COVID-19-associated parotitis and sublingual gland sialadenitis

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SUMMARY

The COVID-19 mainly affects the respiratory system; however, a variety of atypical manifestations of this disease have been also reported. Herein, we report a case of a man in his late 50s with severe COVID-19 presenting with parotitis and sublingual gland sialadenitis. Six days after admission, swelling in the bilateral preauricular and lower jaw areas developed. CT demonstrated parotid and sublingual gland enlargement with surrounding fat stranding, indicating sialadenitis. This case suggests that, in the present COVID-19 pandemic, COVID-19 should be included in the differential diagnosis of sialadenitis and prompt isolation should be considered to reduce the spread of infection.

BACKGROUND

The COVID-19 is caused by SARS-CoV-2 infection. COVID-19 has spread worldwide rapidly since December 2019, and over 500 million people have been affected. Its most common symptoms are fever, fatigue, dry cough and shortness of breath.[1] However, a variety of atypical presentations of COVID-19, even in the absence of respiratory symptoms, have been also reported, including myocarditis,[2] gastrointestinal and liver damage,[3] ocular manifestations,[4] stroke[5] and various neurological manifestations.[6] Recognition of the atypical presentations of COVID-19 is important for clinicians since it contributes to correct diagnosis of COVID-19, effective management of such patients and isolation precautions to minimise the transmission of SARS-CoV-2. In this article, we describe a case of COVID-19-associated parotitis and sublingual gland sialadenitis.

CASE PRESENTATION

A man in his late 50s was referred to our hospital for the treatment of acute respiratory failure caused by a SARS-CoV-2 infection. He had developed malaise, diarrhoea and shortness of breath 6 days prior. His symptoms exacerbated 2 days prior and he was admitted to a hospital. He was diagnosed with COVID-19 after a reverse-transcriptase-loop-mediated isothermal amplification test for SARS-CoV-2 via a nasopharyngeal swab. The patient then underwent tracheal intubation and artificial ventilation. He also received dexamethasone 6 mg daily and tocilizumab 8 mg/kg (560 mg) intravenously. He was then transferred to our hospital for intensive care. On physical examination, the patient was sedated for tracheal intubation. No swelling of the face and neck was observed. The cervical lymph nodes were not palpable. Laboratory findings showed leucopenia (white cell count: 3.4×10^9 cells/L) and an elevated C reactive protein level (2.11 mg/dL). Radiography of the chest revealed bilateral vague hazy densities and left mid to lower lung opacities. We continued treatment with artificial ventilation and administration of dexamethasone. We also administered ceftriaxone in consideration of the complication of bacterial pneumonia.

INVESTIGATIONS

The patient's condition did not change significantly; however, we observed swelling without erythema or induration in the bilateral preauricular and lower jaw areas on day six at our hospital (figure 1). The presence of pain could not be determined as the patient was on sedatives and analgesics. Clear saliva was spontaneously discharging. No pus was excreted from the parotid glands. Contrast-enhanced CT revealed enlarged bilateral parotid and sublingual glands with surrounding fat stranding, indicating salivary gland inflammation (figure 2A,B). No fluid collection, obstructing stones, dilatation of salivary duct, masses or abscesses were observed.

DIFFERENTIAL DIAGNOSIS

A nasopharyngeal swab was processed for SARS-CoV-2 by reverse transcriptase PCR and the result was positive. The results of the serological test for mumps virus were negative for IgM and positive for IgG, which was consistent with the patient's history of vaccination in childhood. An HIV screening test was negative. Since the patient's parotitis was bilateral and missing erythema or induration, excretion of pus was not observed from the parotid glands, and the patient were receiving ceftriaxone intravenously, we did not suspect bacterial parotitis. Since saliva was normally discharging and no obstruction of the salivary ducts was revealed by CT, we did not think that salivary gland enlargement was due to ventilation therapy. The patient did not have a medical history such as sarcoidosis or Sjogren syndrome, which can cause non-infectious salivary gland enlargement. We considered that COVID-19-associated parotitis and sublingual gland sialadenitis were most likely.

OUTCOME AND FOLLOW-UP

On day 10, CT revealed no remarkable changes in the parotid and sublingual glands. On day 14, the patient died from respiratory failure.

DISCUSSION

A variety of microorganisms can cause salivary gland infections and the parotid gland is most commonly

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Figure 1 Physical examination findings. The preauricular and lower jaw areas are swollen (white arrow heads).

affected.[7 8] Viral salivary gland infections are most commonly associated with the mumps virus, the only aetiologic organism known to cause epidemic parotitis before the development and dissemination of an effective mumps vaccine.[7] Other viruses that have been reported in the minority of parotitis cases include enteroviruses, adenoviruses, cytomegalovirus, influenza, parainfluenza, Epstein-Barr, helps simplex and herpesvirus 6 viruses.[7–9] Sialadenitis is an uncommon manifestation of COVID-19, and only a total of 25 cases of parotitis associated with COVID-19 have been reported.[10–15] One case also involved the submandibular gland.[10] Our case may be the first report showing involvement of the sublingual gland as well as the parotid glands in a patient with COVID-19. In the previous 25 cases of COVID-19-associated parotitis, most cases happened in adults, while mumps parotitis commonly affects children aged 5–9 years old.[16] This may be related to the fact that diagnoses of COVID-19 are few in children. Additionally, 23 patients (92%) with COVID-19-associated parotitis reported unilateral parotitis, while approximately 75% of mumps parotitis are bilateral.[8] Three patients with COVID-19-associated parotitis underwent MRI, which revealed intraparotid lymphadenitis in an otherwise well-preserved gland.[11] This finding of intraparotid lymphoid tissue inflammation suggests different pathogenesis of parotid swelling due to mumps virus, which replicates within parotid glandular tissues and causes oedema and necrosis of acinar and epithelial duct cells.[17] It is not determined when parotitis develops after SARS-CoV-2 infection. The date of parotitis development is not clearly described in many reports. Some cases reported that parotitis developed 1–3 days after the commencement of COVID-19 symptoms.[11 12] Lim *et al* reported 9 days after illness onset.[14] This may indicate that multiple factors are related to the development of sialadenitis in patients with COVID-19.

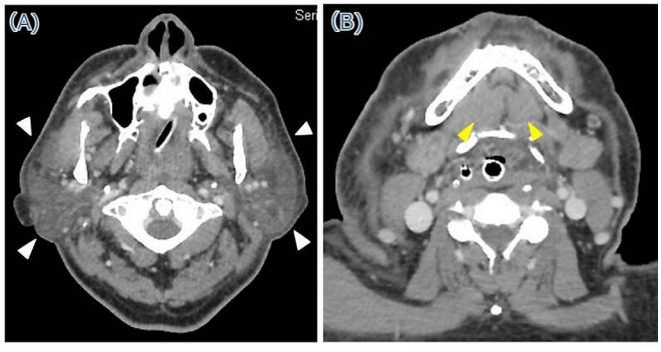

Figure 2 Contrast-enhanced CT shows swelling of the bilateral parotid (white arrow heads) (A) and sublingual glands (yellow arrow heads) (B) with surrounding fat stranding.

The pathogenesis of COVID-19-associated sialadenitis remains to be elucidated. One hypothesis is the direct passage of the virus to the salivary glands. Animal models of the highly related SARS-CoV-2 virus showed direct infection of the epithelial cells on the salivary gland through ACE 2 receptors, which are required for entry into host cells.[18 19] The detection of SARS-CoV-2 in saliva in patients with COVID-19[20] and the finding that 56% of patients with COVID-19 report xerostomia[21] indirectly suggest that the invasion of SARS-CoV-2 into the glands is one of the pathogeneses of COVID-19-associated parotitis. Another thought is that sialadenitis may be caused by the systemic immune-inflammatory response to the SARS-CoV-2 infection. SARS-CoV-2 is known to cause cytokine storm derived from an excess release of cytokines, which leads to cytokine release syndrome.[22] It is characterised by a rise of proinflammatory cytokines such as interleukin (IL)-2, IL-6, IL-10 and interferon-γ in the lung or in the bloodstream, from which the salivary glands are affected.

This case showed that parotitis and sublingual gland sialadenitis can manifest complications in patients with COVID-19. However, it is necessary to study more number of the cases to clarify the specific characteristics of COVID-19-associated sialadenitis. Some cases may have been overlooked, particularly when the patients show parotitis-like symptoms mainly. This case suggests that, in the present COVID-19 pandemic, COVID-19 should be included in the differential diagnosis of sialadenitis in order not to miss COVID-19 and not to expand the risk of transmission.

Learning points

- Sublingual gland sialadenitis, as well as parotid glands, can be complicated with COVID-19.
- In the present COVID-19 pandemic, COVID-19 should be included in the differential diagnosis of sialadenitis in order not to spread the infection.
- Although most COVID-19-associated parotitis have been reported to be unilateral, it can occur bilaterally.

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REFERENCES

1 Wiersinga WJ, Rhodes A, Cheng AC, *et al*. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19). *JAMA* 2020;324:782–93.
2 Wang D, Hu B, Hu C, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020;323:1061.
3 Mao R, Qiu Y, He J-S, *et al*. Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2020;5:667–78.
4 Wu P, Duan F, Luo C, *et al*. Characteristics of ocular findings of patients with coronavirus disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 2020;138:575–8.
5 Fifi JT, Mocco J. COVID-19 related stroke in young individuals. *Lancet Neurol* 2020;19:713–5.
6 Ellul MA, Benjamin L, Singh B, *et al*. Neurological associations of COVID-19. *Lancet Neurol* 2020;19:767–83.
7 Wilson KF, Meier JD, Ward PD. Salivary gland disorders. *Am Fam Physician* 2014;89:882–8.
8 Lau RK, Turner MD. Viral mumps: increasing occurrences in the vaccinated population. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2019;128:386–92.
9 Elbadawi LI, Talley P, Rolfes MA, *et al*. Non-mumps viral parotitis during the 2014-2015 influenza season in the United States. *Clin Infect Dis* 2018;67:493–501.
10 Chern A, Famuyide AO, Moonis G, *et al*. Sialadenitis: a possible early manifestation of COVID-19. *Laryngoscope* 2020;130:2595–7.
11 Lechien JR, Chetrit A, Chekkoury-Idrissi Y, *et al*. Parotitis-Like symptoms associated with COVID-19, France, March-April 2020. *Emerg Infect Dis* 2020;26:2270–1.
12 Capaccio P, Pignataro L, Corbellino M, *et al*. Acute parotitis: a possible precocious clinical manifestation of SARS-CoV-2 infection? *Otolaryngol Head Neck Surg* 2020;163:182–3.
13 Fisher J, Monette DL, Patel KR, *et al*. COVID-19 associated parotitis. *Am J Emerg Med* 2021;39:254.e1–254.e3.
14 Lim ZY, Ang AXY, Cross GB. COVID-19 associated parotitis. *IDCases* 2021;24:e01122.
15 Ekemen Keles Y, Karadag Oncel E, Baysal M, Keles YK, Oncel EK, *et al*. Acute parotitis in a 4-year-old in association with COVID-19. *J Paediatr Child Health* 2021;57:958–9.
16 Galazka AM, Robertson SE, Kraigher A. Mumps and mumps vaccine: a global review. *Bull World Health Organ* 1999;77:3–14.
17 Rubin S, Eckhaus M, Rennick LJ, *et al*. Molecular biology, pathogenesis and pathology of mumps virus. *J Pathol* 2015;235:242–52.
18 Wang C, Wu H, Ding X, *et al*. Does infection of 2019 novel coronavirus cause acute and/or chronic sialadenitis? *Med Hypotheses* 2020;140:109789.
19 Xu H, Zhong L, Deng J, *et al*. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci* 2020;12:8.
20 Wyllie AL, Fournier J, Casanovas-Massana A, *et al*. Saliva or nasopharyngeal swab specimens for detection of SARS-CoV-2. *N Engl J Med* 2020;383:1283–6.
21 Biadsee A, Biadsee A, Kassem F, *et al*. Olfactory and oral manifestations of COVID-19: sex-related Symptoms-A potential pathway to early diagnosis. *Otolaryngol Head Neck Surg* 2020;163:722–8.
22 Borgia F, Li Pomi F, Alessandrello C, *et al*. Coronavirus disease 2019 and pityriasis rosea: a review of the immunological connection. *J Dermatol* 2022;49:948–56.