Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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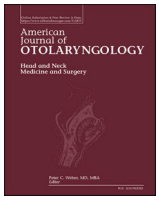

Facial paralysis as the only symptom of COVID-19: A prospective study

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ABSTRACT

Purpose: Idiopathic facial palsy is called as Bell's palsy and reports showed that facial paralysis increased during COVID-19 pandemic period. There are many reports about the relationship between COVID-19 and facial paralysis but there is no prospective study. SARS-CoV-2 IgG and IgM antibodies increase in COVID-19. Our purpose is to investigate SARS-CoV-2 IgG + IgM antibody in the Bell's palsy.

Methods: Prospective cross-sectional study was planned. Patients with acute peripheral facial paralysis with no reason and diagnosed as Bell's palsy was included in the study. In order to investigate SARS-CoV-2 in the etiologies of these patients, SARS-CoV-2 IgM + IgG (total) test was studied. SARS-CoV-2 IgG + IgM was measured by using the ADVIA Centaur® test kit. Test reports result in index values and as nonreactive or reactive. The results were analyzed.

Results: Forty-one patients were included in the study. The average age of the patients was 41,7. 17 (41,4%) were female and 24 (58,6%) were male. 21 patients had left-sided; 20 had right-sided paralysis.

SARS-CoV-2 IgG + IgM values were measured two times of the patients. First control was in the first week of facial paralysis, 10 (24,3%) positivity was found. The average index of the positive patients were 6,74 (min.1,39–max.10) in the first control and 9,585 in the second control (min.8,7–max. 10).

Conclusion: We found that the SARS-CoV-2 IgM + IgG antibody test was positive in 24.3% of the patients with Bell's palsy. The results are higher than the seroprevalence studies conducted in asymptomatic individuals. Facial paralysis could be the only symptom of COVID-19 but further studies must be done.

1. Introduction

Bell's palsy is an acute, peripheral facial nerve paresis or paralysis. The exact mechanism of Bell's palsy is not clear. Many different theories including viral infection, inflammation, ischemia, and immune disorders have been considered in the etiopathogenesis [1–4].

Numerous diagnostic tests have been used in the evaluation of the patients with Bell's palsy, including serum laboratory testing, viral serological testing, computed tomography, magnetic resonance imaging (MRI), and electrodiagnostic tests, with different diagnostic and prognostic values. Facial nerve palsy can be mostly associated with HSV (herpes simplex virus) and VZV (varicella zoster virus) infections. HIV, Lyme disease, and *Mycobacterium tuberculosis* infections can also be related to facial paralysis. Non-infectious reasons like sarcoidosis and neoplasms can cause facial paralysis. Neurotropic viruses, for example HSV and VZV, are thought to be related to neural spread and viral replication by causing inflammation and demyelination of the facial nerve [5–9].

Neurologic symptoms in COVID-19 is an up-to-date issue and various case studies are published in this regard. It is known that coronaviruses have neuroinvasive propensity and COVID-19 may present neurological symptoms [10].

Acute facial paralysis is considered as one of the neurological symptoms of COVID-19; [11–13] however, there is no study about this subject.

SARS-CoV-2 IgM can be detected from the blood samples of COVID-19 patients after 5 days of symptom onset, lasts for 1 month and then gradually decreases. The median duration of SARS-CoV-2 IgG antibody detection is 14 days. It is suggested that SARS-CoV-2 IgM and IgG was helpful for the diagnosis of COVID-19 after the corresponding window periods [14,15].

In the present study, SARS-CoV-2 IgG + IgM antibody was investigated in patients with acute facial paralysis, who were considered to be diagnosed as Bell's palsy during the pandemic period.

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2. Material and methods

A prospective cross-sectional study was planned. Forty-one patients with Bell's palsy, who had acute facial paralysis during the pandemic period but no reason could be found as a result of etiologic studies, were included in the study. All the patients included in the study applied to our clinic with acute facial paralysis complaint; detailed anamnesis, ear nose throat examination, neurological evaluation, complete blood count, biochemical blood tests, viral serologies (especially HSV, HIV, VZV), and cranial and temporal MRI were applied as a routine process in order to investigate the etiology of facial paralysis. The patients, who completed these tests, but no etiologic reason could be found, were diagnosed as Bell's palsy and 1 mg/kg/day prednisone treatment was started. All of the patients had the same therapeutic protocol, which included prednisone 1 mg/kg/day, tapered and stopped in two weeks.

These patients were called for routine controls for facial paralysis. In order to investigate SARS-CoV-2 in the etiologies of these patients, who were followed up for Bell's palsy, SARS-CoV-2 IgM + IgG (total) test was done during the first week of facial paralysis. After the first control; patients were called for second control after 14 days.

This test is applied for the determination of immune response to SARS-CoV-2 virus and antibodies that develop against the virus in the human serum and plasma during and after COVID-19 infection related to SARS-CoV-2.

The patients included in the study were those, who were followed up for Bell's palsy and who did not have any COVID-19 symptoms thus no PCR test was applied. The patients who were previously infected by COVID-19 were not included in the study. Also, while investigating the etiology of acute facial paralysis, patients who had a cause, for whom 10 days passed after facial paralysis were not included in the study.

2.1. Laboratory

SARS-CoV-2 IgG + IgM (total) was measured by using the ADVIA Centaur® test kit (Siemens Healthcare Diagnostics Inc). The test is a chemiluminescent immunoassay intended for qualitative detection of total antibodies (including IgG and IgM) to SARS-CoV-2 in human serum and plasma. The system reports result in index values and as nonreactive or reactive.

Nonreactive is accepted as lower than 1.0 Index. These samples are considered negative for SARS-CoV-2 antibodies. Reactive is accepted as higher than and equal to 1.0 Index. These samples are considered positive for SARS-CoV-2 antibodies. Higher than 10 index value considered as 10 by the laboratory.

2.2. Statistical analysis

Data were analyzed by using the SPSS version 21.0 software program (Statistical Package for Social Sciences v.21, IBM, Chicago, IL). Descriptive statistics were done for the analysis.

2.3. Ethical consideration

Because this research includes human subjects, ethical approval was taken from the Ministry of Health and the local ethical committee. All patients were informed about the study and informed consent was obtained.

3. Results

Forty-one patients were included in the study. The average age of the patients was 41,7. Of them, 17 (41,4%) were female and 24 (58,6%) were male. 21 patients had left-sided; 20 had right-sided paralysis. The etiology causing paralysis could not be found in any of the patients and they were followed up with the diagnosis of Bell's palsy.

First control was done during the first week of the facial paralysis complaint. 24,3% (10 patients) was found positive for SARS-CoV-2 IgG + IgM. The average index of the positive patients were 6,74 (min.1,39–max.10) in the first control. SARS-CoV-2 PCR was done to the antibody positive patients and all PCR's was found negative. The patients again questioned about COVID-19 classic symptoms. None had any symptoms. Their e-government codes were checked for positive COVID-19 history or direct contact to COVID-19 patient but the patients had no history. Both 41 patients had risky residential home address for COVID-19 according to e-government system. Second control for the study was done 14 days after the first control. SARS-CoV-2 IgG + IgM was found negative again in the negative patients. 10 patient was found positive again. The average index of the positive patients were 9585 (min.8,7–max.10). (Table 1.)

Among 41 patients 2 patients could not have the MRI due to claustrophobia. One had a metal foreign body due to a history of a traffic accident and could not have the MRI. Other patients all had MRI and 28 had facial nerve enhancement. Ten had normal MRI findings. Of patients who had positive SARS-CoV-2 antibodies 70% had facial enhancement in the MRI scan; 20% had normal and 10% had no MRI scan. Patients who had negative SARS-CoV-2 antibodies 67,7% had facial enhancement in the MRI scan. 25,8% had normal and 6,5% had no MRI scan.

4. Discussion

The results of the present study have indicated that the SARS-CoV-2 IgG + IgM test was positive in 24.3% of patients with Bell's palsy. In addition, these patients had no history of any COVID-19 symptoms like fever, cough, sore throat, or shortness of breath in their personal history.

Acute facial nerve paresis or paralysis that appears in less than 72 h without any reason is called Bell's palsy [9]. Neural ischemia, autoimmune diseases, and viral inflammation of the facial nerve paralysis are found to be responsible, but the etiology is unclear [16].

Many studies have been conducted to find out the etiology. Rheumatologic mechanisms occurring after a common cold has been found to be responsible. Embolus or vasospasm in vasa nervorum of the seventh cranial nerve may cause Bell's palsy. Other factors in the etiology are viral inflammation and edema in the nerves [4,17–19].

COVID-19 is a complex disease that aggravates rheumatologic mechanisms, thrombus, and embolus [20,21]. In addition, it is a viral disease that can cause viral inflammation [22].

Studies have been published regarding the increased peripheric acute facial paralysis during COVID-19 pandemic. Direct viral neurophism or immune-mediated mechanism secondary to increased proinflammatory cytokines may cause facial paralysis in COVID-19 [11–13,23–25].

Except for some reports there is no controlled study about COVID-19 and facial paralysis.

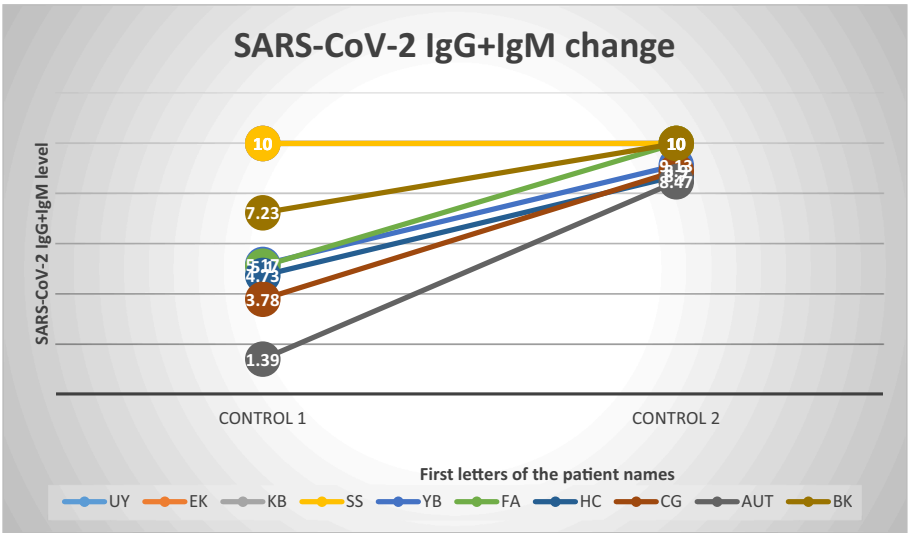
It was suggested that neurotropic viruses like herpesviruses have a relation with facial paralysis and SARS-CoV-2 is known as a neurotropic virus [26].

The frequency of taste and smell alterations are ranging from 19.4% to 88% among COVID-19 patients. The exact pathogenesis of these chemosensitive disorders has not yet been clarified but the neurological invasion is one of the potential pathogenesis reason [27–30].

It has been reported that up to 36.4% of COVID-19 patients have developed neurologic manifestations like Guillain-Barre syndrome, encephalopathy, and strokes. Cases of facial paralysis lead us to investigate the patients with Bell's palsy during the pandemic and a strong relation is found between facial paralysis and COVID-19 [31–34].

Host cell entry receptor of the SARS-CoV-2 is the angiotensin-converting enzyme 2 (ACE2). ACE2 receptors in the neurons and glial cells make the nervous system a potential target; however, the mechanism is unknown. SARS-CoV-2 may access to the blood circulation, reach cranial circulation, and spread to the nerves. Another possible route is specified by invading the olfactory nerves and retrogradely transferring into the nervous system. On the other hand, SARS-CoV-2

Table 1
Changes of SARS-CoV-2 IgG + IgM levels of the patients.



may trigger an immune response which can damage the neuronal tissues [35–39].

Asymptomatic individuals from the randomly selected sample participated in a Spanish study investigated COVID-19 IgG and/or IgM and the prevalence was found as 5.47% [40]. The seroprevalence of SARS-CoV-2 IgG and/or IgM antibody in asymptomatic individuals was found to be 2.39% in Wuhan [41]. The highest prevalence of SARS-CoV-2 antibodies in the literature was found among asymptomatic people in Sergipe, Brazil. SARS-CoV-2 IgG was found as 8.3% and as 11.9% for IgM [42].

In a study from Turkey about seroprevalence among health care workers was preprinted. SARS-CoV-2 IgG was found in 6% among cleaning staff, 4% among physicians, 2,2% among nurses and 1% among radiology technician [43].

In the current study, it was found that SARS-CoV-2 IgM + IgG antibody test was positive in 24.3% of the patients with Bell's palsy. The results are higher than the seroprevalence studies conducted in asymptomatic individuals.

Among the limitations of the study, the limited number of patients and the lack of SARS-CoV-2 PCR test on the first admission to the hospital of the patients could be considered. However, these patients had no complaints except facial paralysis. PCR test was conducted in our patient group, who had positive SARS-CoV-2 IgG + IgM after the antibody test and all were found to be negative. Another limitation is not analyzed SARS-CoV-2 IgG and IgM separately but in our center we had no facility.

5. Conclusion

In our study we found that facial paralysis could be the only symptom of COVID-19 but further studies with larger patients groups must be done. PCR test on the first admission of the patients could be done to clarify the etiology. Also SARS-CoV-2 antibody test for measuring IgG and IgM separately could be done.

Financial support

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Data availability

Data is available on request from corresponding author.

Ethical statement

Ethical approval was taken from the Ministry of Health and the local ethical committee (protocol: 2020-10-14T00_45_49).

Consent about participate and publication

All patients were informed about the study and informed consent was obtained.

CRediT authorship contribution statement

All authors declare that they all meet the author criteria.

Declaration of competing interest

No conflict of interest.

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No.

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