline 200 mg per day for 6 weeks plus streptomycin 1 g per day for 3 weeks resulted in significant clinical and radiological improvement (Fig.3) that were followed by a complete resolution of the pain.

Fig. 3. T2 weighted image from the L3-L4 vertebral bodies and the relative intervertebral disc space obtained in May 1999 showing improvement of the bone and disc lesions.

In May 1999 the patient's wife presented to our department complaining of continuous fever, with evening spikes reaching 39°C preceded by chills and followed by profuse sweating, and steadily worsening lumbar pain. Blood and urine cultures were repeatedly negative. Brucellar spondylodiscitis was diagnosed based on a positive Wright's agglutination test (titre 1:400) and on MRI showing involvement of the disk space between L2 and L3, with broad destruction of the lower end plate of L2, and more limited involvement of the L3 vertebral body.

Discussion

An extensive anamnesis revealed that in July 1998 both patients and their family had consumed fresh, unpasteurized goat cheese produced and imported from an endemic Italian region. Indeed one son, who had suffered intermittent fever and monolateral epididymo-orchitis 4 months after consumption of the cheese, tested positive for brucellar antibodies (titre 1:400).

Brucellosis exists worldwide, especially in the countries around the Mediterranean basin, and it should be investigated in all patients showing fever of unknown origin when a history of potential exposure (contact with animals, ingestion of raw milk/cheese or raw liver, and/or a family history of brucellosis) is reported in association with non-specific signs and symptoms such as sweating, malaise, anorexia headache, and back pain with either an acute or an insidious onset (Table I) (1).

Table I. Symptoms and signs in patients with brucellosis due to *Brucella melitensis* (9).

Symptoms and signs	% of pts.	Symptoms and signs	% of pts.
Lack of energy	95	Lymphoadenopathy	32
Fever	93	Ill appearance	25
Aches	91	Splenomegaly	25
Sweating	87	Cough	24
Joint and back pain	86	Pallor	22
Chills	82	Testicular pain/epididymoorchitis	21
Hedhache	81	Hepatomegaly	19
Loss of appetite	78	Rash	14
Weight loss	65	Diarrea	7
Spinal tenderness	48	Central nervous system abnormalities	4
Constipation	47	Cardiac murmur	3
Abdominal pain	45	Jaundice	1
Arthritis	40	Pneumonia	1
Sleep disturbances	37		

Table II. Diagnostic procedures for the assessment of brucellar spondylitis.

Exams	Common findings	Comments
Blood, disc or bone tissue specimen culture	Positive in most cases	False negative result is possible if inadequate microbiological techniques are used or if the patient has previously been administered antimicrobial agents
Serology	Positive: titre >1:160 for standard tube agglutination test and >1:320 for Coomb's test	False negative reactions possible due to prozone phenomenon, or false positive results due to cross-reactions with antibodies to Tularemia, cholera, or Yersinia
Magnetic resonance	Low signal intensity on T1-weighted images, hyperintensity on T-2 weighted images of the intervertebral disc and the adjacent vertebral bodies in acute infection. Non-homogeneous signal intensity in the vertebral bodies on T-1 weighted images in chronic infection	Soft-tissue masses of small or moderate size are very common, and the decrease is correlated with a good good clinical outcome.
CTscanning	In the early stages destruction is confined to the upper end plate anteriorly	Provides a more detailed picture of spinal changes than plain x-ray
Radionuclide scintigraphy	Increased uptake on technetium bone scan and rarely decreased	Very sensitive and well suited for total body assessment of the extent of musculoskeletal involvement
Plain radiograms	Very frequently positive	Low sensitivity in the first 2-4 weeks of the disease

Table III. Radiologic features of the main spinal pathologies that should be considered in the differential diagnosis of brucellar spondylitis.

	Magnetic resonance	Radionuclide scintigraphy	Other features
Tuberculous spondylitis	Lack of an abnormal signal in intervertebral disc space, presence of a gross paraspinal soft tissue mass, involvement of the posterior vertebral bodies and arches, involvement of many VB, and the presence of a large paraspinal mass. Higher frequency of thoracic involvement and spinal deformity.	Increased signal, 95% sensitivity, multicentricity in 25% of cases	Higher frequency of lack of fever and neurological deficit
Pyogenic spondylitis	Few or no differences with respect to the brucellar spondylitis pattern		Diabetes mellitus, intravenous drug abuse, focal infections, bacteremia and surgery. Leucocytosis, neutrophilia, very high ESR and C-reactive protein values.
Vertebral metastases	Involvement of the intervertebral discs. VB show no contrast enhancement.	Decreased uptake on technetium bone scan	History of malignancy or the presence of other suggestive elements

The diagnosis of brucellosis can be made with certainty when brucellae are recovered from blood, bone marrow or other tissues (Table II). The rate of isolation from the blood ranges from 15% to 70% depending on the method used and the period of incubation, while a higher yield can be obtained with culturing of bone marrow. In the absence of bacteriological confirmation, a presumptive diagnosis can be made on the basis of high or rising titres of specific antibodies (Table II).

Although brucellosis is a systemic infection in which any organ or system of the body may be involved, osteoarticular complications are the symptom most frequently encountered (2, 3). In particular, spondylitis can occur in up to 53% of patients with brucellosis and the lumbar spine is involved in up to 58% of cases (4-6). Thus, back pain can be the main symptom raising the suspicion of brucellosis, especially in older patients (4). However, brucellar spondylitis may be difficult to diagnose, particularly in non-endemic areas such as Tuscany (7-9), and the differential diagnosis in patients with acute lumbar pain and radiographic evidence of straightening of the spine and narrowing of the disk space, with or without paraspinal abscess (9), should be aimed at excluding tuberculous or pyogenic spondylitis and vertebral metastases (Tables II and III).

To this end, MRI is very useful since it can distinguish between these abnormalities. In particular, in acute brucellar infections MRI shows low signal intensity in T1-weighted images and hyperintensity on T2-weighted images of the intervertebral disc and the adjacent vertebral bodies, while in the case of metastatic lesions of the spine the intervertebral disks are not involved and the affected vertebral bodies show no contrast enhancement (10). Tuberculous spondylitis is characterized by the lack of an abnormal signal in the intervertebral disk space, the presence of a gross paraspinal soft tissue mass, involvement of posterior vertebral bodies and arches, and usually involves

Table IV. The treatment of brucellar spondylitis.

Treatment	Comments
Doxycycline 200 mg/day for 6-12 weeks + gentamicin 240 mg/day for 3 weeks *or* streptomycin 1 g/day for 2-3 weeks	Brucellar spondylitis may require a longer duration or therapy. Sometimes several courses of treatment are needed, especially in the presence of large paravertebral abscesses.
Surgical intervention	Indicated for patients with neurological deficits
Percutaneous drainage or aspiration of the epidural or paravertebral abscesses	May represent an alternative to surgery and can be indicated for patients who are poor surgical candidates
Analgesics and immobilization	

many vertebral bodies (11) (Table III). The treatment for brucellar spondylitis is reported in Table IV. Immobilization and the administration of antibiotics and anti-inflammatories are the mainstay of the therapy, while CT-guided percutaneous drainage is necessary only in the presence of a large paravertebral abscess. The duration of antibiotic therapy for brucellar spondylitis is 6-12 weeks, longer than that usually recommended for systemic brucellosis without spondylitis (9). Some patients respond only partially or temporarily to this regime however and require several courses of antibiotic treatment. Failure of antimicrobial therapy rarely represents actual resistance of the bacteria to antibiotics, but is usually due to the presence of a large paravertebral abscess (12). When the inflammatory process responds well to treatment, the changes in signal intensity tend to regress within a period of 6 weeks to several months, due to regression of the inflammation with the formation of fibrous tissue and bone (10).

In our male patient, the x-ray and MRI findings were compatible with the diagnosis of brucellar spondylitis, but the confounding finding of decreased uptake on ^{99m}technetium bone scan and the history of malignancy gave rise to a misinterpretation of the clinical picture, resulting in a significant delay in the diagnosis and, unfortunately, progression of the vertebral lesions. The diagnosis could have been made much earlier if brucellar etiology had been included in the differential diagnosis of the epididymo-orchitis affecting the son. Since even in non-endemic areas more than half of all cases also report brucellosis in other family members (2,3), brucellosis found in a patient should prompt an extensive search to exclude this etiology in other family members presenting with clinical manifestation compatible with brucellar infection.

This report indicates that a high degree of suspicion and a correct methodological approach are mandatory to reduce the delay in diagnosis and treatment of the disease. This strategy may prevent the occurrence of difficult-to-treat complications, and allows an accurate and extensive epidemiological evaluation to identify the other members of the family who may have been exposed to the risk of infection.

References

1. MADKOUR MM: *Brucellosis*. London, Butterworths, 1989.
2. YOUNG E: An overview of human brucellosis. *Clin Infect Dis* 1995; 21: 283-90.
3. SOLERA J, MARTINEZ-ALFARO E, ESPINOSA A: Recognition and optimum treatment of brucellosis. *Drugs* 1997; 53: 245-256.
4. COLMENERO JD, REGUERA JM, MARTOS F *et al.*: Complications associated with *Brucella melitensis* infection: a study of 530 cases. *Medicine (Baltimore)* 1996; 75: 195-209.
5. GONZALEZ-GAY MA, GARCIA-PORRUA C, IBANEZ D, GARCIA-PAIS MJ: Osteoarticular complications of brucellosis in an Atlantic area of Spain. *J Rheumatol* 1999; 26: 141-5.
6. Al-SHABED MS, SHARIF HS, HADDAD MC, AABED MY, SAMMAK BM, MUTAIRI MA: Imaging features of musculoskeletal brucellosis. *Radiographics* 1994; 14: 333-48.
7. APPLEBAUM GD, MATHISEN G: Spinal brucellosis in a southern California resident. West J Med 1997; 166: 61-5.
8. CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL: Weekly clinicopathological exercises. Case 37-1986: a 50-year-old woman with back pain, extensive travel, and exposure to farm animals. *N Engl J Med* 1986; 315: 748-54.
9. SOLERA J, LOZANO E, MARTINEZ-ALFARO E, ESPINOSA A, CASTILLEJOS ML, ABAD L: Brucellar spondylitis: review of 35 cases and literature survey. *Clin Infect Dis* 1999; 29: 1440-9.
10. HARMAN M, UNAL O, ONBASI KT, KIYMAZ N, ARSLAN H: Brucellar spondylodiscitis MRI diagnosis. *J Clin Imaging* 2001; 25: 421-7.
11. SMITH AS, WEINSTEIN MA, MIZUSHIMA A *et al.*: MR imaging characteristics tuberculous spondylitis vs. Vertebral osteomyelitis. *Am J Radiol* 1989; 153: 399-405.
12. ARIZA J, GUDIOL F, VALVERDE J *et al.*: Brucellar spondylitis. A detailed analysis based on current findings. *Rev Infect Dis* 1985; 7: 656-64.