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ORIGINAL ARTICLE

Serum Viral and Toxoplasma Gondii Antibody Titers in Vestibular Neuronitis

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Objective: To evaluate patients with vestibular neuronitis serologically and to try to demonstrate that the viral infectious agents or toxoplasma gondii causes the disorder.

Materials and Methods: The study was conducted on 38 vestibular neuronitis and 30 age-matched control patients whose only health problem was headache due to rhinosinusitis and tension type headache. Serum IgM antibody levels of herpes simplex virus, varicella-zoster virus, cytomegalovirus, EB virus, adenovirus, influenza virus, parainfluenza virus, mumps virus, rubella virus, measles virus, respiratory syncytial virus, and toxoplasma gondii were measured by ELISA method. The rates of antivirus and anti–T. gondii IgM antibody positivities between the vestibular neuronitis patient group and the control group were compared by using chi-square test.

Results: Nineteen out of 38 vestibular neuronitis cases and 9 out of 30 control cases showed significant change in serum viral IgM antibody level. But there was no case which showed high serum toxoplasma gondii IgM antibody There was no statistically significant difference between the patients and the control group (p=0.157). When the viruses were compared between each other there were no statistically significant difference between the herpes simplex virus, EB virus, adenovirus, influenza virus, mumps virus, and respiratory syncytial virus (p=0.37, p=0.99, p=0.99, p=0.78, p=0.99, p=0.25, respectively).

Conclusions: Althogh viral infection of the vestibular nerve and/or labyrinth is believed to be the most common cause of vestibular neuronitis, our study showed that serological evaluation is not a useful method to identify viral agents and also it is difficult to say that toxoplasma gondii could play an important role in the aetiology of vestibular neuronitis.

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Introduction

Vestibular neuronitis is the one of the most common cause of persistent vertigo and lasts more than 24 hours. It has been thought to result from a selective viral inflammation of the vestibular nerve [1]. Unilateral signs and symptoms of vestibular hypofunction accompanies and it has been characterized by the acute onset of vertigo that gradually resolves over days. The typical complain of patients is a subacute onset of spinning vertigo over hours but occasionally symptomatic onset may occur over several minutes. The sensation of vertigo is intense and nausea and vomiting are almost always associated with vertigo. This disease is also termed neuronitis because both the labyrinth and vestibular nerve can be affected [2,3]. Vestibular neuronitis occurs commonly in middle-aged adults and about 30% of the patients had a common cold prior to the disease [4].

Epidemiologic studies support a viral cause for vestibular neuronitis, but viruses have rarely been identified in individual cases [5] Recently a 3 tesla Magnetic Resonance Imaging (MRI) study showed gadolinium enhancement of the vestibular nerve on the affected side that has been consistent with the concept of a viral and/or inflammatory aetiology [6].

The most convincing evidence of the viral cause of vestibular neuronitis is the temporal bone studies of Schuknecht and Kimura. Isolated atrophy of the vestibular nerve or parts of the vestibular nerve in four patients who reported prolonged vertigo attack suggestive of vestibular neuronitis. Besides the atrophy of vestibular nerve there were also additional atrophy in the vestibular end-organ. The atrophy of the end-organs and nerves were similar to patients with vertigo who had well documented viral disorders such as mumps and measles [7,8]. Another suspected cause of vestibular neuronitis is reactivation of herpes simplex virus type 1 in the vestibular ganglion [1,4] but this has never been demonstrated. Adenovirus infection was also reported as a cause of vestibular neuronitis [4].

Acquired toxoplasmosis can cause neurological symptoms or syndromes imitating various

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neurological or mental disorders. The most frequently described disorders are: various psychotic states, as well as dementia, depression, sleep disorders, i.e. insomnia or recurring somnolence such as in Kline-Levin syndrome, and also non-specific symptoms such as headache, vertigo, loss of appetite and energy, suspicion, irritation, emotional instability [9]. Thus, toxoplasma gondii was demonstrated as a potent pathogenetic factor in acute inner ear disturbances in laboratory animals and it was suggested as a potential risk factor in cases with sudden deafness and vertigo without obvious other cause [10].

In previous studies viral agents have been evaluated serologically but viruses have rarely been identified in individual cases. To the best of our knowledge in the literature, there is no study evaluating toxoplasma gondii in vestibular neuronitis. In this study we evaluated vestibular neuronitis patients serologically and tried to demonstrate the infectious agents caused the disorder.

Materials and Methods

In routine clinical practice, the diagnosis of vestibular neuritis mainly depends on the medical history and the clinical findings of the patients and the physical examination supports the diagnosis This study was conducted on patients describing their vertigo as a sense that they or their surroundings were spinning, increasing with head movement and lasting more than 24 hours and suffering from acute vertigo as leading complaint and accompanying spontaneous, unidirectional and horizontal nistagmus. Vertigo was associated with nausea and vomiting. All of the patients underwent a brief neurologic examination and patients who have neurologic symptoms such as weakness, vision or hearing changes, altered level of consciousness, truncal ataxia, vertical nystagmus, cranial nerve deficits or other changes in sensory and motor function favor the presence of a central cause of vertigo such as cerebrovascular disease, neoplasm, or multiple sclerosis were not included in the study. All of the participants were subjected to history taking and otoscopy, complete neurootologic examination including bedside vestibular examination, to differentiate peripheral versus central vestibular lesion, basic audiologic evaluation, and cranial magnetic resonance imaging with Gadolinium enhancement using a 1.5 Tesla system unit. Patients who have hearing loss, history of external or middle ear problems, ototoxic drug intake, previous neurologic disorders, and trauma were not included in the study. The control group was formed from attendants of headache outpatient clinic of the Department of Neurology and was composed of 30 age-matched subjects whose only health problem was headache due to tension type headache, according to the criteria of the International Headache Society [11]. The study was approved by the Local Ethics Committee of Afyon Kocatepe University and was performed in accordance with the latest version of Declaration of Helsinki. All participants gave informed consent prior to their inclusion in the study. Serum IgM antibody presence of herpes simplex virus (HSV), varicella-zoster virus (VZV), cytomegalovirus (CMV), Epstein-Barr Virus (EBV), adenovirus, influenza virus, parainfluenza virus, mumps virus, rubella virus, measles virus, respiratory syncytial virus (RSV), and Toxoplasma gondii are measured by ELISA method.

The rates of anti-virus and anti–T. gondii IgM antibody positivities between the vestibular neuronitis patient group and the control group was compared by using chi-square test.

Five milliters blood samples were obtained from all patients and healthy volunteers under sterile conditions by venipuncture. The sera were separated from whole blood shortly after collection and were stored at −20°C until the analysis. We used the ELISA method for anti-virals and anti-T.gondii IgM antibodies.

In ELISA, the appropriate antigen is bound to a solid support in microtiter wells. The specimen to be tested is added and reacts with the already present antibody. Washing then removes unbound test material, after which enzyme-linked antibody is added, which reacts with the antibody of the test material. An additional washing removes all unbound material, and finally a solution that reacts with the remaining enzyme to produce a color change is added. This change (the intensity of the color) is measured colorimetrically at 450 nm. ELISA kit provided from CHORUS commercial manufacturer. The technique was performed according to the manufacturer's instructions. The immune status ratio (ISR) value of each specimen was calculated by dividing the sample absorbance by the calibrator value based on the manufacturer’s guide, and ISR < 0.90 was interpreted as negative, ISR > 1.10 as positive, and 0.90-1.10 as doubtful. In this study, there were no equivocal samples.

Results

Nineteen out of 38 cases showed viral IgM antibody evidence in serum samples (herpes simplex virus, 4 cases; EBV, 1 case; adenovirus, 1 case; influenza virus, 9 cases; mumps virus, 1 case; and RSV, 3 cases). But there were no cases showing high serum toxoplasma gondii IgM antibody level in vestibular neuronitis cases. Six patients (15%) had preceding infections (five non-specific upper respiratory tract infections and 1 tonsillitis). Among age-matched healty control subjects, 9 out of 30 cases showed significant change in serum viral IgM antibody level (HSV, 1 case; EBV 1 case; adenovirus 1 case; influenza virus, 6 cases). None of the control cases showed high serum toxoplasma gondii IgM antibody levels. There was no significant difference between the patients and the control group (p=0.157). Comparison of the Ratios of Antiviral IgM Antibodies Between Vestibular Neuronitis and Control Groups are listed in Table 1.

Discussion

Vestibular neuronitis is the most common peripheral cause of vestibular vertigo and the diagnosis rests on three clinical diagnostic criteria: usually sudden onset of vertigo, an absence of cochlear symptoms or signs (deafness and tinnitus) and an absence of associated neurological symptoms and signs [12]. The central feature of vestibular neuronitis is sudden onset vertigo and is decribed in 73% of cases [13]. Spontaneous, unidirectional and horizontal nistagmus with the fast phase oscillations beat toward the healthy ear or positional and apparent only when gazing toward the healthy ear or during Dix-Hallpike maneuvers [5,14] accompanies the disease.

Association of vestibular neuronitis with preceding or concurrent infectious ilness occurs in between 43% [13] and 46% of cases. Most of these infections have been found to be non-secific upper respiratory tract infections, [4,9,10,15] influenza, [16,17] or focal sepsis of the upper respiratory tract such as tonsillitis, and dental sepsis [12].

In our study 6 (15%) patients had preceding infections. An infective aetiology in the development of vestibular neuronitis has long been hypothesized [12, 15,18,19] because of its association with infections and its frequent occurence [14] Shimizu et. al. were evaluated 57 cases of vestibular neuronitis for viral infection by means of serum antibody titer [18]. The viruses tested were HSV, VZV, CMV, EBV, adenovirus, influenza virus A, influenza virus B, parainfluenza virus 3, mumps virus, rubella virus and measles virus. They found significant change in 26 cases in viral antibody titer and only one case showed high HSV 1 IgM antibody level by ELISA method. Thus vestibular neuronitis in this case was assumed to have a close relation to viral infection. In another study, Hirata et. al. were evaluated 44 patients and 17 out of 36 patients showed significant change in serum antibody titers. These viruses were HSV, 2 cases, CMV, 1 case, EBV, 7 cases, rubella, 2 cases, adenovirus, 2 cases, influenza A, 1 case, influenza B, 2 cases. In these cases, infection caused by these detected viruses were assumed to play an important role in the onset of vertigo in each case [17].

In our study, we evaluated 38 vestibular neuronitis patients. The viruses tested were HSV, VZV, CMV, EBV, adenovirus, influenza virus, parainfluenza virus, mumps virus, rubella virus, measles virus, and RSV. 19 out of 38 cases showed significant IgM antibody level in serum (HSV, 4 cases; EBV, 1 case; adenovirus, 1 case; influenza virus, 9 cases; mumps virus, 1 case; and RSV, 3 cases). Also 6 (15%) of the cases had preceding infectious illness (five non-specific upper respiratory tract infections and 1 tonsillitis). When we evaluated control group, we found 9 out of 30 cases showed significant serum IgM antibody level (HSV, 1 case; EBV 1 case; adenovirus 1 case; influenza virus, 6 cases). There was no statistically significant difference in the number of antiviral IgM antibody positive subjects between the patients and the control group (p=0.157). When the

Table 1. Comparison of the Ratios of Antiviral IgM Antibodies Between Vestibular Neuronitis and Control Groups

	Vestibular Neuronitis n(%)	Control n(%)	p value
Herpes Simplex Virus	4(10.5)	1(3.3)	0.37
Ebstein Barr Virus	1(2.6)	1(3.3)	0.99
Adenovirus	1(2.6)	1(3.3)	0.99
Influenza Virus	9(23.6)	6(20)	0.78
Mumps Virus	1(2.6)	0	0.99
Respiratory Syncytial Virus	3(7.8)	0	0.25

viruses were compared between each other there were no statistically significant difference between the HSV, EBV, adenovirus, influenza virus, mumps virus, and RSV (p=0.37, p=0.99, p=0.99, p=0.78, p=0.99, p=0.25, respectively).

In the study of direct, local, hematogenous, and intracisternal infection of the guinea pig cochlea with toxoplasma gondii, three of ten directly inoculated and one of five hematogenously infected guinea pigs showed a severe labyrinthitis in electron and light microscopy. Thus, toxoplasma gondii was demonstrated as a potent pathogenetic factor in acute inner ear disturbances in laboratory animals and it was suggested as a potential risk factor in cases with sudden deafness and vertigo without obvious other cause [10]. Also vertigo was reported between the neurological disorders caused by acute toxoplasmosis [9]. To the best of our knowledge, Toxoplasma gondii was not evaluated in vestibular neuronitis patients. However, there was no significant difference between in our patients and in control group, for the evidence of anti- Toxoplasma gondii IgM antibody in serum. Thus it is difficult to assume that toxoplasma gondii could play an important role in the onset of vertigo.

Histopathologic degeneration of vestibular ganglion cells in vestibular neuronitis [7,8]; gadolinium enhancement of the vestibular nerve on the affected side in 3Tesla MRI study [6]; temporal bone studies of Schuknecht and Kimura [7-8] and the relief of vertigo with the administration of antiviral medication in vestibular neuronitis provide practical evidence of a viral neuropathy in patients with vestibular neuronitis [20]. As mentioned above, in previous serum viral antibody titer in vestibular neuronitis studies, [17-18] some viruses showed significant IgM antibody levels by ELISA. Similarly, we found significant antiviral IgM antibody levels in 19 out of 38 patients. But when we compared our results with control group there were no significant difference between the antiviral IgM antibody levels in vestibular neuronitis and control groups.

In the isolation of viruses antigen detection, polymerase chain reaction (PCR) assay, virus isolation, and serology could be used. In our study we used ELISA to identify viruses. In the literature adenovirus was also reported as a cause of vestibular neuronitis. However, it is well known that adenovirus can be excreted for prolonged periods without any symptoms [4]. Therefore the presence of the virus does not necessarily imply associated vestibular neuronitis and in our study there was no significant difference between the adenovirus IgM titers of vestibular neuronitis patients and controls group.

In conclusion, we did not find significant difference between the antibody presences of viruses or T. gondii between the vestibular neuronitis patients and controls group serologically and although viral infection of the vestibular nerve and/or labyrinth is believed to be the most common cause of vestibular neuronitis, serology does not appear to be clinically useful in the aetiological evaluation of vestibular neuronitis. Additionally, it is difficult to say that toxoplasma gondii can play a role in the aetiology of vestibular neuronitis. Obviously, like other studies, our study also has some limitations; the most important of which to our mind is the sample sizes of study and control groups. Further studies involving greater number of patients would be helpful to extend and support our findings in this study.

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