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Covid-19 and Bell Palsy: Could it Be Neurotrophic Involvement?

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ABSTRACT

Objective: Idiopathic cases are common, and the etiology is not clearly explained. The purpose of this study is to compare the frequency, clinical-radiological characteristics and response to the treatment of peripheral facial paralysis patients who visited the otorhinolaryngology clinic during the Covid-19 pandemic and in the same period of the previous year, and to discuss this data in the light of the literature.
Materials and Methods: Otoscopic examination findings, audiological results, application and post-healing grade information according to House Brackmann Staging system were obtained from all the patients' files. Temporal Bone Computed Tomography, which is included in the routine practice of our clinic, and Cranial & Diffusion Magnetic Resonance Imaging examinations for the elimination of central causes were applied to the patients. Facial nerve tympanic, mastoid, labyrinth segment and geniculate ganglion diameters were measured separately for the diseased side and the healthy side.
Results: In the study, Group 1 consisted of 42 patients (43%), and Group 2 consisted of 56 patients (57%). 56 (57%) of the patients were male and 42 (43%) were female. The left and right-side facial paralysis admissions were equal, but no statistically significant difference was found (p=0.068).
Conclusions: Peripheral facial paralysis is a very common case in ear, nose, and throat practice and requires priority treatment and follow-up. Since the Covid-19 virus is a new entity for the world, we think that it has a neurotrophic affinity for the facial nerve although our knowledge about this virus is limited.

Keywords: Bell palsy, COVID-19, facial nerve, radiology, steroids

INTRODUCTION

Peripheral facial paralysis (PFP) is a self-limiting disease that starts suddenly and often causes a unilateral inability to control the voluntary movement of facial muscles. Idiopathic cases are common, and the etiology is not clearly explained. Anatomical, immune, inflammatory, and ischemic mechanisms are among the most frequently emphasized reasons. In Magnetic Resonance Imaging (MRI) studies, it was reported that the facial nerve showed increased gadolinium uptake near the labyrinthine segment and geniculate ganglion during the acute phase of PFP (1,2). In addition, in histopathological and electron microscopic studies, an inflammatory reaction showing more lymphocyte infiltration, demyelination, and axonal degeneration was found in the intratemporal facial nerve (FN) in patients with acute-onset PFP (3,4). All these studies suggested that the intratemporal facial nerve was stuck in the narrow bone canal of the FN due to inflammation and edema, and as a result, it caused paralysis in the facial muscles. In addition, some studies have shown that herpes simplex virus (HSV) reactivation plays a role in the development of PFP by causing cell infiltration and demyelination through neural inflammation. For example, Bell's Palsy (BP) demonstrated HSV genomic DNA in the facial nerve of patients by polymerase chain reaction (PCR) (5,6). In animal studies, it was shown that they developed acute transient facial paralysis as a

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result of HSV inoculation into the tongue and auricles of mice, and diffuse inflammatory edema, and HSV was found in the histopathological examination of the facial nerve of these animals. It has been reported that this edema is mostly concentrated in the geniculate ganglion region (7-9).

The coronavirus outbreak that started in Wuhan province of China in December 2019 spread all over the world and created a serious pandemic. The clinical picture in Covid-19 patients constitutes a wide spectrum ranging from asymptomatic disease to multiorgan failure. Although the most prominent otorhinolaryngologic symptoms of the disease are taste and smell disorders, PFP cases have also been frequently reported. Codeluppi et al. reported that they observed more PFP cases in the emergency department in the first phase of the Covid-19 pandemic during February-May 2020 than during the same period of the previous year (7.1 and 4.1 per 100,000, respectively) and that the average age of these patients was reported to be lower than the actual one (10). Brisca et al., on the other hand, reported that there was a higher increase in pediatric PFP cases admitted to the emergency department in the same period compared to the last five years (11). Again, in this period, the publication of case reports with PFP that were Covid-19 positive in the literature revealed the idea that this virus could create a PFP clinical picture.

In this study, the demographic characteristics, radiological facial nerve segment diameters, clinical presentations, and treatment responses of the patients who visited our clinic due to PFP during the period of 10.03.2020 -10.06.2020, when the number of Covid-19 patients peaked in Turkey during the pandemic, and in the same period the previous year were evaluated comparatively. We aim to investigate whether Covid-19 has a significant effect on PFP.

MATERIALS AND METHODS

The files of the patients who applied to the Otorhinolaryngology Clinic of Adana City Research and Training Hospital between 10.03.2019-10.06.2019 and between 10.03.2020 -10.06.2020 with the diagnosis of Bell Palsy (BP) were evaluated retrospectively. 42 patients with PFP before the pandemic (Group 1) and 56 patients with PFP after the pandemic (Group 2) were included in the study. Records of patients' age, gender, PFP side, admission grade, post-healing grade, presence of additional disease, receiving steroid treatment, results of Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), and the diameters of the facial nerve tympanic-mastoid-labyrinthine-geniculate ganglion were taken from the files. Those with missing radiological examinations were excluded. Ethics committee approval was obtained for our study, and written informed consent was obtained from all patients (Date:08.07.2021, No: 984).

Otoscopic examination findings, audiological results, application, and post-healing grade information according to the House Brackmann Staging system were obtained from all the patients' files. Temporal Bone CT, which is included in the routine practice of our clinic, and Cranial & Diffusion MRI examinations for the elimination of central causes were applied to the patients. FN tympanic, mastoid, labyrinth segment diameters, and geniculate ganglion diameters were measured separately for the diseased side and the healthy side. All patients included in the study were patients with idiopathic peripheral facial paralysis.

Computed tomography was used for facial nerve (FN) segment measurements. A 128-detector Multidetector Computed Tomography (MDCT) unit (Philips Ingenuity 128, Eindhoven, The Netherlands) was used for CT imaging. The technical parameters utilized were as follows: 120 kvP, 200-400 mAs automatic tube current modulation, rotation time 0.42 s, pitch 0.6, slice thickness: 1 mm. Axial images of the temporal tomography scans were reformatted in sagittal planes.

Statistical analysis

Normal distribution control of continuous variables was evaluated with Shapiro-Wilk statistics. Variables compatible with normal distribution were examined using two independent groups t-tests to examine the differences between the groups. For the variables in a categorical structure, the Chi-Square test was used. In summary statistics, mean ± standard deviation values were given for numerical variables, while frequencies and percentages were used for categorical variables. The statistical significance level was taken as $p<0.05$. All analyses were done with IBM SPSS 22 (USA) package program trial version.

RESULTS

In the study, there were 42 patients (43%) in Group 1 before the pandemic and 56 (57%) patients in Group 2 after the pandemic. 56 (57%) of the patients were male and 42 (43%) were female. The ages of the patients were between 7 and 87, and the average age was 45. 88. There was no additional

Table 1: Diameter values in all patients

	Minimum	Maximum	Average	Standard deviation
Right labyrinthine segment (mm)	0.80	1.71	1.14	0.16
Right geniculate ganglion (mm)	0.99	2.63	1.74	0.31
Right mastoid segment (mm)	1.40	2.34	1.94	0.21
Right tympanic segment (mm)	0.70	1.62	1.10	0.23
Left labyrinthine segment (mm)	0.75	1.54	1.12	0.21
Left geniculate ganglion (mm)	1.01	2.03	1.64	0.27
Left mastoid segment (mm)	1.50	2.30	1.95	0.19
Left tympanic segment (mm)	0.75	1.42	1.08	0.19

Table 2: Grades of Bell Palsy patients at the time of admission to the hospital and facial nerve diameters on the same side of the disease

	Grade 2	Grade 3	Grade 4	Grade 5	Grade 6	P values
Right labyrinthine segment (mm)	1.15±0.15	1.13±0.17	1.09±0.05	1.02±0.25	0.97±0.14	0.279
Right geniculate ganglion (mm)	1.78±0.33	1.71±0.29	1.68±0.25	1.84±0.08	1.50±0.48	0.542
Right mastoid segment (mm)	1.94±0.22	1.97±0.18	1.96±0.21	1.59±0.16	1.72±0.33	0.051
Right tympanic segment (mm)	1.08±0.23	1.12±0.22	1.17±0.37	0.96±0.02	1.22±0.35	0.693
Left labyrinthine segment (mm)	1.16±0.18	5.43±25.47	1.01±0.01	0.99±0.16	1.04±0.24	0.788
Left geniculate ganglion (mm)	1.64±0.27	1.66±0.26	1.68±0.20	1.62±0.12	1.50±0.48	0.878
Left mastoid segment (mm)	1.96±0.20	1.97±0.15	2.01±0.13	1.65±0.19	1.78±0.37	0.075
Left tympanic segment (mm)	1.07±0.18	1.10±0.21	1.14±0.37	0.96±0.06	1.07±0.23	0.794

Table 3: Affected side and diameters

	Effected side left	Effected side right	P values
Right labyrinthine segment (mm)	1.12±0.15	1.15±0.17	0.265
Right geniculate ganglion (mm)	1.77±0.34	1.72±0.28	0.442
Right mastoid segment (mm)	1.92±0.21	1.95±0.22	0.501
Right tympanic segment (mm)	1.07±0.21	1.13±0.25	0.161
Left labyrinthine segment (mm)	1.42±0.29	1.15±0.16	0.297
Left geniculate ganglion (mm)	1.66±0.26	1.63±0.28	0.612
Left mastoid segment (mm)	1.95±0.18	1.95±0.20	0.958
Left tympanic segment (mm)	1.08±0.20	1.08±0.19	0.990

disease in 91% of the patients. Diabetes Mellitus ranks first with 27% among patients with additional disease. The total number of right and left BP was 98: right BP was 51 in Group 1 and left BP was 47 in Group 2. In Group 1 and Group 2, the highest reference grade was grade 2 (58.5%) and then grade 3 (37.5%). All of the left BPs regressed to grade 1 and showed complete recovery. 1 of the patients with right BP regressed to grade 2; 3 of them regressed to grade 3, and all the rest showed complete recovery by regressing to grade 1. In Group 1, the post-healing grade of all the patients was grade 1. In Group 2, the post-healing grades of the patients: 1 was grade 2; 3 of them were observed as grade 3 and the remaining 52 patients were observed as grade 1. The post-healing grade of all the patients in Group 1 decreased to 1. Post-healing grades in group 2 are as follows: 52 patients - Grade 1, 1 patient - Grade 2, and 3 patients - Grade 3. 47 (48%) of the patients are right BP; 51 (52%) of them are in the form of left BP. The fact that BP is on the right or left has no effect on recovery; all the patients on the left side and 92% of them on the right side were completely grade 1 (p=0.068). Steroid treatment was given to all patients in the pre-pandemic period. (As the routine practice of our clinic, oral methylprednisolone is started at a dose of 1 mg/kg, reduced within days, and then stopped.) In the period after Covid-19, since the results of the use of steroids in the first days are not known, no steroid was given to any patient in this period. Groups and gender did not have a statistically significant effect on healing (before or after Covid-19) (p=0.534, p=0.100, respectively). There is a statistically significant difference between the post-healing grade and comorbidity (p=0.049). The probability of staying as BP grade 3 in patients with additional disease is 20%. The healing rate of those who do not have any additional disease as grade 2 or 3 is 1.1% for both. There is a statistically significant difference between the post-healing grade and the reference grade (p=0.005). The low level of the post-healing grade (improvement) is statistically and significantly associated with the low level at the first application. The average of the diameters of the facial nerve segments in all patients is given in Table 1.

There is no statistically significant difference between the hospital admission grade of BP patients and the facial nerve geniculate, labyrinth, mastoid, and tympanic segment diameters on the same side of the disease (Table 2, p> 0.05 for all segments).

Facial nerve diameters by the affected side are shown below (Table 3).

Between Group 1 and Group 2, right tympanic segment diameters (p <0.001) in the patients with right BP, left tympanic segment diameters (p=0.006) in the patients with left BP, and right geniculate ganglion diameters in the patients with right BP (p=0.014), there is a statistically significant difference in terms of variables. In Group 2, the right tympanic segment diameters are wider in the patients with right BP compared to Group 1. (p <0.001). In Group 2, left tympanic segment diameters are wider in the patients with left BP compared to Group 1. (p=0.006). In Group 1, the right geniculate ganglion diameter is larger in the patients with right BP compared to Group 2. It is wider in Group 1 (p=0.014) (Table 4).

There is a statistically significant difference between the comorbid disease groups only in terms of the left mastoid segment variable (p=0.035). In other words, the left mastoid segment diameter was found to be narrower in patients with additional disease. While there is no statistically significant relationship between comorbidity and admission grade (p=0.326), there is a statistically significant relationship between comorbidity and the post-healing grade (p=0.049).

Table 4: The FN segment diameters of the groups

	Group 1	Group 2	P Values
Right labyrinthine segment(mm)	1.17±0.11	1.11±0.19	0.052
Right geniculate ganglion (mm)	1.86±0.24	1.66±0.33	0.014
Right mastoid segment (mm)	1.98±0.20	1.90±0.22	0.821
Right tympanic segment (mm)	0.96±0.11	1.20±0.24	<0.001
Left labyrinthine segment (mm)	1.20±0.17	3.86±20.43	0.087
Left geniculate ganglion (mm)	1.69±0.26	1.61±0.27	0.691
Left mastoid segment (mm)	1.99±0.15	1.92±0.21	0.118
Left tympanic segment (mm)	0.99±0.14	1.15±0.20	0.006

Complete recovery in facial paralysis is less common in patients with comorbidities. There is no statistically significant difference in age between the post-healing grade groups (2-3-4-5-6) (p=0.052). However, the lowest mean age is grade 4, and the highest average age is grade 3.

The post-healing grade of all 42 patients who took steroids decreased to grade 1. The post-healing grades of patients not receiving steroids are grade 1 in 52 patients, grade 2 in 1 patient, and grade 3 in 3 patients. There was no statistically significant difference in the age variable between pre and post-Covid-19 groups (p=0.751). There is no significant difference in age between Group 1 and Group 2. The age distribution of patients with BP during the pandemic period is similar to the previous year.

DISCUSSION

Facial paralysis publications associated with Covid-19 in the literature are mostly in the form of case reports. The number of articles submitted to the literature for the virus considered to be neurotrophic is expected to increase in time. There are articles in the literature presenting variable data in terms of female and male distribution. According to the information obtained from the presented cases, PFP can be the first finding in Covid-19, or it can develop in the first 10 days (10-16). In addition, bilateral or unilateral PFP cases associated with Guillain-Barré syndrome (GBS) have been reported in Covid-19 patients in the literature (17-22). In our study, the pre-Covid period group is Group 1 and the post-Covid period group is Group 2. While all the patients in Group 1 took steroids, the patients in Group 2 did not take any. There is no significant statistical difference between the groups in terms of the post-healing grade. However, the number of patients in Group 2 is higher. We think that Covid-19 is a neurotropic virus and increases PFP.

Although the main cause of idiopathic PFP (Bell's Palsy) has not been fully elucidated in the literature, the detection of herpes simplex virus type 1 (HSV-1) genome in the endoneurial fluid obtained from FN in these patients is the most likely pathogenic mechanism in the geniculate ganglion and meatal foramen, and it supports the view of inflammation due to HSV-1 reactivation in the segment of the labyrinth (9-11). The mechanism of PFP formation due to Covid-19 is probably demyelination induced by an inflammatory process, as in PFP due to the neurotropic herpes viruses HSV and varicella zoster virus

Table 5: Isolated PFP cases in the Covid-19 Period

	Age	Gender	Side	Grade	Treatment	Conclusion
Wan et al.28 (2020)	65	Female	Left	4	The symptoms of left facial paralysis relieved after antiviral treatment with arbidol and ribavirin	Complete
Goh et al.29 (2020)	42	Male	Left	3	Prednisone and valacyclovir, as well as lopinavir/ritonavir in an attempt to reduce SARS-CoV-2 viral replication	Complete
Lima et al. (2020)	43*	Female	Right	3	Oral steroids	Partial
	25*	Female	Right	2	Oral steroids + acyclovir	Complete
	33	Female	Right	3	Oral steroids + acyclovir	Partial
	26	Female	Left	2	Oral steroids	Complete
	50	Female	Left	3	Oral steroids	Partial
	38	Female	Left	2	Supportive	Complete
	39	Female	Right	2	Oral steroids	Complete
	34	Female	Left	2	Intravenous steroids	Complete
Figueiredo et al. (13)	35	Female (pregnant)	sol	3	Corticosteroid therapy (10-day tapering prednisolone course, starting at 60mg/day) was initiated in order to optimize functional recovery	Partial
Mehta et al. (16)	36	Male	Right	3	prednisone and eye lubrication,	Complete

*As the first symptom of Covid-19 and the main reason for patients' admission to the hospital. PFP: Peripheral facial paralysis.

(VZV). Some authors have reported that demyelination may occur in cranial nerves due to a secondary delayed immune response as a result of Covid-19 viremia (12,14,23). In addition, the fact that Covid-19 has been associated with various neurological diseases, such as anosmia, acute ischemic stroke, encephalopathy, and GBS, indicates that this virus may cause cranial nerve involvement (24). Neurological findings have been reported in approximately 36.4% of Covid-19 (11,17). For this reason, additional symptoms should be questioned in patients presenting with isolated FPP, cranial nerve examinations should be performed, and MRI should be requested if necessary.

Correa et al. published cranial nerve (CN) (1st, 2nd, 6th, and 7th CN) abnormalities and magnetic resonance imaging (MRI) results of these patients in six Covid-19 positive cases (25). FN involvement was present in four of the six patients published. One patient had unilateral PFP, while the other had unilateral PFP and ipsilateral abducens nerve paralysis. Bilateral PFP was observed in the other two patients. One of the bilateral PFP cases was associated with GBS. He reported that FN had increased gadolinium uptake in the canalicular segment, labyrinth segment, and/or geniculate ganglion on MRI of the patients. In addition, the patient who had abducens paralysis with unilateral PFP had significant contrast enhancement in the caudal of the pons, FN mastoid segment, and abducens nerve on MRI. However, in a series of eight cases by Lima et al. (12), MRI was performed in five of the cases, and it was reported that contrast enhancement increased in FN only in one of them. Komori et al. (26) selected five regions along the intratemporal facial canal as the measurement sites of the facial nerve diameters: (1) the meatal foramen, (2) the cochleariform process, (3) the stapes, (4) the pyramidal eminence, and (5) the dike segment of the chorda tympani. Measurements as left and right were as follows, respectively (mm); meatal foramen (MF) 0.99±0.05 (0.87-1.11); 0.99±0.06 (0.89-1.15), Cochleariform process (CP) 1.39±0.10 (1.25-1.57); 1.39±0.09 (1.23-1.55), Stapes (S) 1.09±0.07 (0.95-1.23); 1.09±0.07 (0.93-1.21), Pyramidal eminence (PE) 1.62±0.07 (1.50-1.75); 1.61±0.07 (1.48-1.71), Emerging point of chorda tympani (EC) 2.14±0.24 (1.63-2.82) 2.15±0.16 (1.75-2.54). Although the same points were not used in our measurements, they are similar to each other. In our study, we measured the segment diameters of the facial nerve using temporal CT and MRI imaging.

In the consensus reports of Herman et al. regarding the use of corticosteroids in otology cases, they recommended the use of short-term corticosteroids in necessary cases according to the severity of the symptoms after the BP cases were well evaluated, and it was decided that they were definitely idiopathic (27). They recommended short-term corticosteroid therapy only in severe forms (Grades 5-6) and in patients without any of the signs and symptoms of Covid-19. They did not recommend routine nasopharyngeal swabs in patients presenting with PFP because PFP was not a definitive finding for Covid-19, and more importantly, the nasopharyngeal swab had limited reliability (40% false negativity). In other patients, only eye protection and follow-up were recommended. They published that BP patients with Covid-19 symptoms should be evaluated on a case-by-case basis by the responsible team after diagnostic tests. Oral antiviral therapy (valaciclovir 3g / day) was recommended only in shingles cases, as previously stated (27). The post-healing grade of all 42 patients who took steroids decreased to Grade 1. The post-healing grades of the patients not receiving steroids remained as Grade 1, one patient as Grade 2, and three patients as Grade 3. Although we understand that steroid therapy works partly, we see that spontaneous regression is more important. Current literature information regarding the Covid-19 period and our article is shown in Table 5 (12, 13, 16, 28, 29).

In a study on the incidence of Covid-19 and Bell's Palsy, it was reported that the incidence did not increase during the pandemic in the last five years. However, the fact that the PCR result of approximately 40% of the patients in this study is unknown may support both hypotheses in all the existing debates that the virus increases or reduces the true incidence of Bell's Palsy (30). Patients presenting with facial paralysis during the heaviest period of the pandemic may have been sent from the hospital without taking swab samples, which may obscure real interpretations.

CONCLUSION

Facial paralysis is a common phenomenon in ear, nose, and throat practice and requires priority treatment and follow-up. When we look at the two same time intervals before and after Covid from the data we have obtained from this study; We see that the frequency of facial paralysis has increased in the post-covid period. It has been emphasized in some studies that Covid-19 is a neurotropic virus. Since the Covid-19 virus is a new entity in the world, we think that it has an affinity for the facial nerve, although our knowledge about this virus is limited. For this reason, clinical follow-up of the facial nerve is important in Covid patients. Although there was no change in the approach to treatment, the patients were given routine Covid treatment. In addition, in accordance with the literature, we did not observe a significant difference in terms of improvement between patients who took steroids and those who did not.

Limitations of the study

In addition, patients were not given corticosteroids treatment for facial paralysis because the effects of corticosteroids were not known at the beginning of the pandemic. In Turkey, the official announcement date of the first patient was 10.03.2020, and we think that that group of patients who did not take a swab in the next three months presents as a neurotrophic symptom of the virus. Unfortunately, swab samples were not sent from those patients who did not have typical respiratory system findings.

Ethics Committee Approval: This study was approved by Adana City Training and Research Hospital Clinical Research Ethics Committee (Date:08.07.2021, No: 984).

Informed Consent: Written informed consent was obtained.

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