Nasal Cerebrospinal Leaks in the Milieu of COVID-19 Pandemic

Vazamentos nasais cerebroespinhais no meio da pandemia de COVID-19

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Abstract

Background The unintentional ingestion of oropharyngeal or gastric contents into the respiratory tract is known as aspiration. Rhinorrhea can cause aspiration pneumonia (cerebrospinal fluid leakage).

Objective There are only a few reports in the literature about pneumonia as a complication of rhinorrhea. There are no reports on how to handle such cases if they present to the clinic at the peak of COVID-19 disease and distinguish between these two conditions.

Methods We reviewed the literature and retrospectively analyzed the clinical information and treatment protocols used to treat the two clinical cases.

Results By screening the COVID-19 PCR and antibodies more than twice, surgery was postponed for 10–14 days in both cases to rule out COVID-19-induced pneumonia. Chest CT scans still revealed ground glass opacities. In both cases, the skull base defect was repaired. In both cases, radiological signs of rhinorrhea-induced pneumonia had completely resolved at the 24- and 30-day follow-ups.

Conclusion CSF aspiration causes radiological changes in the lungs in rhinnorhea. This is a short-term local decrease in lung tissue airness (partial filling of alveoli with fluids), which is visible radiographically (ground-glass opacities). To rule out COVID-19 infection, surgery should be postponed for 10–14 days, and PCR and antibodies (IgG, IgM) should be performed at least twice. If the COVID-19 screening test is negative, repair surgery can be scheduled.

Keywords
- CSF liquor rhea
- COVID-19
- aspiration
- pneumonia
- skull base repair surgery

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Resumo

Introdução A ingestão não intencional de conteúdo orofaríngeo ou gástrico no trato respiratório é conhecida como aspiração. A rinorréia pode causar pneumonia por aspiração (vazamento de líquido cefalorraquidiano).

Objetivo Existem poucos relatos na literatura sobre pneumonia como complicação da rinorréia. Não há relatos sobre como lidar com esses casos se eles se apresentarem à clínica no pico da doença COVID-19 e distinguirem entre essas duas condições.

Métodos Revisamos a literatura e analisamos retrospectivamente as informações clínicas e os protocolos de tratamento utilizados para tratar os dois casos clínicos.

Resultados Ao rastrear a PCR e os anticorpos da COVID-19 mais de duas vezes, a cirurgia foi adiada por 10 a 14 dias em ambos os casos para descartar pneumonia induzida pela COVID-19. A tomografia computadorizada de tórax ainda revelou opacidades em vidro fosco. Em ambos os casos, o defeito na base do crânio foi reparado. Em ambos os casos, os sinais radiológicos de pneumonia induzida por rinorréia foram completamente resolvidos nos acompanhamentos de 24 e 30 dias.

Conclusão A aspiração do LCR causa alterações radiológicas nos pulmões na rinorreia. Esta é uma diminuição local de curto prazo na leveza do tecido pulmonar (preenchimento parcial dos alvéolos com fluidos), que é visível radiograficamente (opacidades em vidro fosco). Para descartar infecção por COVID-19, a cirurgia deve ser adiada por 10 a 14 dias e a PCR e anticorpos (IgG, IgM) devem ser realizados pelo menos duas vezes. Se o teste de rastreio da COVID-19 for negativo, pode ser agendada uma cirurgia reparadora.

Palavras-chave

- Ema licorosa do LCR
- COVID 19
- aspiração
- pneumonia
- cirurgia de reparo da base do crânio

Introduction

Nasal liquorrhea is a leakage of cerebrospinal fluid from the cranial cavity into the nasal cavity or paranasal sinuses caused by a congenital or acquired defect in the bones and meninges of the skull base.[1]

Meningitis, meningoencephalitis, pneumocephalus, and brain abscess are all potentially fatal complications of rhinorrhea. Complications such as aspiration bronchopneumonia and gastritis are possible.[2,3] With pronounced outflow of cerebrospinal fluid in the supine (horizontal) position, cerebrospinal fluid can frequently enter the lower respiratory pathways from the nasal cavity/nasopharynx, resulting in aspiration bronchopneumonia and patients presenting clinically with complaints of cough that is most often reproduced in the supine position.[4] The epidemiology of pneumonia has been reported to be between 5 and 10 cases per 1000 inhabitants in Europe and North America.[5] According to one study, more than 1.5 million of the country's adult population suffers from pneumonia, and the death rate can reach thousands each year.[6] The statistics presented here emphasizes the importance of early diagnosis and treatment of the condition. Viral pneumonia is the most difficult to diagnose, and it has a seasonal nature, occurring primarily during the winter session. A new epidemic of coronavirus infection caused by SARS-CoV-2 occurred in December 2019.[7–11] The primary manifestation of the disease is pneumonia, but asymptomatic or mildly symptomatic involvement of the upper respiratory tracts may also occur, which resolves within a week of infection.[12,13] The detection of viral RNA with real-time reverse transcription test (PCR) is currently the gold standard for the diagnosis of COVID-19, and the combination of computed tomography data with PCR false-negative results in COVID-19 suspected patients is another important addition for the differential diagnosis.[14,15] We present the diagnosis and treatment modalities of our two cases with rhinorrhea and COVID-19 positivity, as well as a review of the relevant literature.

Case Presentation

Clinical Case-1

Sixty-seven-year-old patient complained of clear fluid discharge from the nose while tilting head down for six months, with a gradual increase later in the course. The patient was initially diagnosed and treated for allergic rhinitis, but no improvement was observed. Three months after the onset of symptoms, the patient developed a high-grade fever (100,4°-102,2°F) and a headache. In this case, suspected meningitis was ruled out, and an MRI revealed a pituitary adenoma with no neurological deficits at the time [►**Fig. 1**]. IgM and IgG antibodies for the (SARS-CoV-2) virus was found to be negative in an RNA PCR test. Chest CT revealed hyper dense opacities in the "ground glass" pattern in the bilateral lower lobes of the lungs and the 3, 4, and 5 segments of the right lung. There was no dilation in the roots of the lungs, and no fluid was found in the pleural cavity. There were no simultaneous diaphragm changes, and the mediastinum was not displaced [►**Fig. 2**]. The patient has no prior knowledge of the Covid-19 case. Leukocytes were 4.351009/l in laboratory tests, neutrophils were 72.4 percent, granulocytes were 1.1 percent, and lymphocytes

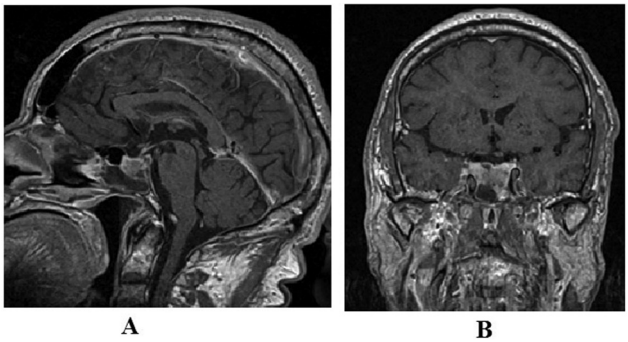

Fig. 1 Endo-infra-sellar lesion of hypophyseal gland. MRI with contrast enhancement in sagital view (A) and coronal view (B).

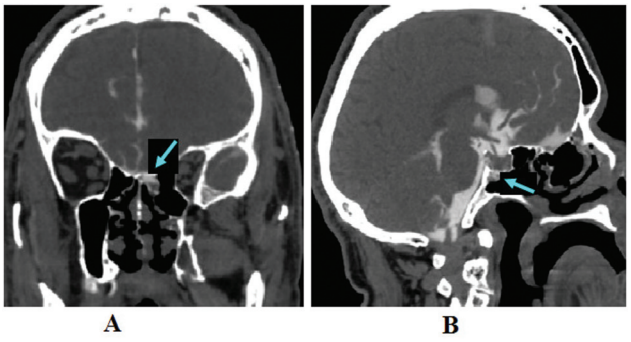

Fig. 3 CT cisternography. Show two defects at different sites of skull base; one at the bottom of Turkish saddle (B), Posterior ethmoid bone cells from the rightside (A). Defects are shown by arrows.

were 0.85109/l. SARS-CoV-2 induced pneumonia was suspected based on the pandemic spread of COVID-19 infection, decreased lymphocytic count, and ground glass opacities in chest CT. In contrast, given the chronic nature of the nasal discharge and chest, CT changes could have resulted from CSF aspiration into the lungs.

As per the protocol in a pandemic, we in our hospital do not hospitalize patients with active or suspected coronavirus infection. The patient's scheduled surgery was postponed for 10–14 days so that dynamic changes in the new chest CT could be evaluated, new swabs from the nose and throat could be administered, blood re-screened for IgG and IgM antibodies could be administered, and a decision about hospitalization and surgical treatment could be made based on the results. However, no COVID-19 RNA was detected by PCR, no IgM and IgG antibodies (ELISA) were found, and a repeat Chest CT done after 16 days revealed multiple focal infiltrative changes in the lungs but no significant dynamic shift in comparison to the previous one. According to a negative PCR for COVID-19 and negative (IgM, IgG) antibodies, chest CT changes were interpreted as a result of CSF aspiration and the resulting CSF induced aspiration Pneumonia, and the patient was admitted to the hospital for surgical repair of the defect.

A CT cisternography was also performed prior to surgery, which revealed defects at two different sites at the skull base, one in the sella floor and the second in the posterior ethmoid bone cells from the right side (►**Fig. 3**). Endoscopic transnasaltranssphenoidal adenoma resection was combined with plasty of the two CSF fistulas, one at the base of sella turcica and the other at the level of posterior ethmoid cells from the right side, using allograft and autograft materials. Pituitary adenoma resection was performed first, followed by soft tissue (fat and fascia) removal from the superolateral aspect of the thigh. The sellar cavity was filled with fat, and a piece of fascia lata was used to close the gap at the level of the posterior ethmoid cells. A free flap of mucosal pedicle with maintained circulation was used to cover and reinforce the defect, which was then fixed in place with fibrin-thrombin glue.

The postoperative period was uneventful. There were no somatic or neurological deficits revealed. There were no signs of nasal liquor rhea after the surgery, and the patient was discharged from the hospital on the ninth day. The histopathological examination confirmed the adenoma diagnosis. The inflammatory changes in the lungs were significantly improved on a repeat chest CT performed 24 days after surgery.

Clinical Case-2

A forty-year-old man presented with complaints of clear nasal discharge for the previous year. The defect was discovered during imaging at the base of the skull, near the sphenoid bone. Plasty of the skull base defect was performed

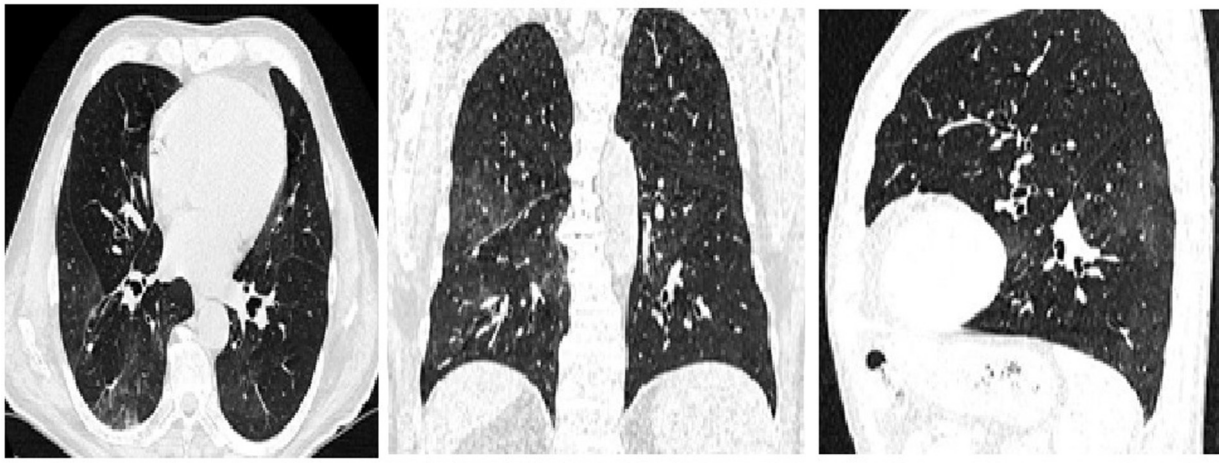

Fig. 2 CT chest prior to surgery.

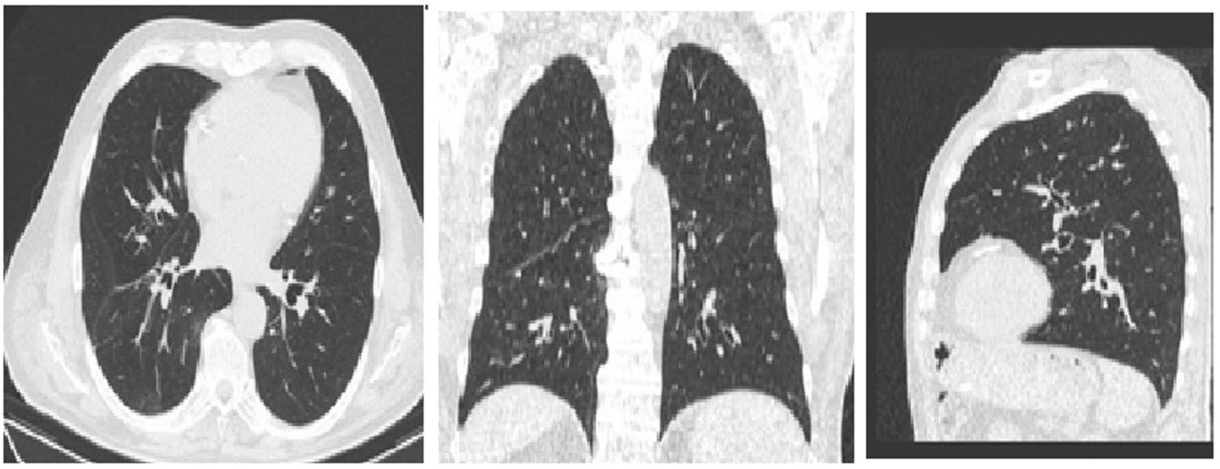

Fig. 4 CT of lungs after plasty of the skull base defects causing liquorrhea (regression of inflammatory changes).

using a transsphenoidal approach, and the patient was discharged with no postoperative leakage complaints. Nonetheless, three months later, the patient complained of nasal liquorrhea, a cough during the night, and headaches. A second defect was discovered in the sphenoid sinus's lateral pocket from the right side during a repeat examination, in addition to the meningoencephalocele (►**Fig. 5**).

In a ground-glass pattern, inflammatory changes were seen bilaterally on chest CT (►**Fig. 6**). A PCR test for SARS-CoV-2 was performed twice, and no coronavirus RNA was detected, as well as no IgM or IgG antibodies to the coronavirus. Clinical and biochemical blood tests were also normal, and there were no signs of intoxication. There was no positive history of contact with the COVID-19 patient, and no family members were also infected with SARS-CoV-2. This patient was also kept under dynamic observation for 14 days, and a repeat SARS-CoV-2 (PCR) analysis was performed, which came back negative, with no IgM/IgG antibodies detected. After a repeat chest CT revealed no dynamic changes, the patient was admitted to the hospital for a second surgical repair of the defect. The defect was plastyed using an endoscopic transnasal approach; the defect was approached via the pterygoid approach, and the meningoencephalocele was removed. The defect was filled with fat, and a large piece of fascia lata was removed from the leg; all layers of plasty were reinforced and fixed with fibrin-thrombin glue. The recovery period was uneventful. There was no nasal liquorrhea in the early postoperative period. Five days after surgery, the patient was discharged with instructions to remain under observation at the regional hospital. The radiological signs of pneumonia on a new chest CT regressed completely in the late postoperative period (one month after surgery), and no antibodies to SARS-CoV-2 were detected.

Discussion

Aspiration refers to the unintentional ingestion of oropharyngeal or gastric contents, liquids, or other hard materials into the lower respiratory tracts. The nature of the aspirated materials, microbiocenosis of the respiratory mucosa, and colonisation by pathogenic microflora all influence clinical response to aspiration.[16,17] Aspiration of CSF into the lungs is possible with severe nasal leaks, which can cause respiratory tract inflammation. Patients suffering from liquor rhea typically complain of coughing while lying in a supine position. There are only a few reports in the literature about

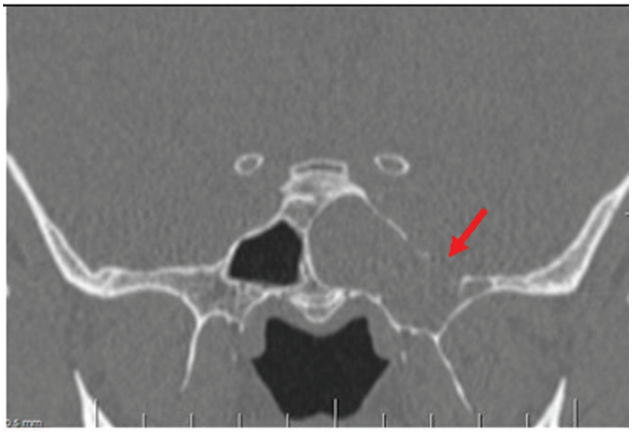

Fig. 5 Defect at the lateral pocket of sphenoid sinus in the right side (red arrow).

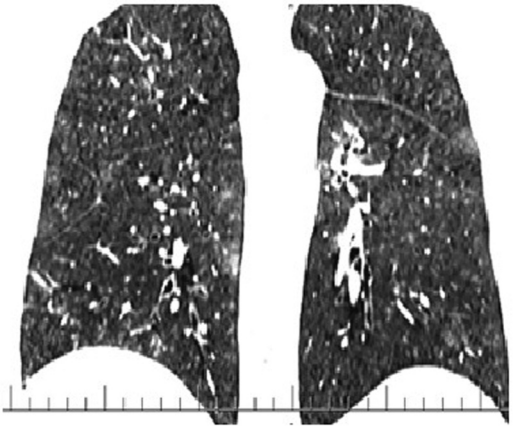

Fig. 6 CT chest of patient with nasal liquor rhea. (Ground glass appearances are present).

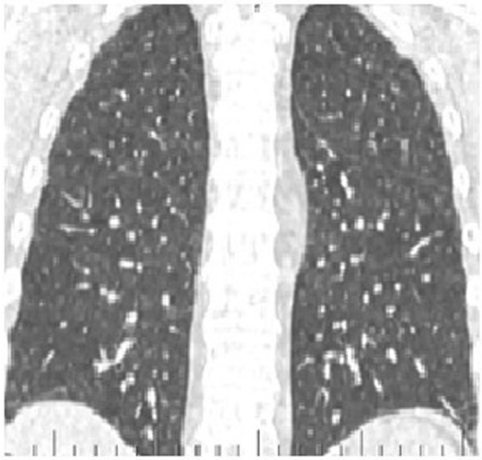

Fig. 7 CT of lungs after plasty of the skull base defect. (regression of inflammatory changes).

pneumonia as a complication of nasal liquor rhea.[18] Until Justin Seltzer et al[19] published their first article on this issue in 2016, reports on this complication were only given in series dedicated to the treatment of nasal liquor rhea. There were no reports on the clinical/diagnostic signs or treatment methods for aspiration pneumonia. It was most likely due to the fact that this complication was not considered important in clinical practice but gained significant importance during the SARS-CoV-2 pandemics.[11,20–26]

From 2016 to 2020, four articles related to aspiration pneumonia were reported in the PubMed search engine, which included nine patients with nasal liquor rhea. ►**Table 1** summarizes the findings of these patients. In the given articles, the average age of the patients was 51 years (33–76 years). Many patients (8,88.9%) were females. 7 (77.8 percent) were overweight, and 5 (55.6 percent) were obese. At the time of presentation, the most common complaints were nasal discharge, cough, and shortness of breath. In 2 (22.2 percent) of the cases, elevated body temperature and classic signs of intoxication were observed. In most cases, radiological studies of the lungs revealed ground glass opacities 7 (77.8 percent). There was no correlation found between the side of the defect and the involvement of the right or left sided lung; in many cases, involvement was bilateral (88.9 percent).

Table 1 Summeries of aspiration pneumonia cases associated with nasal liquor rhea

Authors	Gender	Age	Etiology of leakage	ИМТ	Complaints	Radiography/ CT chest	Localization of defect
[Justin Seltzer][19]	F	44	Spontaneous	36,5	Discharge from the right nostril, cough, dyspnea during physical stress, snoring	Deranged respiratory exchange in bilateral lower lobes of lungs	Roof of ethmoid sinus from the right side
[Maya Or][27]	F	76	Spontaneous	37	Discharge per right nostril, dyspnea, cough	Peri-bronchial ground glass opacities in all lobes	Roof of ethmoid sinus from the right side
[Maya Or][27]	F	51	Spontaneous	36	Discharge from right nostril, periodic cough, meningitis	Bilateral ground glass opacities, thickening of bronchial walls	Sphenoid sinus from the right
[Maya Or][27]	F	44	Spontaneous	37	Periodical discharge from right nostril, dyspnea during physical stress, snoring.	Bilateral disturbance of respiratory gas exchange in lungs (left > right)	Lamina cribrosa from the right side
[Maya Or][27]	F	54	Spontaneous	41	Discharge from left nostril, headache	Ground glass opacities in right side.	Roof of ethmoid sinus from the left side
6[Maya Or][27]	F	36	Spontaneous	31	Discharge from left nostril, cough, dyspnea, snoring	Ground glass opacities in bilateral in both upper lobes + left lowere lobe.	Roof of ethmoid sinus from the left side
[Maya Or][27]	M	64	Spontaneous	21	discharge from left nostril	ground glass appearance bilaterally, thickening of the bronchial wall, bronchiectasis	Pyramids of Temporal bone
[Mark G Jones][28]	F	33	Spontaneous	no given	Nasal discharge, cough, chest discomfort and pain in chest, raised temperature	Ground glass opacities in both lungs	Lamina Cribrosa
[Wasgewatta][29]	F	53	Spontaneous	35	Nasal discharge, cough, raised temprature.	Bilateral Ground glass opacities in lower lobes.	Lamina cribrosa from the right side

Justin Seltzer et al.[19] and Mark G Jones et al.[19] report that they were unable to exclude nasal liquorrhea as the causative agent of pneumonia at the outset. In both cases (patients 1 and 8), they receive several courses of antibiotic therapy as well as other symptomatic treatment; however, the symptoms of pneumonia recur and worsen after the antibiotics are discontinued. Following that, a lung biopsy was performed in both cases, which revealed no evidence of chronic pneumonitis or bronchiolitis. Following a joint discussion, the hypothesis of aspiration induced pneumonia was advanced, and endoscopic endonasalplasty of the skull base defect was performed in both cases after the diagnosis of nasal liquor rhea. According to the authors, after performing a control chest CT in both cases, complete resolution of pneumonia was observed in the postoperative period.

Maya O.R et al.[27] reported on six cases of pneumonia caused by nasal liquorrhea. According to the authors, they performed plasty of the skull base defect without treating pneumonia in the pre and postoperative periods. In all the cases presented, the signs of pneumonia regressed in the postoperative period following treatment of the defect closure. Sanjiwika Lalanjani Wasgewatta et al[16] described a case of spontaneous nasal liquorrhea and pneumonia during CPAP therapy for obstructive sleep apnea syndrome. Following CPAP treatment, the patient developed a cough, headache, nasal discharge, and fever. Following that, the patient underwent endoscopic endonasalplasty of the skull base defect as well as ventriculoperitoneal shunting. A week after the operation, a repeat CT of the chest was performed, and the signs of lung tissue involvement vanished. In our cases, the patients' pneumonia completely resolved after the CSF fistula was closed. During the rapid spread of COVID-19 infection, the neurosurgery center continued to provide patients with cutting-edge medical care. An algorithm was developed to reduce and prevent the nosocomial spread of infection among patients, considering epidemiological data (history of contact with patients infected with COVID-19), laboratory data (detection of SARS-CoV-2 virus RNA by PCR), and data from chest CT before hospitalization.

COVID-19 lung changes are quite variable; however, most authors agree that the most common and distinctive findings are parenchymal thickening in the form of ground glass opacities (single or multiple) or a combination of these changes with consolidation and/or reticular changes (cobblestone changes).[30] The appearance of bilateral changes in the lungs, predominantly in sub-pleural localization and in the absence of pleural effusion, is one of the most common chest CT manifestations of covid-19 pneumonia. However, the dorsal allocation of CT changes with involvement of multiple lobes of the lungs, particularly the lower ones. In our case, the patient's chest CT revealed ground glass opacities. This sign, however, is not pathognomonic; rather, it is an indicator of lung tissue thickening and an indication of interstitial type of infiltration. Certain areas of the lungs with "ground glass" opacities have a moderately reduced airiness index. The occurrence of this phenomenon is caused by thickening of the inter-alveolar septa as well as partial filling of the alveoli with inflammatory contents.[31,32] In the context of the COVID-19 pandemic, it is now necessary to perform a chest CT on all patients to look for the disease's characteristic "ground glass" opacities. Patients with profuse nasal liquor rhea pose a serious problem in terms of differential diagnosis in this scenario, as they have similar chest CT findings, which is dangerous during hospitalization of these patients in hospitals where patients with corona virus are also treated. In our opinion, dynamic observation of chest CT findings, repeated tests for IgG and IgM antibodies, and PCR for COVID-19 RNA allow us to exclude or confirm the diagnosis of COVID-19 and determine a further plan of care for such cases. In cases of nasal liquor, detection of CSF-induced aspiration pneumonia is possible by performing a chest CT scan; however, due to the current COVID-19 pandemic, PCR for coronavirus RNA is recommended in such cases, along with IgM and IgG antibodies for at least two times. If the results of both tests are negative and there are no clinical signs/symptoms of COVID-19, there are no contraindications to general anesthesia and surgery, and the patient can be hospitalized in a separate ward and plastic surgery of the skull base defect can be performed.

Conclusion

Aspiration of cerebrospinal fluid causes radiological changes in the lungs in patients with nasal liquorrhea. In such cases, radiological changes may manifest as a short-term local decrease in the airiness of lung tissue ("ground glass" opacities), representing the partial filling of the alveoli with fluids but with no clinical manifestations. In such cases, patients should have a PCR diagnostic test for SARS-CoV-2 virus RNA and antibodies (IgM, IgG) performed at least twice, as well as a CT of the chest. If there are signs of ground-glass opacity, it is recommended that the operation be postponed for 10–14 days to reassess chest CT changes and repeat the coronavirus detection test to rule out the viral nature of the lung tissue involvement.

Consent for Publication

Proper informed and written consent in local understandable language was taken from the patient regarding the publication of the same cases.

Ethics Approval

There is no ethics issue in this paper.

Data Availability Statement

The data will be available from address of correspondence on reasonable request.

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Conflicts of Interest

There are no conflicts of interest.

Acknowledgment
Nothing to Declare.

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