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Research

Comparison of Facial Palsy Cases before and during the Pandemic Coronavirus Disease-2019

Koronavirüs Hastalığı-2019 Pandemisi Öncesi ve Sırasında Fasiyal Paralizi Olgularının Karşılaştırılması

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ABSTRACT

Objective: The pandemic coronavirus disease-2019 (COVID-19) is caused by a novel type of coronavirus named severe acute respiratory syndrome coronavirus-2 and is rapidly spreading all over the world. In addition to various neurological symptoms, acute facial palsy was diagnosed as the main neurological symptom in some COVID-19 patients. The current study aimed to analyze the variation and any possible association in the case numbers or medical symptoms of patients with facial palsy before and during the COVID-19 pandemic.

Methods: The clinical files of patients who were diagnosed with facial palsy in the Neurology Department of Medicalpoint Hospital, University of Economics Faculty of Medicine, İzmir were retrospectively investigated. To compare the facial palsy cases according to different periods, two patient groups were formed: before the COVID-19 pandemic and during the COVID-19 pandemic. The pandemic group was further divided into two subgroups as COVID-19-positive and COVID-19-negative patients to compare the effects of COVID-19 on facial palsy.

Results: During the specified COVID-19 period (May 2020-January 2021) of the study, 38 patients were admitted to the hospital for facial palsy; 34 facial palsy patients were admitted in the same calendar period as the two previous years (May 2018-January 2019). There was no significant difference in the frequency of facial palsy between these two time periods. There were significant differences between before and during the COVID-19 pandemic groups regarding response to cortisone therapy (p<0.001), facial palsy grade (p<0.001), electromyography findings (p=0.005), denervation (p<0.001), and 6 months recovery (p<0.001) data. There were also significant differences between the COVID-19-positive and COVID-19-negative subgroups regarding response to cortisone therapy (p=0.015) and facial palsy grade (p=0.001).

Conclusion: The current study findings support the possible association between the severity of the clinical course of facial palsy and COVID-19. Further studies are needed to prove a direct association between facial palsy and COVID-19.

Keywords: Severe acute respiratory syndrome, facial palsy, electromyography, COVID-19 pandemic, SARS-CoV-2, neurologic symptoms

ÖZ

Amaç: Koronavirüs hastalığı-2019 (COVİD-19) pandemisi, şiddetli akut solunum sendromu koronavirüs-2 adı verilen yeni bir koronavirüs türünden kaynaklıdır ve hızla tüm dünyaya yayılmıştır. Çeşitli nörolojik semptomlara ek olarak, COVİD-19 hastalarında bazı olgularda ana nörolojik semptom olarak akut fasiyal paralizi tanısı konulmuştur. Bu çalışma, COVİD-19 pandemisi öncesi ve sırasında fasiyal paralizi olan hastaların olgu sayılarındaki veya tıbbi semptomlarındaki varyasyonları ve olası ilişkileri analiz etmeyi amaçlamıştır.

Metot: Medicalpoint Hastanesi Nöroloji Kliniği, Ekonomi Üniversitesi Tıp Fakültesi, İzmir'de fasiyal paralizi tanısı alan hastaların klinik dosyaları retrospektif olarak incelenmiştir. Fasiyal paralizi olgularını farklı dönemlere göre karşılaştırmak için COVİD-19 pandemisinden önce ve COVİD-19 pandemisi sırasında olmak üzere iki hasta grubu oluşturulmuştur. İkinci grup (COVİD-19 pandemi sürecindeki grup), COVİD-19'un fasiyal paralizi üzerindeki etkilerini karşılaştırmak için COVİD-19 pozitif ve COVİD-19 negatif hastalar olarak iki alt gruba ayrılmıştır.

Bulgular: Çalışmanın belirlenen COVİD-19 döneminde (Mayıs 2020-Ocak 2021) 38 hasta fasiyal paralizi için hastaneye başvurmuştur; önceki iki yılın aynı takvim döneminde (Mayıs 2018-Ocak 2019) ise 34 fasiyal paralizi hastası başvurmuştur. Bu iki dönem arasında fasiyal paralizi görülme sıklığında anlamlı bir fark saptanmamıştır. Çalışma grupları (COVİD-19 pandemisi öncesi ve COVİD-19 pandemisi sırasında) arasında kortizon tedavisine yanıt (p<0,001), fasiyal paralizi derecesi (p<0,001), elektromiyografi bulguları (p=0,005), sinir blokajı (denervasyon) (p<0,001) ve 6 aylık iyileşme (p<0,001) verileri açısından anlamlı farklılıklar bulunmuştur. Ayrıca COVİD-19 pozitif ve COVİD-19 negatif alt gruplar arasında kortizon tedavisine yanıt (p=0,015) ve fasiyal paralizi derecesi (p=0,001) bakımından anlamlı farklılıklar saptanmıştır.

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Sonuç: Mevcut çalışma bulguları, fasiyal paralizinin klinik seyrinin şiddeti ile COVİD-19 arasındaki olası ilişkiyi desteklemektedir. Fasiyal paralizi ve COVİD-19 arasında doğrudan bir ilişki olduğunu kanıtlamak için daha ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Şiddetli akut solunum sendromu, fasiyal paralizi, elektromiyografi, COVİD-19 pandemisi, SARS-CoV-2, nörolojik semptomlar

INTRODUCTION

The pandemic coronavirus disease-2019 (COVID-19) is caused by a novel type of coronavirus named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and has rapidly spread all over the world since its first report in December 2019 in China (1). This virus primarily affects the respiratory system but can penetrate many other organs of the body. Neurological system symptoms are generally the first indication of the disease or they accompany respiratory abnormalities and include headaches, hyposmia, dizziness, confusion, cerebrovascular diseases, and encephalopathies (2). In addition to these neurological symptoms, acute facial palsy was diagnosed in COVID-19 patients as the main neurological symptom in some of the cases and was observed as unilateral or bilateral and idiopathic (Bell's palsy) (3,4). This condition has also been reported in children (5) and pregnant women (6). Facial palsy implies lower motor neuron failure of the facial nerve and can occur because of various medical conditions and events such as trauma, malignancy, autoimmune disorders, vaccination, surgery, and viral infections just as in the COVID-19 cases (7,8). Although the exact pathogenesis of viral infection-related facial palsy is still unclear, it is suggested to be associated with axonal transmission and viral reproduction leading to inflammation and demyelination (9). Some physicians noticed that facial nerve palsy cases increased after the COVID-19 pandemic compared to previous years and consistently reported literature increased recently; however, broad analysis and further research are required to reveal the exact interaction between them (2,10).

The current study aimed to analyze the variation and any possible association in the case numbers or medical symptoms of patients with facial palsy before and during the COVID-19 pandemic.

METHODS

The clinical files of patients who were diagnosed with facial palsy in the Neurology Department of Medicalpoint Hospital, University of Economics Faculty of Medicine, İzmir were retrospectively investigated. To compare the facial palsy cases according to different periods, two patient groups were formed: before the COVID-19 pandemic and during the COVID-19 pandemic. Before the COVID-19 pandemic group consisted of 34 facial palsy patients (collected data from hospital visits only between May 2018-January 2019) and during the COVID-19 pandemic group consisted of 38 facial palsy patients (collected data from hospital visits only between May 2020-January 2021). The pandemic group was further divided into two subgroups as COVID-19-positive and COVID-19-negative patients, and only cases with confirmatory tests (SARS-CoV-2 reverse transcriptase-polymerase chain reaction test) at first admission were included. Patients with inadequate clinical data or who could not be followed up for 6 months after diagnosis were excluded. In these groups, patients were compared concerning their demographic data (age and sex) and several clinical features [pregnancy, having diabetes mellitus (DM), presence of an autoimmune disease, presence of any other comorbidity, immunosuppressive therapy, corticosteroid therapy, facial palsy side and grade, electromyography (EMG) recordings, denervation, and recovery level on the control visit after 6 months]. Electrophysiological studies were conducted using the Nihon Kohden (Japan) MEB-9400K Neuropack S1 EMG/EP measuring system. Facial palsy was graded using the House-Brackmann scale (11). The study was approved by the Non-Interventional Clinical Research Ethics Committee of İzmir Bakırçay University (decision no: 634, date: 15.06.2022). All patients provided written informed consent. The research process is in accordance with the ethical standards of the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed using PASW Statistics for Windows, Version 18.0. (SPSS Inc., Chicago, IL, USA). A p-value of <0.05 was set as statistically significant. The descriptive statistical data were expressed as numbers and percentiles for categorical variables and as mean, standard deviation, median, and minimum-maximum (range) for numerical variables. The normal distributions of variables were tested by visual (histograms and probability graphics) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk) test methods. For categorical variables, in two group comparisons, the Pearson chi-square test was used when applicable (expected value >5) and when not, Fisher's Exact test was used, and for ordinal variables, the Mantel-Haenszel test was used. For numerical variables in two group comparisons, the Mann-Whitney U test was used when data were not normally distributed.

RESULTS

During the specified COVID-19 period (May 2020-January 2021) of the study, 38 patients accessed the hospital for facial palsy (median age 37.0 years, range 22-60 years) and 34 facial palsy patients (median age 38.5 years, range 26-61 years) were found in the same calendar period of two previous years (May 2018-January 2019). There was no significant difference in facial palsy incidence between these two time periods. Pregnancy was in only two (9.5%) patients in the during COVID-19 group and in one (6.3%) patient in the before COVID-19 group.

Demographic data and clinical features and the comparison of these parameters between the two groups (during COVID-19 and before COVID-19) are summarized in Table 1. According to the data, there were no significant differences between these two groups regarding sex (p=0.487), age (p=0.433), facial palsy side (p=0.718), presence of comorbidity (except DM and autoimmune disease) (p=0.649), presence of DM (p=0.898), presence of autoimmune disease (p=0.463), receiving immunosuppressive therapy (p=0.599), and receiving steroid therapy (p=0.063). On the other hand, there were significant differences between the two groups regarding response to cortisone therapy (p<0.001), facial palsy grade (p<0.001), EMG findings (p=0.005), denervation (p<0.001), and 6 months recovery (p<0.001) data. In terms of cortisone therapy, in the during COVID-19 group, the full response ratio was 13.2%; partial response ratio was 52.6%; non-response ratio was 15.8%, and 18.4% of the patients did not receive the therapy, and in the before COVID-19 group, these values were 70.6%; 20.6%; 2.9%; and 5.9%, respectively. In terms of facial palsy grade, in the during COVID-19 group, mild grade ratio was 10.5%; moderate grade ratio was 39.5%; moderately severe grade ratio was 28.9%; severe grade ratio was 18.4%, and total paralysis ratio was 2.6%, and in the before COVID-19 group, these values were 52.9%; 35.3%; 8.8%; 2.9%, and 0%, respectively. In terms of EMG recordings, in the during COVID-19 group, the ratio of axonal findings was 31.6%; the ratio of demyelinating findings was 10.5%, and the ratio of mixed patterns was 57.9%, and in the before COVID-19 group, these values were 64.7%; 14.7%; and 20.6%, respectively. The denervation ratio of the patients in the during COVID-19 group was 78.9%, whereas this ratio was 38.2% in the before COVID-19 group. In terms of 6 months recovery, in the during COVID-19 group, the full recovery ratio was 28.9%; partial recovery ratio was 63.2%, and non-recovery ratio was 7.9%, and in the before COVID-19 group, these values were 88.2%; 11.8%; and 0%, respectively.

Table 2 shows the comparison of demographic and clinical data between the COVID-19-positive and COVID-19-negative subgroups within the COVID-19 group. Accordingly, of 38 patients, 9 were COVID-19-positive (2 of them were diagnosed at the admission to the hospital for facial palsy and 7 of them had COVID-19 before) and 29 were COVID-19-negative. The results were similar in these two subgroups regarding sex (p=0.984), age (p=0.345), facial palsy side (p=0.634), presence of comorbidity (except DM and autoimmune disease) (p=0.578), presence of DM (p=0.559), presence of autoimmune disease (p=0.134), receiving immunosuppressive therapy (p=0.237), receiving steroid therapy (p=0.650), EMG findings (p=0.055), denervation rate (p=0.650) and 6 months recovery rate (p=0.056). However, there were significant differences between the two subgroups regarding response to cortisone therapy (p=0.015) and facial palsy grade (p=0.001). In terms of cortisone therapy, in the COVID-19-positive subgroup, the full response ratio was 11.1%; partial response ratio was 33.3%; non-response ratio was 55.6%, and none of the patients received the therapy, and in the COVID-19-negative subgroup, these values were 13.8%; 58.6%; 3.4%; and 24.1%, respectively. In terms of facial palsy grade, COVID-19-positive subgroup, mild grade ratio was 10.5%; moderate grade ratio was 39.5%; moderately severe grade ratio was 28.9%; severe grade ratio was 18.4%, and total paralysis ratio was 2.6%, and in the COVID-19-negative subgroup, these values were 13.8%; 48.3%; 27.6%; 10.3%, and 0%, respectively.

DISCUSSION

The comparison of the clinical results revealed that the cases during the COVID-19 period had a significantly lower response to cortisone therapy, worse facial palsy grades, higher denervation ratios (almost 2-folds), worse EMG findings with a higher mixed pattern, and worse 6 months recovery than those before the COVID-19 period. Consistently, in the subgroup comparisons, significantly lower response to cortisone therapy and worse facial palsy levels were seen in COVID-19-positive patients than in COVID-19-negative patients; however, denervation, EMG findings, and 6 months recovery data were similar. These findings may support the association between facial palsy and COVID-19, especially from the aspect of the clinical course of facial palsy. On the other hand, the current study showed that the number of peripheral facial paralysis cases during the COVID-19 pandemic was similar to previous years' data from the same center. This result is in line with other similar studies where no significant difference was

Table 1. Demographic and clinical characteristics of the two patient groups: during the COVID-19 pandemic and before the COVID-19 pandemic

	During COVID-19 n=38	Before COVID-19 n=34	p
Sex, n (%)			
Female	21 (55.3)	16 (47.1)	0.487*
Male	17 (44.7)	18 (52.9)	
Age, median (range)	37.0 (22-60)	38.5 (26-61)	0.433**
Facial palsy side, n (%)			
Left	18 (47.4)	18 (52.9)	
Right	19 (50.0)	16 (47.1)	0.718*
Bilateral	1 (2.6)	0 (0.0)	
Comorbidity (except DM and autoimmune disease), n (%)	2 (5.3)	2 (5.9)	0.649†
DM, n (%)	6 (15.8)	5 (14.7)	0.898*
Autoimmune disease, n (%)	3 (7.9)	5 (14.7)	0.463†
Immunosuppressant therapy, n (%)	1 (2.6)	2 (5.9)	0.599†
Steroid therapy, n (%)	30 (78.9)	32 (94.1)	0.063*
Cortisone therapy response, n (%)			
Total	5 (13.2)	24 (70.6)	
Partial	20 (52.6)	7 (20.6)	<0.001‡
Non-response	6 (15.8)	1 (2.9)	
Not-received	7 (18.4)	2 (5.9)	
Facial palsy grade, n (%)			
Mild	4 (10.5)	18 (52.9)	
Moderate	15 (39.5)	12 (35.3)	
Moderate severe	11 (28.9)	3 (8.8)	<0.001‡
Severe	7 (18.4)	1 (2.9)	
Total paralysis	1 (2.6)	0 (0.0)	
EMG, n (%)			
Axonal	12 (31.6)	22 (64.7)	
Demyelinating	4 (10.5)	5 (14.7)	0.005*
Mixed	22 (57.9)	7 (20.6)	
Denervation, n (%)	30 (78.9)	13 (38.2)	<0.001*
6-months recovery, n (%)			
Full	11 (28.9)	30 (88.2)	
Partial	24 (63.2)	4 (11.8)	<0.001‡
Non-recovery	3 (7.9)	0 (0.0)	

COVID-19: Coronavirus disease-2019, DM: Diabetes mellitus, EMG: Electromyography
*Pearson chi-square test, **Mann-Whitney U test, †Fisher's Exact test, ‡Mantel-Haenszel test

Table 2. Demographic and clinical characteristics of the two patient subgroups during the COVID-19 pandemic as COVID-19 positive and COVID-19 negative

	COVID-19 positive n=9	COVID-19 negative n=29	p
Sex, n (%)			
Female	5 (55.6)	16 (55.2)	0.984*
Male	4 (44.4)	13 (44.8)	
Age, median (range)	41.0 (23-51)	35.0 (22-60)	0.345**
Facial palsy side, n (%)			
Left	5 (55.6)	13 (44.8)	
Right	4 (44.4)	15 (51.7)	0.634*
Bilateral	0 (0.0)	1 (3.4)	
Comorbidity (except DM and autoimmune disease), n (%)	0 (0.0)	2 (5.3)	0.578†
DM, n (%)	1 (11.1)	5 (17.2)	0.559†
Autoimmune disease, n (%)	2 (22.2)	1 (3.4)	0.134†
Immunosuppressant therapy, n (%)	1 (11.1)	0 (0.0)	0.237†
Steroid therapy, n (%)	8 (88.9)	22 (75.9)	0.650†
Cortisone therapy response, n (%)			
Total	1 (11.1)	4 (13.8)	
Partial	3 (33.3)	17 (58.6)	
Non-response	5 (55.6)	1 (3.4)	0.015‡
Not-received	0 (0.0)	7 (24.1)	
Facial palsy grade, n (%)			
Mild	0 (0.0)	4 (13.8)	
Moderate	1 (11.1)	14 (48.3)	
Moderate severe	3 (33.3)	8 (27.6)	0.001‡
Severe	4 (44.4)	3 (10.3)	
Total paralysis	1 (11.1)	0 (0.0)	
EMG, n (%)			
Axonal	1 (11.1)	11 (37.9)	
Demyelinating	0 (0.0)	4 (13.8)	0.055*
Mixed	8 (88.9)	14 (48.3)	
Denervation, n (%)	8 (88.9)	22 (75.9)	0.650†
6-months recovery, n (%)			
Full	1 (11.1)	10 (34.5)	
Partial	6 (66.7)	18 (62.1)	0.056‡
Non-recovery	2 (22.2)	1 (3.4)	

COVID-19: Coronavirus disease-2019, DM: Diabetes mellitus, EMG: Electromyography *Pearson chi-square test, **Mann-Whitney U test, †Fisher's Exact test, ‡Mantel-Haenszel test

found in the occurrence of the cases between the pandemic period and previous years (10,12). In contrast, Codeluppi et al. (4) reported higher incidence rates of facial palsy in the pandemic period compared with the previous year. There are a few studies on the effect of COVID-19 on facial palsy incidence comparisons, and further analyses with more comprehensive and wider samples could help to clarify any possible significant variation.

In the current study, facial palsy was the first clinical symptom of COVID-19 in 2 of 9 COVID-19-positive patients. Similarly, in another study from Türkiye, 5 of 8 COVID-19 patients (9) and in a case study, 3 of 8 patients had facial palsy as the first symptom (12). Several studies have reported facial palsy as the initial symptom of COVID-19, which have been presented in detail in literature reviews (2,3). In addition, several studies have demonstrated facial palsy as the only main symptom of COVID-19 (3,13). Furthermore, in a cohort study in Singapore, facial neuropathy was found to be the most common (71.4%) COVID-associated mononeuropathy (14). These results support the suggestion that facial palsy should be added to the COVID-19-associated neurological manifestations as a nonspecific symptom (10,12).

Neurological issues in COVID-19 are unfolding as one of the most prominent clinical outcomes of this pandemic (8,9). The most common are anosmia/ageusia, encephalitis, encephalopathy, cerebrovascular complications, myelitis, Guillain-Barré syndrome, myalgia, and facial palsy/Belly's palsy (3,12). Although there are several approaches to the possible effects of SARS-CoV-2 on the nervous system, the exact mechanism remains unclear. These approaches can be classified as hypoxia, angiotensin-converting enzyme 2 receptor downregulation, immune injury, or direct involvement via infection, and by these ways, SARS-CoV-2 can induce cytokine storms (2,15). Meticulous clinical, diagnostic and epidemiological research is required to identify the neurological disorder manifestations of COVID-19 (16). Potential mechanisms suggested for nerve damage in facial palsy include vasa nervorum ischemia and demyelination induced by viral replication and inflammation (12,17). Microthrombi and other vascular changes, through viral damage or an autoimmune reaction, may also be contributing mechanisms to dysfunction (12).

The clinical findings of facial palsy in the current study suggested a highly noticeable worse outcome when occurred in the COVID-19 period compared to a previous period for the clinical parameters stated above. Even though the parameters with significant differences were less in the subgroup comparisons, the two parameters were

still significantly worse in COVID-19-positive patients than in COVID-19-negative, reflecting the association between facial palsy and COVID-19. These alterations may be due to patients who were deemed COVID-19-negative but had previously had asymptomatic COVID-19. fears during a pandemic lead individuals to delay or avoid accessing hospitals, even for COVID-19 tests. In another comparison study, although it was reported that higher incidence rates of facial palsy were found during the pandemic period, the evaluated clinical results were similar between the pandemic group and the previous year In a case study with 8 COVID-19-positive patients with facial palsy, complete recovery was observed in 5 patients, and the facial palsy grades were mild for 5 and moderate for 3 patients (12). In the current study, the ratio of mild grade facial palsy in the before COVID-19 group (52.9%) was significantly higher than that in the during COVID-19 group (10.5%), whereas there was a slight difference in moderate grade facial palsy ratios between these two groups (35,3% and 39.5%, respectively). In addition, the complete recovery ratio in the before COVID-19 group (88.2%) was significantly higher than that in the during COVID-19 group (28.9%). In parallel, in another study from Türkiye, the complete recovery rate was reported to be 37.5% in COVID-19-positive patients with facial palsy (9). Furthermore, in subgroup comparisons of the present study, the overall complete recovery ratio was quite low (28.9%), which may support the negative clinical effects of COVID-19 on facial palsy.

As far as it is concerned, this is the first facial palsy comparison study for COVID-19 that includes not only data from different periods but also detailed clinical data including information such as EMG findings and denervation. Few works of literature restrict the exact comparison of all the current findings. Other limitations are the small sample size and performing the study in only one center.

CONCLUSION

The recent literature reveals that SARS-CoV-2 can cause several neurological symptoms and disorders, and facial palsy seems to be one of these issues. The current study findings support the possible association between the severity of the clinical course of facial palsy and COVID-19. Large-scale and postmortem studies are needed to prove a direct association between facial palsy and COVID-19.

ETHICS

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