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Orbital Cellulitis, Sinusitis and Intracranial Abnormalities in Two Adolescents with COVID-19

We review two cases of adolescents with orbital cellulitis, sinusitis and COVID-19 presenting to emergency rooms in New Jersey within a 24 hour period. SARS CoV-2 samples obtained within 24 hours were positive, supporting prior infection despite relatively limited early symptoms of COVID-19. Unusual clinical and radiographic characteristics included hemorrhagic abscess with blood of varying age in the first, intracranial epidural abscess in the second, radiographic signal consistent with hemorrhagic or thrombotic phenomena, retro-maxillary antral fat changes, and meningeal enhancement or extension in both cases. Radiographic findings thereby mimic fungal infection, although further investigation for allergic and invasive fungal disease remain negative to date. These cases highlight potential orbital presentations of COVID-19, and aspects raise the possibility that COVID-19 might work synergistically with the underlying, presumably bacterial, processes, to potentiate what might otherwise be a more moderate infection.

Keywords: COVID-19; SARS-CoV-2; orbital cellulitis; thrombosis; hemorrhage

Introduction

Novel coronavirus Disease 2019 (COVID-19) has resulted in a global pandemic of unprecedented modern scale, and public health and government authorities remain engaged in a concerted effort to mitigate the spread. Achievement of this goal will require a more comprehensive understanding of the full spectrum of COVID-19. To date, symptoms of dry eye (20.9%), blurred vision (13.9%), foreign body sensation (11.8%), “ophthalmalgia” (4.1%),¹ conjunctival congestion (0.8-31.6%),^{1,3} and conjunctival secretion (9.7%) have been described as ocular manifestations of COVID-19.¹ We report the unique orbital presentation of COVID-19 in two adolescent patients with orbital cellulitis, sinusitis, local hemorrhage or thrombosis, retromaxillary antral fat changes, and intracranial radiographic changes.

Clinical Courses

Case 1

A 12 year old Egyptian male with seasonal allergies developed a 3 day history of progressive painful unilateral orbital swelling and was transferred to our institution for further management after the initiation of parenteral vancomycin and ceftriaxone. Physical findings included normal visual acuity, trace right afferent pupil defect, severe unilateral right upper and lower eyelid edema with mild erythema requiring digital force to open the eyelids (Figure 1a), unilateral mild/moderate non hemorrhagic conjunctival chemosis, 3-4 mm proptosis, severe limited supraduction, moderate limited abduction (60%) and mild limited adduction (90%) [Figure 1 near here]. He reported mild nasal congestion for 2 weeks and denied fever, chills, rhinorrhea, anosmia, dysgeusia, lower respiratory symptoms, myalgias, diarrhea, and symptoms of chronic sinusitis. The patient was afebrile (98.6 degrees Fahrenheit) and remained so throughout his course, despite mild tachycardia (106 beats per minute). A peripheral blood smear had a normal white cell and platelet count with the exception of 20% eosinophilia. D-dimer and transaminases early in his course were normal.

Computed tomographic imaging (CT) (Figure 2) of the orbit showed ipsilateral frontal, maxillary and anterior ethmoid sinusitis, and hyperdense material within the sinuses, associated with a complex extraconal superior subperiosteal fluid collection with trace peripheral enhancement, and orbital cellulitis. There was subtle infiltration of the periantral fat. The nasolacrimal ducts appeared aerated [Figure 2 near here]. Vancomycin and ceftriaxone were initiated, and the patient underwent superior orbitotomy with drainage of the subperiosteal muco-pyocoele and subperiosteal irrigation with concentrated

bacitracin/polymyxin on the evening of presentation. The contents were mucoid intermixed with purulence, and deeper dissection drained thin brown fluid followed by larger blood clots. Gram stain of fluid contents had few polymorphonuclear leukocytes (pmns) with no organisms and cytologic analysis revealed few eosinophils, histiocytes and rare atypical epithelioid histiocytes without Charcot-Leyden crystals nor allergic mucin.

Rapid clinical improvement ensued on parenteral vancomycin, ceftriaxone, metronidazole, fluticasone and oxymetazoline nasal sprays, and topical ocular tobramycin ointment. Operative cultures and initial ocular swab (both after antibiotic initiation) remained negative 14 days following collection. Nasopharyngeal swab for SARS-CoV-2 RNA, obtained within six hours of his presentation to a medical facility as a preoperative precaution, was positive. An orbital Magnetic Resonance Imaging (MRI) scan in the postoperative period demonstrated the additional finding of small area of frontal dural enhancement (Figure 2).

Case 2

A 15 year old obese male with mild asthma developed a three day history of progressive painful unilateral orbital swelling, mild rhinorrhea, resolved recent migraine headache, a few loose stools per day associated with mild crampy pain, and mild bouts of vomiting. He was transferred to our institution for further management after the initiation of parenteral vancomycin and ceftriaxone. He denied lower respiratory symptoms, anosmia, dysgeusia, myalgia and dyspnea. A low grade fever was followed by fever spikes to 104°F.

Examination revealed an obese black male with axillary striae in no acute distress, normal pulmonary, and cardiac auscultation, mild diffuse epigastric tenderness,

and a normal neurologic evaluation. He had normal visual acuity, absence of a relative afferent pupil defect, severe right sided upper and lower eyelid and periorbital edema requiring force to manually open his eyelids (Figure 1b), scant crusty discharge, mild non-chemotic conjunctival hyperemia, moderate supraduction deficit and 3-4 mm of right eye proptosis.

CT imaging demonstrated opacification of the right paranasal sinuses, with clear sinuses on the left. The sinuses were filled with hypodense fluid, and there was evidence of subtle invasion of the right periantral fat (Figure 3). There was also thrombophlebitis of the right superior ophthalmic vein (SOV). MRI imaging on day 1 of admission (Figure 3) showed acute sinusitis, predominantly involving the right frontal ethmoid and maxillary sinuses, with diffusion restriction concerning for bacterial superinfection [Figure 3 near here]. The right orbit had marked enhancement of the periorbita, nasolacrimal area, extensive intra and extraconal fat infiltration and enhancement without organized abscess. SOV thrombus extended retrograde toward the facial vein, sparing the orbital apex, cavernous sinus and dural venous sinuses. The right optic nerve was straightened with traction and tenting of the posterior globe in the setting of the orbital edema and proptosis. Pachymeningeal enhancement was noted over both frontal lobes, with formation of a small epidural abscess just posterior to the right frontal sinus, 1.6 cm in greatest dimension.

Laboratory evaluation revealed a normal white count ($8.3 \times 10^3/\mu\text{l}$) with relative monocytosis (23.5%), mild microcytic anemia with low total iron and iron binding capacity, normal aminotransferases, mild hypokalemia, normal gastrointestinal pathogen panel, ferritin of 1382 ng/ml, an ESR of 35mm/hr, and a CRP which increased from <1 to 169mg/L within the first 24 hours of admission to our hospital.

Nasopharyngeal swab for SARS-CoV-2 RNA, collected within 19 hours of his

presentation to a medical facility as a preoperative precaution, resulted positive.

Moderate respiratory decompensation ensued at 48 hours after admission.

He underwent endoscopic frontal sinusotomy, total ethmoidectomy and maxillary antrostomy, with intraoperative observations significant for purulence, thickened tissue and polypoid mucosa. Sinus content gram stain had moderate pmns and gram-positive cocci, but cultures did not produce bacterial growth (sinus cultures drawn three days after initiation of antibiotics). Negative fungal stains, serum 1-3 beta-D-glucan and galactomannan, were concordant with fungal cultures exhibiting no growth at 12 days post collection. An eye swab culture grew few diphtheroids and coagulase negative cocci interpreted as normal bacteria flora, and a throat swab grew group C beta-hemolytic streptococcus. His clinical course was marked by persistent fevers, moderate diffuse worsening of ocular motility without the development of consolidated orbital abscess with serial neuro-imaging, increasing conjunctival chemosis with small areas of hemorrhage, and episodes of dyspnea and mild chest pain with brief desaturations to 89% which corrected on face mask non-rebreather oxygen to 100%. A portable chest radiograph on day four post admission showed mild patchy bilateral opacities. In the setting of compromised oxygen saturation, he was transferred to a dedicated pediatric COVID-19 unit in an affiliated hospital. He was maintained on parenteral vancomycin, ceftriaxone, metronidazole, enoxaparin 2mg/kg divided into twice daily dosing, hydroxychloroquine (400 mg bid loading dose followed by 200 mg po bid), zinc (3 day course), vitamin C and thiamine. Adjuvant treatments included ocular tobramycin ointment, nasal fluticasone and oxymetazoline, and levetiracetam for seizure prophylaxis (due to epidural abscess). His pulmonary decompensation remained limited in extent; he did not develop disseminated intravascular coagulation (DIC) nor require intubation. Yet, he remained febrile on a continuous course of broad-spectrum

intravenous antibiotics, with near resolution of his orbital findings and stability of his small epidural fluid collection.

Discussion

These two cases, presenting within a 24-hour period to different New Jersey emergency rooms, had very unusual but quite similar local manifestations and both were COVID-19 positive. To our knowledge, COVID-19 presenting with primary orbital signs is unreported, although a large case series described “ophthalmalgia” (PubMed and Google Scholar English language search, keywords: “COVID-19”, “corona virus”, “orbit”, “signs”, “symptoms”, “hemorrhage”, “thrombosis” etc.).¹

It is unclear if SARS-CoV-2 is coincidental or pathogenic in these two cases, but findings and the clinical course in these two adolescents support that secondary sinusitis in the setting of COVID-19 related disease lead to compromise of mucociliary clearance, obstruction, and secondary orbital infection in both, with the development of frontal meningeal enhancement in case 1 and intracranial spread to cause epidural abscess in case 2. In neither case was a clinical diagnosis of COVID-19 suspected initially, albeit both were placed in droplet isolation status on admission to our unit. The acquisition of COVID-19 testing within six hours of first presentation for case 1 and within 19 hours for case 2 makes the likelihood that both had smoldering disease at presentation rather than nosocomial infection nearly certain, even if initially unrecognized. COVID-19 infection may be asymptomatic in a significant proportion of cases, with an estimated frequency a recently published study of 78%.⁴ The presentation in children is still less well described than in adults, and this is partly due to the relatively indolent course described in many children. A study of over 2000 pediatric patients in China showed that 56% of children with confirmed COVID-19 were

asymptomatic or had mild symptoms.⁵ Another study from China published in *Lancet Infectious Diseases* put this estimate at 47%.⁶

We also suggest that our clinical observations in the first case of a complex collection more suggestive of aging hematoma than mature abscess on imaging, supported by the operative findings of a muco-pyocoele with subacute hemorrhage of varying age composition, and in the second case, the SOV thrombosis with facial vein extension, may be related to SARS-CoV-2. Hemorrhagic and thrombotic complications of SARS-CoV-2 related disease appear to be increasingly recognized as the pandemic evolves, and we are aware of patients in our institution (Esther A Nimchinsky, phone call, April 2020)* and reports of pulmonary emboli,^{7,8*} acute necrotizing hemorrhagic encephalitis,⁹ multifocal intracranial infarcts with anticardiolipin antibodies,¹⁰ extremity gangrene,* and gastric bleeding as well as DIC in newborns of COVID-19 infected mothers.¹⁰ Thrombotic complications have also rarely been reported in the predecessor SARS-CoV.¹¹ Early literature suggests that COVID-19 associated thrombotic/hemorrhagic phenomena occur more frequently with severe disease manifestations (e.g., shock, DIC), as do abnormalities in serum ferritin, IL-6, D-Dimer, platelets, fibrinogen/fibrinogen degradation products, prothrombin and thrombin times.¹²⁻¹⁵ Abnormalities of these inflammatory markers may be less prevalent, and more incompletely defined in children who also typically follow a more indolent or even asymptomatic course.^{13,16} For instance, in the study of Qiu⁶ et al describing pediatric COVID-19 cases in China, only 3 of 36 patients had an elevated D-Dimer. This generally attenuated severity of disease presentation in children may explain the paucity of current literature addressing the issue of thrombotic/hemorrhagic complications in pediatric patients. We anticipate that the communication of our

pediatric encounters will spur the reporting of similar cases from which a pattern may emerge.

These cases also demonstrate unusual imaging characteristics. Case 1 was characterized by dense and T1 hyperintense sinus contents, believed to represent inspissated secretions and/or deposition of calcium salts or metals such as Mg, Mn and Fe,¹⁷ and typically seen with chronic invasive or allergic fungal sinusitis.¹⁸ However, both cases demonstrated features typically associated with acute or invasive disease. Case 2 was characterized by hypodense, fluid signal contents, unlike the increased density seen with chronic invasive or allergic fungal sinusitis,¹⁸ and seen more commonly with acute invasive disease. Both cases were strictly unilateral, which is less common in allergic fungal sinusitis than in invasive disease, although it is more commonly seen in children than in adults.¹⁹ Moreover, in both cases, there was subtle involvement of the periantral fat, a finding relatively specific for invasive fungal sinusitis,²⁰ which was not expected in either case, as neither patient was immunosuppressed. Interestingly, COVID-19 has been observed to mimic angio-invasive fungal infection in the lungs, manifested as hemorrhagic pulmonary nodules,²¹ and this has been observed more commonly in the pediatric age group.²² In our cases, these unusual findings raise the possibility that COVID-19 might work synergistically with the underlying, presumably bacterial, processes, to potentiate what would otherwise be a more moderate infection.

Disclosure of Interest:

The authors report no conflicts of interest

References

1. Chen L, Deng C, Chen X, et al. Ocular manifestations and clinical characteristics of 534 cases of COVID-19 in China: A cross-sectional study. *medRxiv [Preprint]*. March 2020. doi:10.1101/2020.03.12.20034678
2. Wu P, Duan F, Luo C, et al. Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China [published online ahead of print March 31, 2020]. *JAMA Ophthalmol*. doi:10.1001/jamaophthalmol.2020.1291. PMID: 32232433
3. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China China [published online ahead of print February 28, 2020]. *N Engl J Med*. doi: 10.1056/NEJMoa2002032. PMID: 32109013.
4. Day M. Covid-19: four fifths of cases are asymptomatic, China figures indicate. *BMJ*. 2020; 369:m1375 doi: <https://doi.org/10.1136/bmj.m1375>
5. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 Among Children in China. *Pediatrics*. Apr 2020, e20200702. doi:10.1542/peds.2020-0702. PMID: 32179660.
6. Qiu H, Wu J, Hong L, et al. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study [published online ahead of print March 25, 2020]. *Lancet Infect Dis*. doi: [https://doi.org/10.1016/S1473-3099\(20\)30198-5](https://doi.org/10.1016/S1473-3099(20)30198-5).
7. Xie Y, Wang X, Yang P, Zhang S. COVID-19 Complicated by Acute Pulmonary Embolism. *Radiology: Cardiothoracic Imaging*. 2020;2(2). doi: 10.1148/ryct.2020200067. PMID: 32227120.
8. Danzi GB, Loffi M, Galeazzi G, Gherbesi E. Acute pulmonary embolism and COVID-19 pneumonia: a random association? [published online ahead of print

March 30, 2020] *European Heart Journal*. doi: 10.1093/eurheartj/ehaa254.

PMID: 32227120.

9. Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19–associated Acute Hemorrhagic Necrotizing Encephalopathy: CT and MRI Features. *Radiology*. 2020:201187. doi: 10.1148/radiol.2020201187. PMID: 32228363.

10. Zhang Y, Xiao M, Zhang S. Coagulopathy and Antiphospholipid Antibodies in Patients with Covid-19 [published online ahead of print April 8, 2020]. *New England Journal of Medicine*. doi:10.1056/NEJM2007575. PMID: 32268022.

11. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*. 2020;9(1):51-60. doi: 10.21037/tp.2020.02.06. PMID: 32154135.

12. Chong PY, Chui P, Ling AE, et al. Analysis of deaths during the severe acute respiratory syndrome (SARS) epidemic in Singapore: challenges in determining a SARS diagnosis. *Arch Pathol Lab Med*. 2004;128(2):195-204. doi: 10.1043/1543-2165(2004)128<195:AODDTS>2.0.CO;2. PMID 14736283.

13. Han H, Yang L, Liu R, et al. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection [published online ahead of print March 16, 2020]. *Clinical Chemistry and Laboratory Medicine*. doi:10.1515/cclm-2020-0188. PMID 32172226.

14. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia [published online ahead of

print April 9, 2020]. *Journal of Thrombosis and Haemostasis*. September 2020.

doi:10.1111/jth.14830. PMID 32172226.

15. Fox SE et al. Pulmonary and Cardiac Pathology in COVID-19: The First Autopsy Series from New Orleans. *medRxiv [Pre-Print]*. April 2020. doi: <https://doi.org/10.1101/2020.04.06.20050575>.

16. Zhang W, Zhao Y, Zhang F et al. The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): the perspectives of clinical immunologists from China *Clin. Immunol.* 2020; 214:108393 doi: 10.1016/j.clim.2020.108393 PMID: 32222466.

17. Zinreich SJ, Kennedy DW, Malat J et al. Fungal Sinusitis: Diagnosis with CT and MR Imaging. *Radiology*. 1988;169:439. doi: 10.1148/radiology.169.2.3174990. PMID: 3174990.

18. Aribandi M, McCoy VA, Bazan C. Imaging features of invasive and noninvasive fungal sinusitis: a review. *RadioGraphics*. 2007;27(5):1283–1296. doi: 10.1148/rg.275065189. PMID: 17848691

19. Rowan NR, Janz TA, Schlosser RJ, Soler ZM. Radiographic nuances in allergic fungal rhinosinusitis. *Am J Rhinol Allergy*. 2019;33:310–316. Doi: 10.1177/1945892419825695. PMID: 30674195.

20. Silverman CS, Mancuso AA. Periantral soft-tissue infiltration and its relevance to the early detection of invasive fungal sinusitis: CT and MR findings. *AJNR Am J Neuroradiol* 1998; 19:321–5. PMID: 9504486.

21. Li X, Zeng X, Liu B, Yu Y. COVID-19 Infection Presenting with CT Halo Sign. *Radiology: Cardiothoracic Imaging*. 2020; 2:1. doi: <https://doi.org/10.1148/ryct.2020200026>.

22. Xia W, Shao, J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in

pediatric patients with COVID-19 infection: Different points from adults. *Pediatr Pulmonol.* 2020;55(5):1169-1174. doi: 10.1002/ppul.24718. PMID 3214205.

Figure 1.

- (a) Moderate to severe upper and lower eyelid edema with injection is noted in patient 1.
- (b) Similar findings including mild crusting noted in patient 2 who developed right sided worsened congestive chemosis with mild hemorrhage (inset) by post-operative day three. Subconjunctival hemorrhage persisted through the second postoperative week.

Figure 2.

- (a) Computed Tomography (CT) of patient 1 on day zero demonstrates opacification of the right-sided paranasal sinuses, which are filled with hyperdense material (red stars). There is a complex subperiosteal collection in the superolateral orbit with only trace peripheral enhancement (red arrow).
- (b) Postoperative Magnetic Resonance Imaging (MRI) on day five demonstrates fluid re-accumulation at the resection site (red arrow). This demonstrated no diffusion restriction to suggest abscess (data not shown).
- (c) There is enhancement surrounding the superior muscle group and the superior ophthalmic vein (red arrow) at the posterior orbit. No thrombus is seen within the vein.
- (d) There is subtle infiltration of the periantral fat with corresponding enhancement on CT (red arrows), suggestive of an invasive process.
- (e) Similar findings to (d) shown on MRI.
- (f) Subtle dural enhancement is noted just posterior to the right frontal sinus, indicating intracranial involvement (red arrow).

Figure 3.

- (a) Computed Tomography of patient 2 demonstrates thrombophlebitis of the right superior ophthalmic vein and hypoattenuating fluid is noted within the sinus (red star).
- (b) Magnetic Resonance imaging of patient 2 demonstrating thrombophlebitis of the right superior ophthalmic vein and extensive enhancement within the intra- and extraconal right orbit.
- (c) There is hypoattenuating fluid within the sinus. Infiltration of the periantral fat is compatible with invasion (red arrow).
- (d) Thrombus extends into the veins of the periorbital tissues (red arrow).
- (e) Note patent veins on the left (blue arrow) but not on the right (red arrow).
- (f) Fluid level within the right frontal sinus indicates acute sinusitis, and there is an epidural abscess just posterior to the inner sinus table.





