Sensorineural hearing loss in neurobrucellosis

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ABSTRACT

يعتبر داء البروسليات العصبية (NB) حالة سريرية نادرة من داء البروسليات، ومن الصعب تشخيص وعلاج هذا النوع نتيجة لقلة فئة التصنيف التشخيصية. طيف الأعراض السريرية قد يتراوح ما بين أعراض عصبية غير محددة ويصل إلى التهاب شديد في الدماغ والسحايا. نذكر هنا تقريراً عن حالة ثلاثة مرضى يعانون من داء البروسليات العصبية (NB)، تكمن المشكلة الرئيسية لديهم في فقدان السمع الحسي (SNHL)، ويتم متابعة حالتهم لدينا في المستشفى منذ ثلاثة السنوات. شخصنا داء البروسليات العصبية (NB) بواسطة نتيجة فحص زراعة السائل النخاعي الشوكي الموجبة (CSF) لدى مريضين، وللبروسيلا الموجبة (IgG)، والتراص الشديد في الدم، ونتيجة السائل النخاعي الشوكي لدى الثالث. يعتبر نقص السمع الحسي (SNHL) من المضاعفات النادرة الحدوث للبروسليات العصبية (NB)، والذي لم يلفت الانتباه بشكل كاف من بين الظواهر المعبرة. يجب على أطباء الأعصاب وأطباء الأذن إعارة المزيد من الاهتمام لهذه الأعراض كوجود سريري لداء البروسليات.

Neurobrucellosis (NB) is a rare clinical presentation of brucellosis. This form is hard to diagnose because of a lack of definite diagnostic criteria, and its treatment is also hard. The clinical spectrum may cover a span between non-specific neurological symptoms to a severe meningoencephalitis. We report 3 patients with NB, whose main complaint was sensorineural hearing loss (SNHL) who were followed up at our hospital for 3 years. We diagnosed NB by positive CSF cultures in 2 patients and by a positive brucella IgG agglutination titer in blood and CSF in the third. Sensorineural hearing loss is a rare complication of NB, which has not attracted enough attention among known manifestations. Neurologists and otologists should be aware of this symptom as a probable clinical presentation of brucellosis.

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Brucellosis may affect any system, however, involvement of the CNS is seen in less than 5% of patients. The most common complication is meningitis. Headache, vomiting, fever, nuchal rigidity, or cranial nerve palsy can be seen in patients with acute meningitis. In neurobrucellosis (NB), transient hemiparesis, psychiatric symptoms, aphasia, convulsions, myoclonia or deafness may occur.[1] In the 1990's, the diagnostic criteria of NB were: i) Neurological signs and symptoms that could not be explained by other neurological disease; ii) Positive agglutination titer for brucella organisms in blood of 1:160; iii) Pleocytosis in CSF; and iv) Clinical worsening despite appropriate therapy.[2] In the 2000's, positive CSF culture for Brucella spp. or positive brucella IgG agglutination titer in CSF gained more importance, after it became easier to isolate the responsible agent. The NB patients are sporadically reported, and cranial nerve involvement is rare.[3-8] We review here the findings of 3 patients with NB, whose main complaints were sensorineural hearing loss (SNHL), among 6 patients with NB in our institute between 2000-2003. Our intention is to emphasize SNHL as a clinical form of NB in endemic regions.

Case Report. *Patient One.* A 39-year-old farmer was admitted with headache, fever, nausea, vomiting, deafness, and difficulty in walking. He had had these complaints for 6 months. He was sent to our hospital after pleocytosis was detected in CSF. We detected nuchal rigidity and meningismus. He was conscious, but cooperation was difficult due to a hearing loss. We detected hearing loss and truncal ataxia in the neurological examination. Other systems and blood biochemical tests were normal. We counted 500 cells/mm^3 in the CSF (normally ≤5/mm^3), with 98% lymphocytosis. Protein amount was 1935 mg/dL (normally ≤40mg/dl), and glucose was 21 mg/dL (normally ≥60% of that in blood) in the CSF. We documented a moderate degree of SNHL by audiometry. Cranial MRI was normal. Standard tube agglutination (STA) test was positive at 1:640 in blood, and at 1:320 in CSF. We started combination therapy with doxycycline, rifampicin, and ceftriaxone (DOX+RIF+CRO). Blood and CSF cultures were positive for Brucella spp. on the fourth day

with BACTEC. The minimal inhibitory concentration (MIC) value for RIF was 0.38 µg/ml, for tetracycline (TE) was 0.016 µg/ml, and for streptomycin (SM) was 0.125 µg/ml with E test. We continued antimicrobial therapy for 6 months.

Patient 2. A 54-year-old man was admitted with headache, deafness, myalgia, and difficulty in walking. He reported visiting his physician for fever, sweating, forgetfulness, and trembling in his hands occurring 18 months ago. These complaints had disappeared after therapy, but were replaced with a progressive hearing loss. Six months before, fever, deafness, and walking deficiency reoccurred. We did not observe neck rigidity or meningismus. He was conscious, but cooperation was difficult due to deafness. Other systems and blood biochemical tests were normal. We counted 52 cells/mm^3 in the CSF. The amount of protein was 179 mg/dL, and glucose was 24 mg/dL in the CSF. We documented bilateral SNHL by audiometry. Rose Bengal test was positive in blood and CSF. The STA test was positive at 1:40 titer in both blood and CSF. We started combination therapy (DOX+RIF+CRO). We performed an EMG because of an ache in his arms and legs, and detected polyneuropathy and radiculopathy. Cranial MRI was normal. High IgG titers in both blood and CSF were found by ELISA. At the end of the first month, his clinical complaints and CSF findings obviously regressed. However, his difficulty in walking persisted. We continued antimicrobial therapy for 6 months.

Patient 3. A 60-year-old man was admitted with headache, deafness, difficulty in walking and balance. He complained of a headache of 3-4 years duration and a hearing loss for one year. Difficulty in walking had occurred 5 months ago. We detected ataxia and deafness, but did not observe nuchal rigidity or meningismus. Other systems were normal. We counted 31 cells/mm^3 in the CSF (normally ≤5/mm^3). The amount of protein was 133 mg/dL (normally ≤40mg/dl), and glucose was 35 mg/dL in the CSF (normally ≥60% of that in blood). We documented bilateral SNHL with audiometry. Cranial MRI was normal. The STA test was positive at 1:80 titer in blood and was negative in CSF. Culture for Brucella spp. in CSF was positive on the third day and Brucella IgG was positive in blood and CSF. The MIC value for RIF was 0.016 µg/ml, for TE was 0.016 µg/ml, and for SM was 0.125 µg/ml with E test. We started combination therapy (DOX+RIF+CRO). The clinical improvement was minimal. We performed a BAER test to detect lesion of the eighth cranial nerve due to SNHL. (**Figure 1**). The patient did not hear any impulse given by the neurologist, which suggests a peripheral pathology in the eighth cranial nerve. We followed him for 6 months.

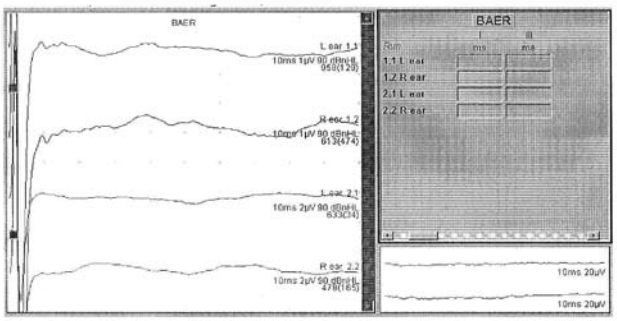

Figure 1 - Peripheric pathology of eighth cranial nerve in the third patient by brainstem auditory evoked responses test.

Discussion. Central nervous system involvement in brucellosis may be seen at every stage of the illness, even long after the convalescence phase. The clinical picture of NB progresses gradually 3 months after the occurrence of symptoms. The frequency of NB in Turkey is unknown. Some authors have reported ratios between 2.7-17.8%.[3,9,10] These different results may have arisen from difficulties in diagnosing NB, and also from geographical differences. The most common form of NB is acute or chronic meningitis. Meningoencephalitis may also be seen.[11] Cranial nerve palsy, hemiparesis, or vasculitis resembling cerebrovascular accident may be seen in chronic meningitis, in addition to the typical picture of meningeal disease.[12] So, clinicians should keep in mind that similar to tuberculosis, brucellosis may cause these manifestations. In these 3 patients, there was no neck stiffness, meningismus or alteration in consciousness, which frequently occurs in acute meningitis, however, they had been suffering from headache, deafness, and ataxia for over 6 months. Cochlea or the eighth cranial nerve may be involved in chronic meningitis. Audiometry is the first step of evaluation for hearing loss. Brainstem auditory evoked responses (BAER) or potentials (BAEP) are the most up-to-date method and help in determining the integrity of primary and secondary auditory pathways between the cochlea and the temporal lobe cortex. The BAEP is specifically performed to evaluate lesions of the eighth cranial nerve.[13] Sensorineural hearing loss was documented by audiometry in these patients, however, BAER test could only be applied to the third patient. According to the result of this test, peripheric pathology of the eighth cranial nerve was determined. There are sporadic case reports of patients with SNHL in NB in the medical literature. In 1990, Bucher et al[4] diagnosed deafness in a Turkish immigrant with severe chronic NB. Thomas et al[5] (as otologists) reported an NB patient with SNHL in 1993. They concluded, "SNHL was a relatively rare manifestation of NB, but otologists should be aware of SNHL as the sole manifestation of NB". More recently, Bodur et al[7] reported a patient

with SNHL in 2001, and Cagatay et al[8] in 2006 in Turkey. At admission, all patients had ataxia and balance defects, indicating a cerebellar syndrome in addition to SNHL. Ataxia occurring months after the beginning of their first symptoms in our 3 patients was accepted as a post-infectious cerebellar ataxia. In patients suggesting NB according to clinical features, diagnosis can be reached by the blood and CSF STA tests. In recent years, blood and CSF culture methods or detection of specific brucella IgG has become more important and valuable tests for diagnosis of brucellosis. Isolation of the responsible agent from blood or CSF samples via the BACTEC system helps to obtain results in a very short time compared with conventional methods.[14] The CSF cultures for Brucella spp. were positive in 3/13 patients in Bodur's study,[9] in 3/9 patients in Heper's study,[10] in 3/10 patients in Aygen's study,[3] and in 2/5 patients in Akdeniz's study[6] in Turkey. In these studies, culture positiveness of CSF was low, but STA tests and Brucella IgG ELISA test positiveness was much higher. We performed ELISA tests for Brucella IgG in CSF for 2 patients, and the results were positive.

Early diagnosis of brucellosis is important due to the destructive complications of a long lasting illness. Neurobrucellosis is an important complication of brucellosis and should be distinguished from other infectious diseases like tuberculosis and non-infectious diseases. Sensorineural hearing loss and cerebellar ataxia are the findings of non-specific neurological manifestations of NB.

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