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The Treatment Paradigm of Chronic Rhinosinusitis with Nasal Polyps in the COVID-19 Era



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As the first wave of coronavirus disease 2019 (COVID-19) ebbs in the United States, many medical practices are preparing to open up cautiously and otolaryngologists are beginning to perform elective endoscopic sinus surgery (ESS) again.¹ In the process of resuming and restructuring care of these patients, how to balance risk and benefit is complicated and affects decisions about patient and provider safety, altering the immune system, and choosing diagnostic and therapeutic approaches. The approval of dupilumab and the upcoming approvals of other biologics have diversified treatment options. The treatment paradigm for chronic rhinosinusitis with nasal polyposis (CRSwNP) in the era of these new drugs was the subject of discussion at a National Institute of Allergy and Infectious Diseases workshop.² How should we be thinking about how to manage CRSwNP in the COVID-19 era given recent events?

SAFETY

Clinical evaluation

Evaluating the patient with CRSwNP poses new risks to patient and provider and requires us to consider a few facts. The upper airway is the first point of entry for this pathogen, and the nose/nasopharynx contains the highest titers of the virus regardless of the presence or absence of symptoms. Aerosolization and droplet transmission of the virus from infected individuals are thought to be the major routes of spread. Tests for COVID-19 have false-negative rates of between 5% and 30% at best.³

These data have led to several recommended modifications that have increased the time needed to see patients with CRS and perform necessary endoscopy for workup. They also led to the need for negative pressure rooms to perform aerosol-generating procedures (eg, debridement) and lengthy protocols for room

sterilization and cleaning, with consequent increased expense and resources, in terms of both personnel and equipment/supplies. Extensive personal protective equipment (PPE) prevents the spread of COVID-19 to health care workers,⁴ but these protective measures increase time and cost. Other changes have been made as well. For example, some have recommended applying topical decongestants and anesthetics by pledgets rather than by sprays to minimize coughing and sneezing.⁵ Others have suggested having the patient wear a mask and performing endoscopy through a small hole.⁶ Authors from locations with relatively high numbers of patients with COVID-19 have even considered computed tomography scan in lieu of endoscopy for the assessment of polyps.⁷ Seeing patients in ways that minimize risk remains a challenge without hard data to guide us.

Surgery

ESS is a medically necessary, time-sensitive surgery⁸ for the treatment of CRSwNP, but poses risks to providers. ESS can involve drilling, which increases the risk of aerosolization of viruses. Whether the microdebrider, which is more frequently used during surgery, causes aerosolization is less likely, but is being evaluated.⁶ Aerosolized viral particles can live on surfaces, including instruments, for up to 3 days, affecting cleaning of rooms and instruments. After aerosolization, viral particles may also remain suspended in the air, with implications for air exchange and filtration.⁵ In addition, general anesthesia suppresses the immune system.⁹ In half the patients undergoing all kinds of surgery with perioperative (before surgery or up to 30 days postoperation) SARS-CoV-2 infection, postoperative pulmonary complications occurred in more than 50% of the patients, with high associated mortality.¹⁰

These concerns affect the safety considerations for patients and surgeons, health care costs, and preoperative and postoperative management. Perhaps the biggest cost, which is difficult to estimate, is when a patient or health care worker requires hospitalization for COVID-19 contracted during care.

Medical therapy

Medical treatments may also carry risks. Saline irrigations may cause virus aerosolization and spread of disease, and there is conflicting data on the effect of systemic steroids, a mainstay of treatment for CRSwNP, on COVID-19.^{1,11,12} Limited work in asthma suggests that inhaled steroids may be protective, but effects in the nose are unknown.¹³ Continuing intranasal corticosteroids for allergic rhinitis has been recommended to avoid sneezing and spread of illness.¹¹ However, others have recommended against their use for the immediate smell loss that appears to characterize COVID-19.¹²

Biologics are another option for the treatment of CRSwNP. So far, biologics do not appear to increase the risk of acquiring

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COVID-19 nor worsen disease in those who are infected.¹⁴⁻¹⁶ Some have recommended that these medications should not be initiated in new patients due to unknown risks, though these recommendations are based on expert opinion, not data.¹⁷ The effect of dupilumab, the only currently approved biologic for CRSwNP in the United States, on acquiring or aggravating SARS-CoV-2 infection has been questioned. How should clinicians approach these issues?

ALTERED IMMUNOLOGIC MECHANISMS

CRSwNP is most commonly T_H2-mediated, which may explain why clinical trials show that dupilumab is effective in about 70% of patients with CRSwNP.¹⁸ Interestingly, T_H2 diseases appear to downregulate angiotensin-converting enzyme 2 (ACE-2), the coronavirus receptor, implying that patients with atopic processes may be protected.¹⁹ The clinical importance of this fact is far from clear. We currently lack data regarding the appropriate use of biologics in patients with CRSwNP overall, much less in the setting of COVID-19. These data led us to formulate a few observations. First, in patients with CRSwNP not taking biologics, a reduced expression of ACE-2 in nasal polyp versus control tissue has been reported.²⁰ In patients with severe asthma, inhaled corticosteroids are associated with decreased ACE-2 expression.¹³ Whether these findings are due to the immune-modulating effects of medications or the disease itself is unclear. Understanding the mechanisms behind this could be useful, both in CRS and more broadly. Second, dupilumab is self-administered at home, and may help avoid repeated surgeries, endoscopies, and debridements. Thus, this medication may prove to be useful, particularly during periods of limited in-person clinical availability and prolonged social distancing precautions. Preliminary data have not identified increased risk of COVID-19 severity in patients taking biologics; however, because of dupilumab's targeted interference with the T_H2 response, the effect on ACE-2 receptor expression and immune response to infection more broadly are relevant and should be further evaluated. It is a challenge to consider how such therapies may alter the immune system in ways that affect risk to patients.

WEIGHING NEW APPROACHES FOR DIAGNOSIS AND THERAPY IN THE COVID-19 ERA

As we transition to the next phase, we believe that the field of rhinology will be dramatically affected. The major challenge we face is how to calculate risk and benefit as we begin to care for our patients in the setting of uncertainty. The risk of viral spread to health care workers can be minimized but not eliminated by high efficiency particulate air filters, PPE, and enhanced cleaning, which reduce efficiency and increase cost and will be required for the foreseeable future. How treatments affect the immune system and health overall remains unclear. Unfortunately, we lack data-driven recommendations regarding best treatment algorithms at this time. Although cost remains a factor for the use of biologics, resources, PPE, and safety concerns have also become significant limitations for both surgical and medical treatments during this time. To minimize risk and increase access, video and phone telemedicine visits have been widely used during the pandemic, but are limited in the management of CRSwNP by an inability to perform nasal endoscopy, although they are likely to play some role in the future.

At most, if not all, centers, patients with CRSwNP with COVID-19 will not receive any treatment (surgery, dupilumab, or oral corticosteroids) until the infection resolves. Should all patients with CRSwNP be tested for COVID-19 before treatment? Perhaps. However, the high false-negative rate, availability, and the time needed to receive results limit utility and impact decision making. Again, clinicians must consider pros and cons. While the pandemic affects population health, clinicians must consider personalized medicine for their patients. Thus, we strongly believe that shared decision making is extremely important during these times, and potential benefits and risks of all options should be disclosed. Making the decision more difficult is that the risk calculus varies by location. As we continue to learn more from the rapidly increasing volume of reported data, flexibility in treatment planning will be paramount as new recommendations emerge.

CONCLUSIONS

The answer to our original question, will COVID-19 change the treatment paradigm of CRSwNP, is a resounding yes. We must all face tough choices as we decide how to optimize outcomes for our patients. How it will change the paradigm is not yet clear. As with the pandemic itself, what we learn about the virus will determine the answer.

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