Visual evoked potentials in neurobrucellosis

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ABSTRACT

Objectives: To investigate whether visual evoked potentials (VEPs) are valuable for distinguishing between brucellosis with or without neurological involvement.

Methods: A total of 23 patients who were admitted to the Department of Infectious Diseases and Microbiology, and Neurology, Ministry of Health Ankara Education and Research Hospital, Ankara, Turkey between December 2004 and August 2005 with a diagnosis of brucellosis were included in this study. After a detailed neurological and ophthalmological examination, VEPs were recorded. The P100 latencies and amplitudes were compared between the group of brucellosis (n=17) and neurobrucellosis (n=6) patients.

Results: Although there was no difference in the mean P100 latencies between the groups (n=17 for brucellosis, and n=6 for neurobrucellosis) (p=0.38), the mean P100 amplitude in patients with neurobrucellosis was significantly lower (p=0.012).

Conclusion: It could be emphasized that VEPs might reflect an underlying axonal pathology as a distinctive feature in neurobrucellosis.

Neurosciences 2008; Vol. 13 (4): 363-365

Brucellosis, a zoonosis, is prevalent in Mediterranean and Middle Eastern countries. Although neurobrucellosis is not a common manifestation of the disease, there are several neurological manifestations of the disease reported in the literature, such as meningitis, meningoencephalitis, myelitis, increased intracranial pressure, headache, demyelinating lesions of CNS or cranial and peripheral nerve involvement.1-3 Although ocular involvement is not common in brucellosis, any ocular structure may become involved.4 Uveitis, episcleritis, papilledema, and optic neuritis have been reported in brucellosis.5 It has been reported that the cranial imaging appearance reflects an inflammatory or demyelinating process, or a vascular insult, and does not always correlate with the clinical picture in neurobrucellosis.6 Visually evoked potential (VEP) is a neurophysiological method that facilitates the examination of the optic nerve and visual pathways. There are few reports on VEP testing in brucellosis in the literature, and they are limited to small numbers of cases.7,8 The aim of this study was to investigate the distinguishing value of VEP in brucellosis with or
without neurological involvement, determining optic nerve, and visual pathways.

**Methods.** This study was carried out in compliance with the Helsinki declaration. All patients gave informed consent and local ethics committee approval was obtained. Patients included were diagnosed as having brucellosis with or without neurological involvement in the Department of Infectious Diseases and Clinical Microbiology, and referred to the Department of Neurology, Ministry of Health Ankara Education and Research Hospital, Ankara, Turkey. The patient group with brucellosis consisted of 23 subjects (10 female and 13 male), aged between 16 and 70 years. The brucella diagnosis was established based on one of the following criteria: 1) isolation of Brucella spp. in blood samples, 2) a clinical presentation consistent with brucellosis in the presence of standard tube agglutination (STA) test equal to or higher than 1:160, or 3) a 4-fold increase in titers of STA. The BACTEC 9050 system had been used to culture both the blood and CSF specimens of the 23 patients, and this incubation had lasted for at least 21 days. A sero agglutination test was also carried out. Detailed neurological and ophthalmological examinations were performed for each patient. Patients who had any refraction and visual field deficits were excluded from the study. To confirm the diagnosis of neurobrucellosis, the symptoms and clinical findings consistent with neurobrucellosis including the criteria below were considered: 1) isolation of Brucella spp. from the CSF and/or demonstration of antibodies to Brucella spp. in the CSF (at any titer) in the presence of any CSF abnormalities, 2) clinical improvement with appropriate therapy. Pattern reversal VEPs were recorded using Synergy-Medelec EMG/EP equipment (Medelec Synergy, Oxford, England). Electrodes were placed at Oz (recording) and Fz (reference) points and the ground electrode was connected to the ear. Black and white, >75% contrast, only one check size (30’), full-field checkerboard pattern and 2/sec stimulation, 300 msecs in 2 mV scanning range were used. The pupils were not dilated, visual acuities were normal. Gaze fixation was provided for all the patients, during VEP recordings. Responses to 2x100 reversals were averaged for monocular recordings. The latency and peak-to-peak amplitudes of first major positive peaks (P100 waves) in each eye were measured. The P100 wave latencies and the peak amplitude values were compared between patients with and without neurological involvement of brucellosis. All recordings were performed before the treatment of brucellosis.

Statistical analysis was performed using SPSS 11.5. Mann-Whitney U test, and chi-square tests were used. *P*-values less than 0.05 were considered significant.

### Results.

A total of 17 patients with brucellosis, composed of 7 (41.2%) females and 10 (58.8%) males, and without neurological involvement, were included in this study. The mean age was 48.7±15.86 years (median 51, ranged 16-71) for patients without neurological involvement. Six patients diagnosed with neurobrucellosis, composed of 3 (50%) males and 3 (50%) females were also included in the study. The mean age of the neurobrucellosis patients was 39.16±9.9 (median 38.5, ranged 23-51). The symptoms and signs of neurobrucellosis patients were as follows; ataxia, headache, vomiting, right hemihypoesthesia, neck stiffness, confusion, fever, pyramidal sign, diplopia, tinnitus, dizziness, dysarthria, lateral gaze palsy, and papilledema (Table 1). There were no statistically significant differences between brucellosis with neurological involvement and brucellosis without neurological involvement, in terms of age (*p*=0.141) or gender (*p*=0.714). All patients had positive Rose-Bengal tests and STA tests. Brucella melitensis was isolated from the blood of 6 patients. The CSF analyses were positive in these patients. There were nonspecific periventricular white matter changes and mild ventricular enlargement in the cranial CT and/or MRs. All the patients with neurological involvement improved after therapy. We calculated the mean values

### Table 1 - Symptoms of patients with neurological involvement.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age</th>
<th>Gender</th>
<th>Symptoms and signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39</td>
<td>M</td>
<td>Fever, meningeal signs, headache, papilledema</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>M</td>
<td>Ataxia, headache, vomiting</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>F</td>
<td>Diplopia, fever, headache, right hemihypoesthesia</td>
</tr>
<tr>
<td>4</td>
<td>48</td>
<td>M</td>
<td>Confusion, neck stiffness, fever, pyramidal sign</td>
</tr>
<tr>
<td>5</td>
<td>38</td>
<td>F</td>
<td>Diplopia, tinnitus, dizziness, headache, dysarthria</td>
</tr>
<tr>
<td>6</td>
<td>36</td>
<td>F</td>
<td>Lateral gaze palsy, diplopia, papilledema</td>
</tr>
</tbody>
</table>

### Table 2 - Mean visual evoked potential (VEP) latencies and amplitudes of eyes in patients with or without neurological involvement.

<table>
<thead>
<tr>
<th>VEP latency and amplitudes value</th>
<th>Brucellosis with neurological involvement (n=12)</th>
<th>Brucellosis without neurological involvement (n=34)</th>
<th><em>P</em>-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P100 latency (msn) ± SD</td>
<td>103.25±4.05</td>
<td>101.83±6.12</td>
<td>0.380</td>
</tr>
<tr>
<td>Amplitude (µv) ± SD</td>
<td>5.95±2.06</td>
<td>7.66±1.75</td>
<td>0.012</td>
</tr>
</tbody>
</table>
of P100 latencies and amplitudes (Table 2). Although we found a slight prolongation of mean P100 latency in the neurobrucellosis, which was not statistically significant ($p=0.38$), mean P100 amplitude was significantly lower in the neurobrucellosis group ($p=0.012$).

**Discussion.** Neurobrucellosis is not a common manifestation of brucellosis (with a prevalence of 5-6.6%), and has not been reported as a specific presentation. In a group of 120 patients, it has been reported that: 0.8% meningitis and 12.5% ocular involvement were found in patients with brucellosis. Brucella cases presenting with meningitis, papilledema, CNS demyelinating lesions, permanent loss of vision and hearing, well-documented optic neuritis, optic disc edema, exudative retinal detachment, and suprasellar lesions have been described in the literature. Cranial nerve involvement in brucellosis is mostly seen in the optic, oculomotor, abducens, facial, trigeminal, and vestibulocochlear nerves. Uveitis and optic neuropathies are the most common ocular manifestations of the disease. There is also a report of an unusual presentation of neurobrucellosis in the literature, which presented with headache, vision loss, confusional state, retrobulbar neuritis, left hemiparesis, and pulmonary involvement. Another case report describes a neurobrucellosis case presenting with irreversible papillitis, ophthalmoparesis, and menigitis.

In our study, there were 17 brucella patients without neurological involvement, and 6 patients with neurobrucellosis. Patients with neurobrucellosis presented with headache, diplopia, papilledema, lateral gaze palsy, meningeal signs, and pyramidal signs, consistent with the literature. In a patient diagnosed with neurobrucellosis and presenting with optic nerve involvement, the VEP findings showed prolonged latencies and decreased amplitudes, which support an axonal and demyelinating process. It has also been reported that axonal degeneration due to inflammatory changes in the optic nerve might cause secondary optic neuropathy in brucella optic neuritis.

In most cases with conduction defects in the optic nerve, latency abnormalities accompany and very often precede amplitude abnormalities. There is little data on the application of VEP in neurobrucellosis. In the present study, although P100 latencies were slightly prolonged in neurobrucellosis, we did not find a statistically significant difference between P100 latencies of brucella patients with neurological involvement and in those without. We found a statistically significant decrease in VEP amplitudes in patients with neurological involvement although visual acuities were normal, and gaze fixations were observed during the test procedure.

We conclude that significantly decreased amplitudes of VEPs in neurobrucellosis should not be underestimated as these might reflect a distinctive axonal pathology in the disease. Our study sample was small, and we recommend further studies with larger groups of neurobrucellosis patients.

**References**