Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Am J Otolaryngol 41 (2020) 102746

Contents lists available at ScienceDirect

Am J Otolaryngol

journal homepage: www.elsevier.com/locate/amjoto

Management of complicated pediatric rhinosinusitis in the COVID-19 era

Conor H. Blanco[a], John B. Stein[a], Gregory L. Barinsky[a], Christina H. Fang[a], Jordon G. Grube[a], Roger E. Turbin[b], Jean Anderson Eloy[a,b,c,d,*]

[a] Department of Otolaryngology – Head and Neck Surgery, Rutgers New Jersey Medical School, Newark, NJ, USA
[b] Department of Ophthalmology and Visual Science, Rutgers New Jersey Medical School, Newark, NJ, USA
[c] Department of Neurological Surgery, Rutgers New Jersey Medical School, Newark, NJ, USA
[d] Center for Skull Base and Pituitary Surgery, Neurological Institute of New Jersey, Rutgers New Jersey Medical School, Newark, NJ, USA

ARTICLE INFO

Keywords:
COVID-19
Coronavirus
Sars-CoV-2
Pediatric rhinosinusitis
Pediatric COVID-19
Complicated sinusitis

ABSTRACT

With the ongoing development of the COVID-19 pandemic, research continues to emerge regarding the pathophysiology, characteristics, and treatment considerations for patients with COVID-19. No reports have highlighted the specific challenges posed in the management of pediatric patients with COVID-19 who present with complicated rhinosinusitis. In this report, we discuss our preoperative, intraoperative, and postoperative multidisciplinary treatment strategy for these cases and provide two examples of complicated rhinosinusitis cases in COVID-19 patients, treated with two different approaches. Pearls, insights, and a brief review of the literature are discussed.

1. Introduction

Complicated rhinosinusitis is defined as the sequelae of direct extension of acute rhinosinusitis to adjacent structures [1,2]. Sequelae of complicated rhinosinusitis include orbital complications, such as preseptal cellulitis, subperiosteal abscess, orbital cellulitis, orbital abscess, and cavernous sinus thrombosis [1–4]. Intracranial complications also can occur, resulting in meningitis, epidural abscess, subdural abscess, intracerebral abscess, and osteomyelitis of the frontal bone [5]. Viral infections are the most common cause of rhinosinusitis and have been found to be a nidus for bacterial superinfection [6].

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which on March 11, 2020 was declared a worldwide pandemic by the World Health Organization (WHO) known as Coronavirus disease 2019 (COVID-19), has not previously been associated with complicated rhinosinusitis. Since the WHO declaration, there has been evidence reporting high viral loads of SARS-CoV-2 in the sinonasal cavity and nasopharynx [7]. As of July 18, 2020, over 14 million cases of COVID-19 have been reported worldwide with over 600,000 global deaths [8]. In the Unites States (US), COVID-19 cases have continued to demonstrate an upward trend since March 2020, now with over 3.6 million documented cases [8]. Despite vast research being performed to elucidate the pathophysiology, patient characteristics, and treatment considerations, no case of complicated rhinosinusitis in COVID-19 patients to our knowledge has been described in the current otolaryngology literature.

2. Illustrative Case I

An obese 15-year-old African American male with recent travel history presented to an outside emergency department (ED) with a three-day history of headaches, subjective fevers, nasal congestion, diarrhea, nausea, emesis, right periorbital swelling, pain, and blurred vision. Computed tomography (CT) revealed right-sided rhinosinusitis and an epidural collection posterior to the right frontal sinus (Fig. 1). He was transferred to our facility. The patient was febrile, tachycardic, and tachypneic, with a right-sided orbital cellulitis on exam. Nasal endoscopy revealed right middle meatal purulence and mucosal inflammation. He was neurologically intact. Table 1 highlights his laboratory values. SARS-CoV-2 ribonucleic acid (RNA) testing was positive.

Multidisciplinary management approach with otolaryngology, ophthalmology, neurosurgery, infectious disease, and pediatrics was initiated. Treatment consisted of vancomycin and ceftriaxone, tobramycin eye drops, nasal saline irrigation, intranasal oxymetazoline and fluticasone, and prophylactic levetiracetam. After no clinical improvement for 24 h, magnetic resonance imaging (MRI) revealed persistent rhinosinusitis, epidural collection, and superior ophthalmic vein

* Corresponding author at: Department of Otolaryngology – Head and Neck Surgery, Neurological Institute of New Jersey, Rutgers New Jersey Medical School, 90 Bergen St., Suite 8100, Newark, NJ 07103, USA.
E-mail address: jean.anderson.eloy@gmail.com (J.A. Eloy).

https://doi.org/10.1016/j.amjoto.2020.102746
Received 9 September 2020
Available online 23 September 2020

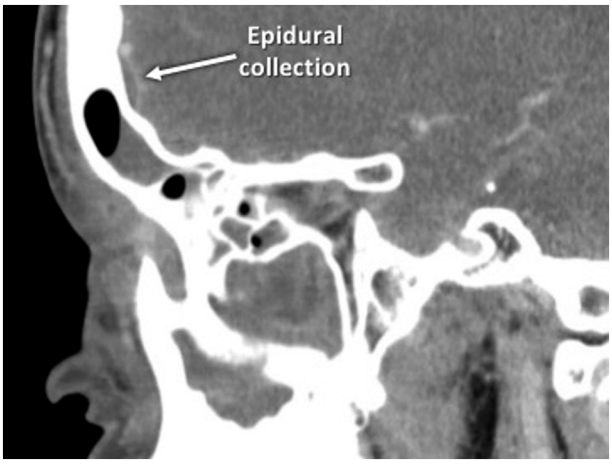

Fig. 1. Preoperative sagittal computed tomography scan of the paranasal sinuses of the patient in Case I depicting rhinosinusitis with a partially opacified right frontal sinus and a small epidural collection posterior to the right frontal sinus posterior table.

thrombosis (SOVT) (Fig. 2).

On hospitalization day 3, he developed worsening chemosis, proptosis, and visual acuity. He was taken to the operating room (OR) for endoscopic right maxillary antrostomy, total ethmoidectomy, and frontal sinusotomy (Fig. 3). Only non-powered instrumentation was utilized. Intraoperative cultures grew coagulase-negative *Staphylococcus*. Postoperatively, he developed hypoxia to 89% on room air. Chest x-ray revealed bilateral, patchy opacities. He was also started on metronidazole, hydroxychloroquine, enoxaparin, zinc, vitamin C, and thiamine. He necessitated transfer to the pediatric intensive care unit (PICU) for bilevel positive airway pressure (BiPAP) therapy. His respiratory status improved with further uncomplicated hospital course. He was continued to metronidazole and ceftriaxone for five weeks after discharge. After completion of his antibiotic regimen, he was subsequently lost to follow-up.

3. Illustrative Case II

A 12-year-old Egyptian male with seasonal allergies and remote history of adenotonsillectomy presented to an outside ED with nasal congestion and progressive right eye swelling for three days. He was evaluated by his pediatrician the day prior and started on oral amoxicillin/clavulanate and ofloxacin eye drops. CT revealed right-sided rhinosinusitis and subperiosteal abscess (Fig. 4). He was transferred to our facility. Table 1 highlights his laboratory values. SARS-CoV-2 RNA testing was positive. Vancomycin and ceftriaxone were administered, and he was taken to the OR expediently by the ophthalmology team for right orbitotomy and drainage of abscess. Intraoperatively, an extraconal collection with mucopurulence and hemorrhagic contents was evacuated. Intraoperative cultures grew no organisms. His postoperative course was uncomplicated. He was continued on vancomycin and ceftriaxone, intranasal oxymetazoline and fluticasone, nasal saline irrigations, and topical ocular tobramycin. His clinical status continued to improve, and he was discharged home with two-week course of amoxicillin/clavulanate and nasal irrigations. He had resolution of his symptoms upon outpatient follow-up. Interval imaging six weeks post discharge did reveal persistent right-sided rhinosinusitis with opacification of the maxillary, ethmoid, and frontal sinuses. He ultimately underwent right-sided endoscopic sinus surgery (ESS) for persistent sinus disease after further testing was negative for SARS-CoV-2 RNA.

4. Discussion

Viral upper respiratory infection (URI) has been linked to the development of acute bacterial rhinosinusitis [6]. This had previously been described by Marom et al., demonstrating the correlation between the presence of *rhinovirus* at initial URI and subsequent development of bacterial sinusitis in children [6]. Our cases highlight this issue in the context of the COVID-19 viral pandemic, and the unique challenges presented in their perioperative management. To our knowledge, despite multiple novel viral pandemics over the past decade, no cases of complicated rhinosinusitis due to Middle East respiratory syndrome (MERS), SARS, or the current COVID-19 have been reported in the otolaryngology literature. This report highlights the challenges presented in the management of acute, complicated rhinosinusitis with both orbital and intracranial complications in pediatric patients with concurrent COVID-19.

COVID-19 as a viral illness in the pediatric population is still not well understood. Xu et al. found that pediatric patients were 2.7 times less likely than adults to contract the illness [9]. Research has suggested less severe disease manifestations in the pediatric population, however pediatric mortalities have been documented in the US [10]. The nasal cavity and nasopharynx are now well known reservoirs for the virus [7]. Additionally, it has previously been hypothesized that the presence of angiotensin-converting enzyme 2 (ACE2) receptors in the nasal epithelium is the underlying pathophysiological mechanism of the high incidence of anosmia reported in COVID-19 infection [11]. Consistent with prior epidemiological analyses regarding complicated rhinosinusitis, adolescents are at increased risk for intracranial complications due to the increased vascularity of the diploic bones [4]. Previous reports of severe COVID-19 infection in pediatric patients have been associated with lymphopenia and elevated c-reactive protein (CRP) [12]. These above findings are consistent with our patients presentation in Case I. While elevated CRP has been found in multiple case series of complicated sinusitis, our patient's presentation CRP of 169 mg/dL is well above the average elevation previously documented in these reports (18 mg/dL) [3].

Previously published COVID-19 guidelines have recommended deferment of operative intervention and initiation of maximal medical therapy for 48–72 h in patients with “complicated acute rhinosinusitis with orbital extension without vision or globe compromise” [13]. This is consistent with a recent systematic review by Wong et al. which recommended 48 h of parenteral antibiotic therapy for postseptal cellulitis in the pre-COVID-19 era [2]. Despite optimizing medical care, the clinical condition of the patient in Case I continued to worsen with the development of SOVT. Derangements in coagulation profiles and the resulting sequalae in patients with COVID-19 have been previously reported throughout the pandemic, including myocardial infarction, ischemic stroke, limb ischemia, and cerebral venous thrombosis among others [14–17]. Urgent ESS in Case I was felt necessary to decrease the risk of developing cavernous sinus thrombosis and further neurologic complications [1]. In contrast, Case II responded well to initial orbital abscess drainage and improved clinically without immediate need for ESS. ESS was eventually required, although this was able to be performed on an outpatient, non-emergent basis after the patient tested negative for SARS-CoV-2 RNA.

In Case I, our patient was noted to experience new onset respiratory deterioration following operative intervention. A retrospective review from Wuhan, China examined 34 patients who underwent surgery during the asymptomatic incubation period [18]. 44% of the patients subsequently required ICU admission for respiratory deterioration with a mortality rate of 20.5%. A more recent and extensive review from 235 hospitals in 24 countries revealed postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 infection. The 30-day mortality in this patient cohort was noted to be 23.8% [19]. Worsening postoperative pulmonary status is consistent with our patient in Case I, highlighted by the necessity of PICU care and maximum non-invasive oxygen supplementation. Possible pulmonary complications from undergoing general anesthesia (up to 10%) is a known risk although patients with concomitant SARS-CoV-2 infection seem to have

Table 1
Laboratory values of pediatric patients presenting with complicated rhinosinusitis.

Lab value	Case I	Case II	RV	Lab value	Case I	Case II	RV
Hemoglobin	13.2	14.1	13.0–16.0 g/dL	Urea	11	10	4–19 mg/dL
Hematocrit	40.1	41.7	37.0–49.0%	Creatinine	0.9	0.55	0.7–1.2 mg/dL
Leukocytes	7.5	6.5	4.5–13.0 × 10^3/μL	CRP	**169**	**22**	0–5 mg/L
Lymphocytes	**10.7**	38.0	20.0–50.0%	ESR	**34**	NA	0–5 mm/h
Monocytes	**13.1**	7.0	2.0–12.0%	Ferritin	**1216**	NA	30–400 ng/mL
Platelets	**122**	281	150-450 × 10^3/μL	Blood culture	Negative	Negative	Negative

RV = reference value. CRP = C-reactive protein. ESR = erythrocyte sedimentation rate. **Bold** represents an abnormal value.

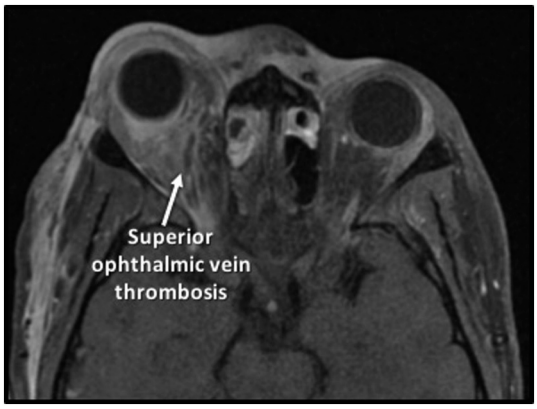

Fig. 2. Preoperative T1-weighted gadolinium enhanced magnetic resonance imaging scan of the brain and orbits of the patient in Case I demonstrating mucosal thickening of the ethmoid sinuses, enhancement of the periorbita, intraconal and extraconal fat infiltration and enhancement, and thrombosis of the right superior ophthalmic vein.

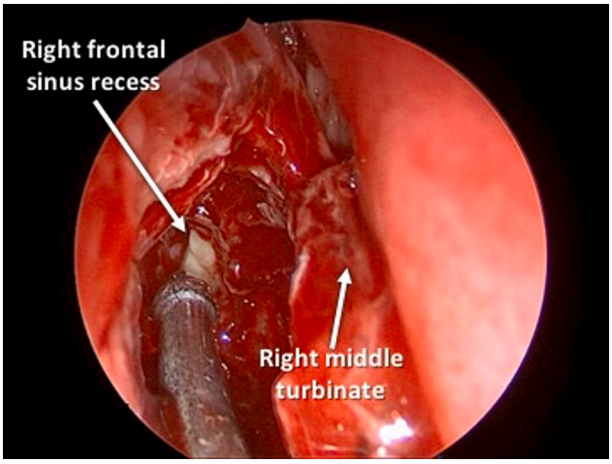

Fig. 3. Intraoperative photograph of Case I after total ethmoidectomy and during Draf2A frontal sinusotomy showing purulence emanating from the right frontal sinus recess.

increased risk, likely due to the pro-inflammatory cytokine and immunosuppressive responses to surgery and mechanical ventilation [20–22]. This provides further evidence to possibly raise the threshold for operative intervention in COVID-19 patients, with need for close postoperative monitoring.

5. Conclusion

COVID-19 remains a novel threat to both the adult and pediatric populations. The cases provided in this report highlight the unique challenge of caring for pediatric patients presenting with complicated rhinosinusitis and concomitant COVID-19 infection. We recommend

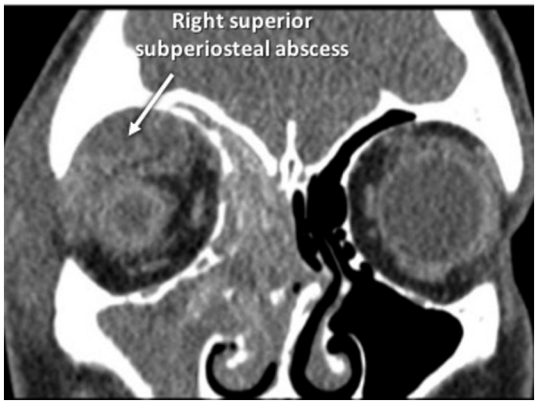

Fig. 4. Preoperative coronal computed tomography scan of the paranasal sinuses of the patient in Case II depicting right-sided rhinosinusitis with a large rim-enhancing complex extraconal superior subperiosteal fluid collection with trace peripheral enhancement, and orbital cellulitis.

utilizing a multi-disciplinary approach in optimizing care of these patients when at all feasible. Further research is still needed to further elucidate the complex pathophysiology and optimal treatment algorithms of SARS-CoV-2 patients with complicated rhinosinusitis.

Financial disclosures

None.

Declaration of competing interest

None.

References

[1] Kou Y-F, Killeen D, Whittemore B, et al. Intracranial complications of acute sinusitis in children: the role of endoscopic sinus surgery. Int J Pediatr Otorhinolaryngol 2018;110:147–51.
[2] Wong SJ, Levi J. Management of pediatric orbital cellulitis: a systematic review. Int J Pediatr Otorhinolaryngol 2018;110:123–9.
[3] Din-Lovinescu C, Mir G, Blanco C, et al. Intracranial complications of pediatric rhinosinusitis: identifying risk factors and interventions affecting length of hospitalization. Int J Pediatr Otorhinolaryngol 2020;131:109841.
[4] Kaplan R. Neurological complications of infections of head and neck. Otolaryngol Clin North Am 1976;9:729–49.
[5] Magit A. Pediatric rhinosinusitis. Otolaryngol Clin North Am 2014;47:733–46.
[6] Marom T, Alvarez-Fernandez PE, Jennings K, Patel JA, McCormick DP, Chonmaitree T. Acute bacterial sinusitis complicating viral upper respiratory tract infection in young children. Pediatr Infect Dis J 2014;33:803.
[7] Zou L, Ruan F, Huang M, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. New England Journal of Medicine 2020;382:1177–9.
[8] John"s Hopkins Coronavirus Center. https://coronavirus.jhu.edu/map.html, Accessed date: 15 July 2020.
[9] Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. Nat Med 2020:1–4.
[10] Bialek S, Gierke R, Hughes M, McNamara LA, Pilishvili T, Skoff T. Coronavirus disease 2019 in children—United States, February 12–April 2, 2020. 2020.
[11] Brann D, Tsukahara T, Weinreb C, Logan DW, Datta SR. Non-neural expression of SARS-CoV-2 entry genes in the olfactory epithelium suggests mechanisms

underlying anosmia in COVID-19 patients. BioRxiv 2020. https://doi.org/10.1101/2020.03.25.009084.
[12] Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. Chem Lab Med. 2020;58(7):1135–8. https://doi.org/10.1515/cclm-2020-0272.
[13] Bann DV, Patel VA, Saadi RA, et al. Best practice recommendations for pediatric otolaryngology during the COVID-1 19 pandemic. Otolaryngol. Head Neck Surg. 2020;162(6):783–94.
[14] Han H, Yang L, Liu R, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. Clinical Chemistry and Laboratory Medicine (CCLM) 2020:1.
[15] Violi F, Pastori D, Cangemi R, Pignatelli P, Loffredo L. Hypercoagulation and antithrombotic treatment in coronavirus 2019: a new challenge. Thromb Haemost 2020;120(6):949–56. https://doi.org/10.1055/s-0040-1710317.
[16] Hughes C, Nichols T, Pike M, Subbe C, Elghenzai S. Cerebral venous sinus thrombosis as a presentation of COVID-19. European Journal of Case Reports in Internal Medicine 2020;7.
[17] Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. J Am Coll Cardiol 2020;75:2950–73.
[18] Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine 2020;21:100331https://doi.org/10.1016/j.eclinm.2020.100331.
[19] Collaborative C. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. Lancet 2020;396:27–38.
[20] Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet 2020;395:497–506.
[21] Kirmeier E, Eriksson LI, Lewald H, et al. Post-anaesthesia pulmonary complications after use of muscle relaxants (POPULAR): a multicentre, prospective observational study. Lancet Respir Med 2019;7:129–40.
[22] Neto AS, da Costa LGV, Hemmes SN, et al. The LAS VEGAS risk score for prediction of postoperative pulmonary complications: an observational study. European Journal of Anaesthesiology (EJA) 2018;35:691–701.