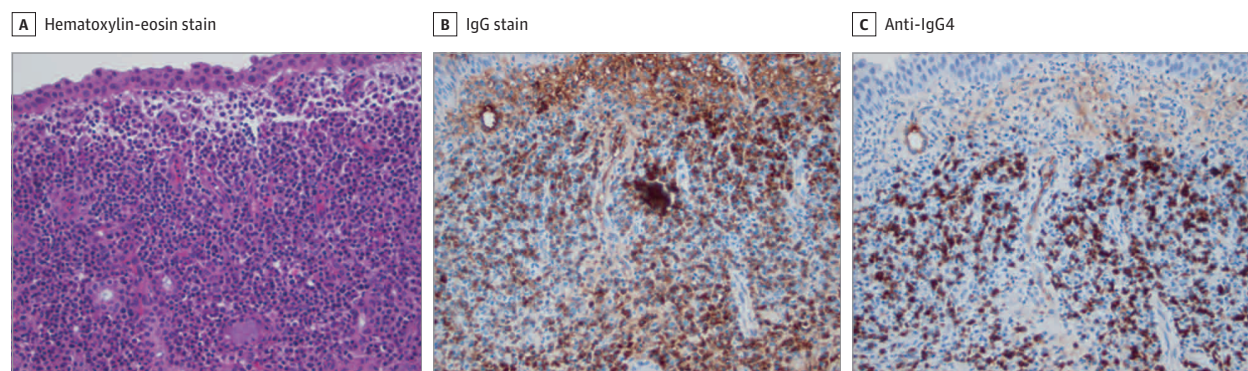


Figure 2. Histopathologic Images



A, A dense band-like infiltrate of lymphocytes and plasma cells was present beneath the epithelium (original magnification  $\times 40$ ). B, IgG stain demonstrates 50 to 100 plasma cells in many high-power fields (original magnification  $\times 40$ ).

C, Most of the IgG-containing plasma cells were IgG4 positive (original magnification  $\times 40$ ).

comprehensive diagnostic criteria for IgG4-RD.<sup>3</sup> Moreover, cultures grew *S. constellatus*, a commensal bacterium associated with orbital invasion,<sup>4</sup> although acute vision loss in rhinosinusitis can occur from other bacteria.

Importantly, this patient's prior SARS-CoV-2 infection suggests a possible relationship between COVID-19 and IgG4-RD. Immunoglobulin G4-RD is mediated by cytotoxic CD4-positive T-cells, an atypical subset of helper T-cells with cytotoxic ability.<sup>1</sup> Increased representation of cytotoxic CD4-positive T-cells was recently discovered in SARS-CoV-2 reactive T-cells, with higher levels associated with hospitalization.<sup>5</sup> This finding signals a possible link between COVID-19 and IgG4-RD, which was suspected earlier in another patient who developed IgG4-related subglottic stenosis after COVID-19.<sup>6</sup>

Overall, COVID-19 may have led to either exacerbation of underlying IgG4-RD or an IgG4 response, with simultaneous precipitation of an acute bacterial rhinosinusitis. Although corticosteroids are standard for IgG4-RD and antibiotics for bacterial rhinosinusitis, simultaneous use of both was effective in this patient who had both diseases. Hence, corticosteroids and antibiotics may be indicated in patients with severe rhinosinusitis until either IgG4-related or bacterial rhinosinusitis can be ruled out.

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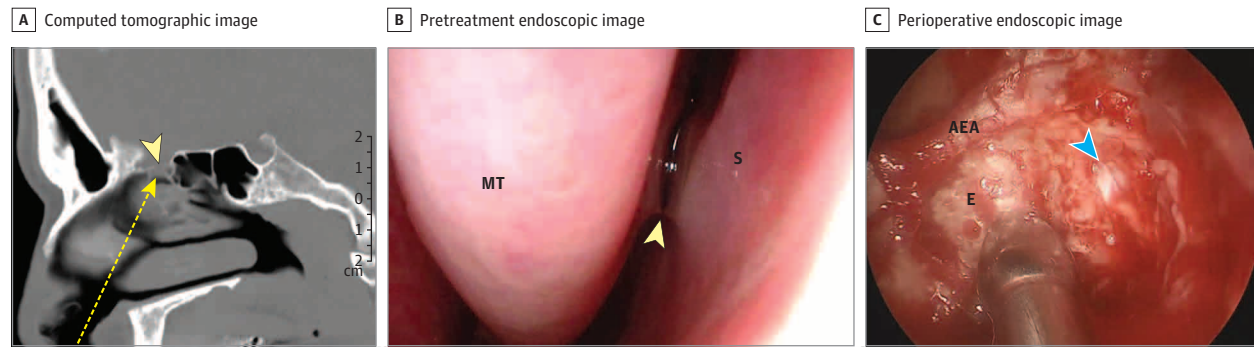
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### Cribriform Plate Injury After Nasal Swab Testing for COVID-19

In March 2020, the World Health Organization characterized the spread of coronavirus disease (COVID-19) as a pandemic. A lot of nasal swabs were used to diagnose COVID-19 to detect the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the upper respiratory tract. We present a case of cerebrospinal fluid (CSF) leak after skull base injury following nasal swab testing for COVID-19 in a patient with a previously intact skull base.

Figure. Computed Tomographic and Clinical Images



A, Computed tomographic scan of the sagittal plane. The yellow arrowhead points at the defect in cribriform plate on the right side of the nasal cavity. The dashed arrow represents the assumed trajectory of the nasal swab. B, Endoscopic image of the right side of the nasal cavity. The yellow arrowhead points to clear secretion between the middle turbinate (MT) and the septum

(S). C, Perioperative endoscopic view of the skull base on the right side of the nasal cavity. The blue arrowhead points at the defect in the cribriform plate. The roof of the ethmoids (E) and canal of the anterior ethmoidal artery (AEA) can be seen in proximity of the defect.

**Report of a Case** | An otherwise healthy man in his 40s presented for right-sided clear water rhinorrhea in December of 2020. Rhinorrhea originated after nasal swab testing and was mistakenly considered to be allergic rhinitis in the patient. The test was performed by a mobile unit at the patient's home in March of 2020. The test was indicated because of previous contact with a woman who had a positive COVID-19 test result 5 days earlier. The patient had no symptoms of COVID-19 infection and RNA of SARS-CoV-2 was not detected by polymerase chain reaction (PCR) testing. The patient had no other symptom except persistent unilateral nasal discharge from March to December 2020. During this period he did not report any signs of meningitis. The first examination at an ENT specialist was done in December 2020, 9 months after the first symptom appeared.

Clear nasal secretion medial to the middle turbinate on the right side was noticeable during nasal endoscopy. On computed tomographic (CT) scan there was a defect in the lamina cribrosa on the right side (Figure). A previous brain CT scan from 2011 showed no skull base defect or other pathology. We collected 3 mL of nasal discharge, and analysis showed a high level of the beta-trace-protein in the nasal secretion (23.7 mg/L; normal range, <6 mg/L). The patient's olfaction was normal, with an Odorized Markers Test score of 11 of 12 points.<sup>1</sup>

Endonasal endoscopic closure was performed in December of 2020 with antibiotic prophylaxis (ciprofloxacin, 400 mg twice daily) that continued for 7 days postoperatively. The defect in the lamina cribrosa was identified and cleaned from surrounding mucosa. Temporal muscle fascia was used as an underlay graft. Mucosa from the middle turbinate was used as an overlay graft and fixed with fibrin glue.

The patient was dismissed on the second day after surgery, instructed to avoid blowing the nose. No unexpected adverse events were observed in the postoperative period. Three weeks after surgery, no crusting or rhinorrhea was observed on nasal endoscopic findings. The patient reported anosmia when trying to sniff with the right side of the nasal cavity. The

score of an Odorized Markers Test was 8 points (hyposmia, testing both sides).

**Discussion** | Laboratory diagnosis of COVID-19 is based on detection of SARS-CoV-2 RNA in the upper respiratory tract by real-time reverse transcription-PCR (RT-PCR). Detection of viral antigens is also a method of choice. The gold standard is collection of the specimen from the nasopharynx through transnasal swab testing. From March 2020 to May 2021, more than 25 million tests were performed in the Czech Republic.

Common complications encountered after nasal swab testing included broken and compacted swabs in the nasal cavity and nosebleed. Rarely the epistaxis required nasal packing or surgical cauterization.<sup>2</sup>

A CSF fistula is a rare but dangerous complication. The iatrogenic CSF leak after nasal swab testing for COVID-19 was reported after trauma to the preexisting skull base erosion.<sup>3,4</sup> To our knowledge, there are no reports of CSF leak after nasal swab testing in patients with no preexisting pathology in nasal cavity or skull base.

**Conclusions** | Complications after nasal swab testing can be expected during the COVID-19 pandemic owing to an increase in nasal swab testing. Every instance of unilateral clear water rhinorrhea that appears after transnasal testing must be considered a potential CSF leak. To our knowledge this is the first case report presenting CSF fistula following the nasal swab testing in a healthy man with no preexisting skull base condition.

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## COMMENT & RESPONSE

### Is There Sufficient Evidence for Continuous Local Anesthetic Wound Infusions as Postoperative Standard of Care in Patients With Head and Neck Cancer?

**To the Editor** We thank Gostian et al<sup>1</sup> for their study demonstrating a reduction in postoperative pain when continuous wound infusion (CWI) was used after head and neck oncological resections. The authors call for CWI to be assimilated into the multimodal postoperative analgesic concept in patients. However, prior to widespread implementation, we find it prudent to draw attention to a few caveats to the study's conclusions.

First, based on trial protocol, patients in the intervention group experiencing pain at Numeric Rating Scale (NRS) greater than 3 at rest were given further analgesia. Intensifying analgesic therapy based on an NRS cutoff would inevitably confound the rating scales in the intervention group in subsequent days. This results in artificially lower daily mean and maximal NRS levels in the intervention group compared with the control group. Given that 47% and 10% of the intervention group received level 1 and 2 analgesic therapy, respectively, the true effect of CWI in suppressing NRS levels (a proxy for pain) is unclear. Therefore, the interpretability of NRS levels for pain control is somewhat limited in this study.

Moreover, although acknowledged by the authors, the effect of the lack of blinding in this study has been understated. Studies have shown both intraoperative (surgical techniques conserving anatomical structures, patient positioning, etc) and postoperative (physical therapy, patient-controlled analgesia) factors have an effect on postoperative pain.<sup>2</sup> In addition, performance bias in the intervention group due to the knowledge of the CWI device in situ also overestimates its effects. These biases, amalgamated with the biological, social and psychological aspects to pain perception,<sup>3</sup> have an unknown level of effect on the favorable results seen in this study.

Apprehension and expectations surrounding the operation cause variations in pain experience, factors that are unique to the individual.<sup>4</sup> This could explain the large standard deviation in the NRS scores, and the study's small sample size exacerbates this. A subgroup analysis on a larger patient pool, categorizing patient data based on rise in pain score before and after surgery in both arms of the study, could be a viable means of circumventing this issue.

Nonetheless, Gostian et al<sup>1</sup> have crucially advocated for local anesthetic use in postoperative pain management for head and neck cancers, thereby reducing systemic analgesic use and improving patients' quality of life. Future research with a more rigorous protocol including a larger sample population, with double-blinding measures, randomization, and placebo control could strengthen conclusions from this study.

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**In Reply** We are pleased to respond to the comments by Vishnu K. and Vishnu K. on our article, "Postoperative Pain Treatment With Continuous Local Anesthetic Wound Infusion in Patients With Head and Neck Cancer: A Nonrandomized Clinical Trial."<sup>1</sup>

The trial protocol mandated that patients of both study groups receive further analgesic treatment in case they experienced pain levels higher than 3 on the Numeric Rating Scale (NRS). Pain intensity was classified using the NRS because it leads to the most valid results, has a low error rate, high acceptance and sensitivity, and is easy to understand and apply.<sup>2</sup> Nevertheless, cutoff points for mild, moderate, and severe pain are not standardized. Gerbershagen et al<sup>3</sup> classified an average pain of NRS of 4 greater as a moderate-to-severe pain and tolerable pain threshold. It was considered to be the cutoff point for intervention and