CLINICAL STUDY

ASSOCIATION BETWEEN COVID-19 AND FACIAL PARALYSIS

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SUMMARY

Objective: To evaluate the records of patients who presented to our clinic with acute facial paralysis during the COVID-19 pandemic and to investigate a potential association between the two conditions.

Methods: A retrospective analysis was made of the patients who presented to our department with facial paralysis in the 1 year preceding the first positive diagnosis of COVID-19 in this country (Group 1), and those presenting with the same complaint within the 1 year after this date (Group 2). The age, gender, COVID-19 swab test result, House-Brackmann staging and side of facial paralysis, audiogram results, treatment is given, time until improvement and the comorbidities and symptoms additional to facial paralysis of each patient were collected.

Results: Included in the study were a total of 45 and 58 patients who presented with facial paralysis for group 1 and group 2 respectively. Of the patients who presented with acute facial paralysis since the pandemic, five were positive for COVID-19 (8.6%) and three had been in contact with someone positive for COVID-19 (5.1%). No statistically significant differences were found between groups 1 and 2 in the compared parameters. A statistically significant improvement was observed in the staging according to the first and last House-Brackman stages of the patients in both groups ($p<0.001$).

Conclusion: These results suggest that there is no clear relationship between COVID-19 and acute peripheral facial palsy. We thus conclude that any association between acute peripheral facial paralysis and COVID-19 during the pandemic may be coincidental.

Keywords: Facial paralysis, pandemic, coronavirus

COVID-19 VE FASİAL PARALİZİ ARASINDAKİ İLİŞKİ

ÖZET

Amaç: COVID-19 pandemisi sürecinde kliniğimize akut periferik fasiyal paralizi ile başvuran hastaları inceleyerek, COVID-19 ile akut periferik fasiyal paralizi arasında potansiyel bir ilişki olup olmadığının değerlendirilmesi amaçlanmıştır.

Yöntem: Çalışmamızda, kliniğimize akut periferik fasiyal paralizi nedeniyle başvuran, ülkemizde ilk COVID-19 pozitifliğinin saptandığı tarih olan 10 mart 2020 tarihinin 1 yıl öncesi(grup 1) ve sonrasındaki(grup 2) hastalar geriye dönük olarak karşılaştırmalı bir şekilde incelenmiştir. Her hasta için yaş, cinsiyet, COVID-19 sürüntü testi sonucu, fasiyal paralizi House-Brackmann evrelemesi ve tarafı, odyogram bilgileri, hastaya verilen tedavi, hastaların iyileşme süreleri, komorbiditeleri ve fasiyal paraliziye ek semptomların verileri toplanmıştır.

Bulgular: Pandemi döneminde 58 hasta, pandemi öncesindeki 1 yıllık süreçte ise 45 hasta izlenmiştir. Pandemi döneminde akut periferik fasiyal paralizisi olan hastalardan 5(%8.6)'i COVID-19 pozitif 3(%5.1)'ü ise temaslı olarak değerlendirilmiştir. Grup 1 ve grup 2 arasında karşılaştırılan parametreler arasında anlamlı istatistiksel fark izlenememiştir. Hem grup 1 hem de grup 2'deki hastalara bakıldığında ilk ve son House-Brackman(HB) evrelemesine göre istatistiksel olarak anlamlı iyileşme izlenmiştir($p<0.001$).

Sonuç: Pandemi dönemi ile öncesindeki bir yıl arasındaki karşılaştırmalarda; değerlendirilen parametreler ve tedaviye verilen cevaplarda iki grup arasında anlamlı istatistiksel fark bulunamamıştır. Çalışmamızdan elde edilen veriler Covid-19 ile akut periferik fasiyal paralizi arasında net bir ilişki olmadığını göstermektedir. Pandemi dörneminde gelen akut periferik fasiyal paralizi hastalarının COVID-19 ile arasındaki ilişkinin rastlantısal olabileceğini düşünüyoruz.

Anahtar Sözcükler: Fasiyal paralizi, pandemi, coronavirüs

INTRODUCTION

The COVID-19 pandemic originated from the SARS-CoV-2 virus outbreak that occurred at the end of 2019 in Wuhan, China, and will likely be with us well into the future due to the lack of global precautions. This virus, which has spread rapidly around the whole world, leads to symptoms that call for the involvement of otolaryngology experts, such as cough, sore throat, nasal obstruction, postnasal discharge, anosmia, and ageusia. In general, fever and respiratory symptoms can be observed in the clinical picture of COVID-19[1], and some neurological symptoms, such as anosmia and ageusia have also been defined[2,3,4]. Coronaviruses have been reported to be neurotrophic in literature[5,6].

Acute peripheral facial paralysis is known to be a problem associated with functional and aesthetic sequela and is frequently encountered by otolaryngologists, neurologists, and emergency medicine specialists. Although peripheral facial paralysis is most frequently idiopathic, infectious agents such as HSV-1, Varicella Zoster virus and Lyme disease are also

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among the common causes[7,8,9], and animal studies support the inclusion of the herpes virus (HSV1) in the etiology[10]. Both unilateral and bilateral facial paralysis have been seen in patients with COVID-19[11,12,13], suggesting that peripheral facial paralysis may be an initial symptom of COVID-19, or may manifest during the clinical course of COVID-19.

The present study evaluates patients who presented to our clinic with acute facial paralysis during the COVID-19 pandemic to investigate the potential association between COVID-19 and facial paralysis.

MATERIAL and METHODS

A retrospective comparative analysis was made of the patients who presented to the ENT Clinic of Pamukkale University with complaints of facial paralysis in the 1 year preceding the first positive diagnosis of COVID-19 in this country on March 10, 2020 (Group 1), and those presenting with the same complaint within the one year after this date (Group 2). The patients who presented since the COVID-19 outbreak constituted the research group. Those who presented in the 1 year following the date of the first positive diagnosis in the country were included in the evaluation of possible differences. Cases with peripheral facial paralysis lasting for more than 1 month were excluded from the study. The age, gender, combined oral and nasal COVID-19 swab test result, House-Brackmann (HB) staging and side of facial paralysis, audiogram results, treatment given, time until improvement, and the comorbidities (diabetes mellitus, hypertension, coronary artery diseases, hyperlipidemia, chronic renal failure, organ transplantations, cancers and thyroid dysfunctions) and symptoms additional to facial paralysis of each patient were collected. Ethics committee approval was obtained from the Pamukkale University clinical research ethics committee. (Date: 02/03/2021 No: E-60116787-020-29321).

The patients diagnosed within the year before the date of the first positive diagnosis of COVID-19 in the country were assigned as Group 1 (March 10, 2019-March 9, 2020), and those diagnosed in the following year were accepted as Group 2 (March 10, 2020-March 10, 2021). The number of presentations to the clinic within the last 5 years and the number of cases with peripheral facial paralysis were also evaluated. In addition to the comparison of Group 1 and Group 2, the status of the Group 2 patients with confirmed or suspected COVID-19 was also analyzed.

Statistical Analysis

The data were analyzed with SPSS version 24.0 software (IBM Corporation, Armonk, NY). Continuous variables were expressed as mean ± standard deviation and range, and categorical variables were expressed as count and percentage. The Students't-test was used for comparison between the two groups. The Chi-square test was used for categorical group comparisons. The statistical significance level was set at $p < 0.05$ in all statistical analyses.

RESULTS

Group 1 was composed of 45 patients who presented to the clinic in the year preceding the first positive diagnosis of COVID-19 in the country. While Group 2 comprised 58 patients who had applied to the clinic with acute peripheral facial paralysis within the 1 year following the first diagnosis. The necessary data of each patient were collected, and the main properties of each group are presented for comparison in Table 1. Among the groups, 25 out of the 45 (55.6%) patients in Group 1, and 40 out of the 58 (69%) patients in Group 2 had been lost to follow-up (p=0.162). Those who had been lost to follow-up were contacted by phone, and the course of their condition was questioned. Among the patients, 24 (60%) of the 40 patients who were lost to follow-up were found to have completely recovered, five had partially recovered (12.5%), one had seen no improvement (2.5%) and 10 (25%) could not be reached. All of the COVID-19 positive (n=5) patients, and those who had been in contact with a person diagnosed as positive for COVID-19 (n=3), were found that they completely recovered, and only 1 patient had continuing anosmia.

No statistically significant differences were found in the age, gender, paralysis site, HB staging on day 1 and day 30, audiogram results, the status of and time to recovery, number of comorbidities, presence of DM, type or treatment, and immunosuppressive treatment status between Group 2 (COVID-19 era) and Group 1 (Table 1).

Among the patients with facial paralysis in Group 2, an RT-PCR nasopharyngeal swab test was positive in five patients (8.6%) and negative in 19 (32.7%) patients; and there were three patients (5.1%) who had been in contact with a person positive for COVID-19. In addition, 31 (53.4%) patients had not undergone a PCR test. Among the five patients with a positive RT-PCR test, the single symptom was facial paralysis with no additional symptoms in two patients, and the remaining three patients were found to have cough and dyspnea in addition to facial paralysis. On the other hand, among the three patients who had been in contact with a COVID-19 positive patient, one was found to have facial paralysis as the single symptom, one had complaints of weakness and arthralgia, and one had a feeling of pressure in the ear in addition to facial paralysis.

A statistically significant improvement was observed in the first and last House-Brackman (HB) stage values of the patients in both groups ($p<0.001$).

The number of patients presenting to the outpatient clinics and patients with acute peripheral paralysis over the last 5 years are presented in Table 2.

Table 1. Demographic data of the patients

	VARIABLES	GROUP 1	GROUP 2	p VALUES
		n=45	n=58	
GENDER	Male	27 (60%)	28 (48.3%)	.237
	Female	18 (40%)	30 (51.7%)	
AGE	Mean	*45.68 [±21] (5-81)*	43,86	.651
	Max-Min		[±21,23]	
			(11-87)	
SIDE	Right	25 (55.6%)	33 (56.9%)	.892
	Left	20 (44.4%)	25 (43.1%)	
HB GRADE		n=45	n=58	
FIRST ASSESSMENT	Mean	patients	patients	.539
	Max-Min	3.65 [±1.03]	3.5 [±1.2]	
		(2-6)	(2-6)	
HB GRADE		n=20	n=18	
ASSESSMENT ON DAY	Mean	patients	patients	.290
30	Max-Min	2.1 [±1.71]	2.33 [±1,45]	
		(1-6)	(1-6)	
AUDIOGRAM	Mean	33.07	23.3	.334
	Max-Min	[±30.29]	[±20.53]	
		(2-120)	(5-120)	
RECOVERY STATUS	Yes	12 (60%)	6 (33.3%)	.254

	Partial	4 (40%)	6 (33.3%)	
	None	4 (40%)	6 (33.3%)	
TIME TO RECOVERY	Mean	52.62	23.3	.077
(DAY)	Max-Min	[±44.18]	[±11.07]	
		(7-165)	(10-45)	
COMORBIDITY	0	20 (44.4%)	29 (50%)	.644
	1	10 (22.2%)	12 (20.7%)	
	2	10 (22.2%)	10 (17.2%)	
	3+	5 (11.1%)	7 (12%)	
DIABETES MELLITUS	Yes	21 (46.66%)	23 (39.65%)	.503
	None	24 (53.33%)	35 (60.34%)	
TYPE OF TREATMENT	Oral Steroid	20 (44.4%)	34 (58.6%)	.136
	Systemic	20 (44.4%)	23 (39.7%)	
	steroids	4 (8.9%)	1 (1.7%)	
	Surgery	1 (2.2%)	0 (0%)	
	None			
IMMUNOSUPPRESSIVE	Present	3 (6.7%)	3 (5.2%)	1.000
TREATMENT	None	42 (93.3%)	55 (94.8%)	

Table 2: Number of patients who applied over the last 5 years

	2016	**2017**	**2018**	**2019**	**2020**
Facial paralysis	41	50	55	45	58
Patients admitted to the outpatient clinic	9477	9441	9990	8750	3450

DISCUSSION

Hypotheses such as vasa nervorum ischemia or demyelination triggered by inflammation have been suggested as possible mechanisms associated with nerve damage in cases of peripheral facial nerve paralysis[14]. Microthrombi and other vascular changes have been reported to play a role in the pathophysiology of peripheral facial nerve paralysis in various postmortem studies[15,16]. An association between acute mononeuropathies and COVID-19 has been reported in some studies[17,18], and neural damage and acute mononeuropathy, as in other infective factors, have been reported to play a possible role in the mechanism of facial paralysis due to COVID-19 in literature.

No statistically significant differences were found in terms of age and gender between Group 1 (pre-pandemic era) and Group 2 (pandemic era), and facial paralysis was reported to have no gender predominance also in earlier

studies[19]. No statistically significant differences were identified between Groups 1 and 2 in any other of the compared parameters, which suggests that the effect of COVID-19 on the clinical picture of peripheral facial paralysis for which it may be responsible is no different than that of other infective agents.

Both unilateral and bilateral (due to Guillain-Barre syndrome) acute facial paralysis has been defined in patients with COVID-19[11,12,13], and these case reports have suggested a possible link between COVID-19 and Guillain-Barre syndrome, although this hypothesis is not supported due to the absence of COVID-19 antibodies in the CSF of a case with COVID-19-positive Guillain-Barre syndrome[20]. These data suggest that the association between COVID-19 and peripheral facial paralysis may be coincidental. In one study, 24.3% of patients with Bell's palsy were found to have positive SARS-CoV-2 IgM + IgG antibody test. It has been stated that facial paralysis may be the only symptom of COVID-19[21].

The number of cases who presented with acute peripheral facial paralysis each year over the last 5 years was similar, with no increase determined in the number of patients presenting with peripheral facial paralysis since the COVID-19 outbreak. No significant difference in the number of patients who applied to the clinic was observed. We believe this was because the patients considered peripheral facial paralysis an emergent condition due to marked functional and aesthetic sequelae on the faces, causing them to present to the hospital despite the pandemic. Among Groups 1 and 2, 25 of the 45 cases (55.6%) and 40 of the 58 (69%) cases, respectively, were lost to follow-up ($p=0.162$). Although the number of patients lost to follow-up was higher following the outbreak, the difference between the two eras was not statistically significant. This, in turn, demonstrated that the profile of the patients with peripheral facial paralysis was similar in the two years included in the study.

According to the RT-PCR nasopharyngeal swab test results of the patients in Group 2, five (8.6%) patients were COVID-19 positive; and there were three (5.1%) patients who had been in contact with a COVID-19-positive patient. Among the five patients with positive RT-PCR test, the single symptom was facial paralysis with no additional symptoms in two patients, while the remaining three presented with cough and dyspnea in addition to facial paralysis. On the other hand, among the three patients who had been in contact with a COVID-19-positive patient, one had facial paralysis as the single symptom, one complained of weakness and arthralgia, and one had feelings of pressure in the ear in addition to facial paralysis. Some 60% of patients with peripheral facial paralysis have been reported in the literature to have viral prodromal symptoms, 50% experienced ear pain, 40% reported numbness in the face, 50% reported changes in taste perception and 20% complained of numbness in the tongue[22]. Peripheral facial paralysis may be seen together with viral prodromal symptoms or as a single symptom in COVID-19, as is the case with any infective agent.

No statistically significant difference was noted in the treatment approaches to Groups 1 and 2, with symptomatic supportive therapy and oral steroids being the basis of treatment[23]. The prognosis of paralysis has been reported to be good in cases of peripheral facial paralysis associated with COVID-19 in studies conducted to date[24,25]. Among the 2,570 patients in a facial nerve study conducted in Copenhagen, 70% of the patients had total facial paralysis, while function returned in 3 weeks in 85% of the cases, and 71% witnessed full recovery[26]. In the present study, a statistically significant improvement was observed in the House-Brackmann (HB) staging of both groups in a 30-day follow-up period ($p<0.001$). In the light of the presented data, no resistance to improvement in cases of facial paralysis was observed during the COVID-19 era.

In conclusion, the number, profile, and prognosis of patients with caused acute peripheral facial paralysis were not affected during the COVID-19 pandemic. No increase in the number of patients who applied to our clinic with acute peripheral facial paralysis was observed when compared to previous years. This suggests that there is no clear association between SARS-CoV-2 and acute peripheral

facial paralysis. We thus conclude that any association between acute peripheral facial paralysis and COVID-19 during the pandemic may be coincidental.

REFERENCES

1. Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720. doi:10.1056/NEJMoa2002032
2. Vonck, K., Garrez, I., De Herdt, V., Hemelsoet, D., Laureys, G., Raedt, R., et al. Neurological manifestations and neuro-invasive mechanisms of the severe acute respiratory syndrome coronavirus type 2. Eur J Neurol. 2020;27(8):1578-1587. doi:10.1111/ene.14329
3. Helms, J., Kremer, S., Merdji, H., Clere-Jehl, R., Schenck, M., Kummerlen, C., et al. Neurologic Features in Severe SARS-CoV-2 Infection. N Engl J Med. 2020;382(23):2268-2270. doi:10.1056/NEJMc2008597
4. Eliezer, M., Hautefort, C., Hamel, A. L., Verillaud, B., Herman, P., Houdart, E., et al. Sudden and Complete Olfactory Loss of Function as a Possible Symptom of COVID-19. JAMA Otolaryngol Head Neck Surg. 2020;146(7):674?675. doi:10.1001/jamaoto.2020.0832
5. Natoli S, Oliveira V, Calabresi P, Maia LF, Pisani A. Does SARS-Cov-2 invade the brain? Translational lessons from animal models. Eur J Neurol. 2020;27(9):1764-1773. doi:10.1111/ene.14277
6. Mao, L., Jin, H., Wang, M., Hu, Y., Chen, S., He, Q., et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. JAMA Neurol. 2020;77(6):683-690. doi:10.1001/jamaneurol.2020.1127
7. Eviston, T. J., Croxson, G. R., Kennedy, P. G. E., Hadlock, T., Krishnan, A. (2015). Bell's Palsy: Aetiology, clinical features and multidisciplinary care. Journal of Neurology, Neurosurgery and Psychiatry, 86, 1356?1361. https://doi.org/10.1136/jnnp-2014-309563
8. Madhok, V. B., Gagyor, I., Daly, F., Somasundara, D., Sullivan, M., Gammie, F., et al. Corticosteroids for Bell's palsy (idiopathic facial paralysis). Cochrane Database Syst Rev. 2016;7(7):CD001942. Published 2016 Jul 18. doi:10.1002/14651858.CD001942.pub5
9. Owusu JA, Stewart CM, Boahene K. Facial Nerve Paralysis. Med Clin North Am. 2018;102(6):1135-1143. doi:10.1016/j.mcna.2018.06.011
10. Morgan M, Moffat M, Ritchie L, Collacott I, Brown T. Is Bell's palsy a reactivation of varicella zoster virus?. J Infect. 1995;30(1):29-36. doi:10.1016/s0163-4453(95)92769-7
11. Goh Y, Beh DLL, Makmur A, Somani J, Chan ACY. Pearls & Oy-sters: Facial nerve palsy in COVID-19 infection. Neurology. 2020;95(8):364-367. doi:10.1212/WNL.0000000000009863
12. Helbok, R., Beer, R., Löscher, W., Boesch, S., Reindl, M., Hornung, R., et al. Guillain-Barré syndrome in a patient with antibodies against SARS-COV-2. Eur J Neurol. 2020;27(9):1754-1756. doi:10.1111/ene.14388
13. Manganotti, P., Bellavita, G., D'Acunto, L., Tommasini, V., Fabris, M., Sartori, A., et al. Clinical neurophysiology and cerebrospinal liquor analysis to detect Guillain-Barré syndrome and polyneuritis cranialis in COVID-19 patients: A case series. J Med Virol. 2021;93(2):766-774. doi:10.1002/jmv.26289
14. Zhang W, Xu L, Luo T, Wu F, Zhao B, Li X. The etiology of Bell's palsy: a review. J Neurol. 2020;267(7):1896-1905. doi:10.1007/s00415-019-09282-4
15. Silberzahn P, Bouhamidi R, Zwain I, Gaillard JL, Martin B (1988) Testosterone blood content is regulated by testicular aromatization- conjugation in the stallion. Steroids 52:353?354. https://doi.org/10. 1016/0039-128x(88)90143-2
16. Duarte-Neto, A. N., Monteiro, R., da Silva, L., Malheiros, D., de Oliveira, E. P., Theodoro-Filho, J., et al. Pulmonary and systemic involvement in COVID-19 patients assessed with ultrasound-guided minimally invasive autopsy. Histopathology. 2020;77(2):186-197. doi:10.1111/his.14160
17. Costello F, Dalakas MC. Cranial neuropathies and COVID-19: Neurotropism and autoimmunity. Neurology. 2020;95(5):195-196. doi:10.1212/WNL.0000000000009921
18. Dinkin, M., Gao, V., Kahan, J., Bobker, S., Simonetto, M., Wechsler, P., et al. COVID-19 presenting with ophthalmoparesis from cranial nerve palsy. Neurology. 2020;95(5):221-223. doi:10.1212/WNL.0000000000009700
19. Katusic SK, Beard CM, Wiederholt WC, Bergstralh EJ, Kurland LT. Incidence, clinical features, and prognosis in Bell's palsy, Rochester, Minnesota, 1968-1982. Ann Neurol. 1986;20(5):622-627. doi:10.1002/ana.410200511
20. Bigaut K, Mallaret M, Baloglu S, Nemoz B, Morand P, Baicry F, et al. Guillain-Barre? syndrome related to SARS-CoV-2 infection. Neurol Neuroimmunol Neuroinflamm 2020;7:e785. doi:10.1212/NXI.0000000000000785
21. Islamoglu Y, Celik B, Kiris M. Facial paralysis as the only symptom of COVID-19: A prospective study. Am J Otolaryngol. 2021 Jul-Aug;42(4):102956. doi: 10.1016/j.amjoto.2021.102956. Epub 2021 Feb 10. [Özet]; PMCID: PMC7972325.
22. Özgirgin N. Fasiyal sinir ve hastalıkları. In: Kıroğlu M, Yiğit Ö, Keleş E, Kara CO, Alkan Z. Kulak burun boğaz ve baş boyun cerrahisi uzmanlık eğitimi Kaynak Kitap-1. Logos Yayıncılık. İstanbul. 2018:599-630.
23. Sullivan, F. M., Swan, I. R., Donnan, P. T., Morrison, J. M., Smith, B. H., McKinstry, B., et al. Early treatment with prednisolone or acyclovir in Bell's palsy. N Engl J Med. 2007;357(16):1598-1607. doi:10.1056/NEJMoa072006
24. Casas, E., Barbosa, A., Rubio-García, E., Cebrián, J., Díaz-Pérez, C., de la Fuente, E., et al. Parálisis facial periférica aislada en un paciente con COVID-19 [Isolated peripheral facial paralysis in a patient with COVID-19]. Rev Neurol. 2020;71(1):40-41. doi:10.33588/rn.7101.2020229
25. Lima, M. A., Silva, M., Soares, C. N., Coutinho, R., Oliveira, H. S., Afonso, L., et al. Peripheral facial nerve palsy associated with COVID-19. J Neurovirol. 2020;26(6):941-944. doi:10.1007/s13365-020-00912-6
26. Kanazawa A, Haginomori S, Takamaki A, Nonaka R, Araki M, Takenaka H. Prognosis for Bell's palsy: a comparison of diabetic and nondiabetic patients. Acta Otolaryngol. 2007;127(8):888-891. doi:10.1080/00016480601075399