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Concurrent Pansinusitis and Orbital Cellulitis Complicated by Extensive Head and Neck Venous Thrombosis in an Unvaccinated Adolescent Patient with COVID-19: A Case Report

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Keywords: pansinusitis; orbital cellulitis; cavernous sinus thrombosis; intracranial abscess; pediatric; Covid-19; SARS-CoV-2; *Streptococcus constellatus*, ophthalmic vein thrombosis; internal jugular vein thrombosis

Abstract

Background: Orbital cellulitis is an infrequent but serious infectious complication of rhinosinusitis, most commonly seen in the pediatric population. Extension into the cavernous sinus, leading to further infection and thrombosis, is a rare but life-threatening complication. While COVID-19 has been linked to an increased risk of venous thromboembolism, most cases involve extremity deep venous thrombosis and/or pulmonary embolism; reports of intracranial or jugular system thrombosis are rare.

Case Report: We describe a case of a 17-year-old female with no significant medical history or thrombotic risk factors found to have orbital cellulitis and severe pansinusitis complicated by multiple venous thromboses in the head and neck requiring emergent surgical intervention and pediatric intensive care admission.

Why Should An Emergency Physician Be Aware of This? Extensive head and neck venous thrombosis and intracranial abscesses are rare complications of pansinusitis and OC, and the thrombotic complications of COVID-19 are well documented. A delay in diagnosis and treatment can lead to potentially devastating consequences.

Keywords: pansinusitis; orbital cellulitis; cavernous sinus thrombosis; intracranial abscess; pediatric; COVID-19; SARS-CoV-2; ***Streptococcus constellatus***, ophthalmic vein thrombosis; internal jugular vein thrombosis

Introduction

Orbital cellulitis (OC) is an infection of the soft tissues within the orbit and is more common in the younger pediatric population compared to adolescents and adults. Clinically, OC is differentiated from the more superficial entity of preseptal cellulitis by the presence of painful extraocular movements, visual deficits, ophthalmoplegia, relative afferent pupillary defect,

chemosis and/or proptosis.(1) OC most often results as a complication of bacterial rhinosinusitis, with Staphylococcus aureus and Streptococcal species being the most frequently identified pathogens.(2-4) If not promptly identified and treated, OC can lead to permanent vision loss, deeper central nervous system infections, and death.(5)

While OC is a rare complication of sinusitis, its associated thrombotic risk is not well known, particularly within the pediatric population. In a retrospective case series covering nearly 37 years, Branson et al reported a total of six cases of septic cavernous sinus thrombosis (SCST) as a complication of OC, four of which initially presented with sinusitis. (6) The only **adolescent** patient of these six was a 12-year-old male that presented with sinusitis complicated by OC and SCST with right internal jugular vein thrombosis.

COVID-19 infection caused by the novel SARS-CoV-2 virus has been linked to an increased risk of thrombosis, (7)with direct endothelial injury posited as a mechanism. (8, 9) Endothelial insult leads to recruitment of inflammatory mediators, cytokines, P-selectin, and von Willebrand factor, resulting in increased platelet aggregation, adhesion, and thrombosis.

In patients with COVID-19 any venous thromboembolism (VTE) is possible, however, most studies describe deep vein thrombosis (DVT) and/or pulmonary embolism (PE) in the adult rather than the pediatric population, and head and neck thrombosis is rare. Additionally, concomitant OC and pansinusitis presentations are rare. We report a case of a COVID-19 positive adolescent patient with untreated preseptal cellulitis that developed OC with extensive septic thromboses of the head and neck.

Case Report

A 17-year-old female with a history of depression presented to a small community Emergency Department (ED) with a complaint of one week of progressive swelling and pain around her right

eye. **Her symptoms began with three days of** dull headache which prompted a visit to her primary care Nurse Practitioner. She denied pain with extraocular muscle movements and had no neurological deficits. A preseptal cellulitis was diagnosed and the patient was prescribed oral amoxicillin-clavulanic acid, but she was unable to fill the prescription. When her right eye redness and swelling rapidly worsened over the next two days, her parents took her to a community ED for evaluation. These more concerning findings prompted computed tomography (CT) imaging of her orbits which confirmed OC (Figure 1-A) and additionally demonstrated internal jugular (IJ) vein thrombosis (Figure 1-B). She was treated with vancomycin 800 mg IV and ceftriaxone 2 grams IV, then transferred to the regional children's hospital.

Upon arrival to the children's ED, the patient was noted to have significant right eye periorbital erythema, edema, and proptosis, with normal intraocular pressures and visual acuity. **Further history revealed no chronic rhinosinusitis, poor dentition or facial trauma. The remainder of her HEENT and neurologic examination was unremarkable**. Laboratory analysis demonstrated elevation in multiple inflammatory markers, including a WBC of 17.8 K/mcL, a CRP of 20 mg/L, an ESR of 93 mm/hr, and a procalcitonin of 4.2 ng/mL. SARS-CoV-2 PCR obtained as an admission screen was positive, although no cycle time was reported. Additional **review of systems after her positive COVID-19 testing was negative for myalgias, malaise, fever, cough or other upper respiratory symptoms**. **At the time of this patient's presentation, Omicron had displaced Delta as the dominant SARS-CoV-2 variant. While COVID-19 vaccination was widely available, she was unimmunized.**

Contrast-enhanced MRI obtained showed extensive thromboses of the head and neck involving the internal jugular veins (Fig. 2-A), bilateral cavernous sinuses, sigmoid sinus, and the right ophthalmic vein (Fig. 2-B). This study also revealed severe bilateral pansinusitis and a right temporal subdural empyema (Fig 2-B and C). Initial neurosurgical intervention was deferred, but a consulting otorhinolaryngologist performed emergent bilateral maxillary

antrostomy, total ethmoidectomy, frontal sinusotomy, and sphenoidectomy, evacuating a significant amount of purulent material. This operative intervention was followed by PICU admission for close neurologic monitoring.

A heparin infusion was started to treat her multiple thrombi, and her antibiotic coverage was broadened by adding metronidazole 500 mg IV three times a day. Levetiracetam 500 mg IV twice daily was administered for seizure prophylaxis, and dexamethasone 4 mg IV four times a day was initiated to lessen the acute inflammatory response. Blood cultures obtained from the outside hospital grew *Streptococcus constellatus*; repeat blood cultures obtained after starting antibiotics were negative. An echocardiogram did not reveal any valvular vegetations.

Due to persistent headache and lack of clinical improvement, a repeat MRI on hospital day five demonstrated worsening subdural empyema, new orbital abscess, and new bilateral temporal lobe abscesses. (Figure 2) The consulting neurosurgeon performed a craniotomy and evacuated the empyema. On hospital day seven the patient was taken back to the OR for repeat sinus debridement. Post-operative MRI on hospital days seven and 12 were stable, thus further operative intervention was withheld.

Postoperatively she was given a 30-day dexamethasone taper. Bilateral internal jugular ultrasounds showed resolution of the thromboses. She was transitioned to rivaroxaban 15 mg by mouth twice daily for 21 days after discharge. A peripherally inserted central catheter was placed to administer eight weeks of ceftriaxone 2 grams twice daily. She continued to improve after discharge and was noted to be doing well on subsequent follow-up visits. Outpatient MRI three months later demonstrated near complete resolution of previously identified abscesses.

Discussion

Sinusitis leading to OC is not uncommon, but the additional complication of head and neck thrombosis appears to be rare. **While this patient had a positive COVID-19 test on admission screening, she lacked other typical symptoms, other than a mild headache**. **Polymerase chain reaction cycle time count can be used as a surrogate for infectivity and viral load; because it was not calculated, it's unclear if she had an active infection or was positive from a prior resolved, but recent COVID-19 infection. While her OC was likely a result of her severe pansinusitis**, **it's possible that a concomitant active COVID-19 infection may have contributed**. **Initial milder COVID-19 respiratory symptoms, eclipsed by the severity of her subsequent illness, may have contributed to bacterial seeding of her sinuses. And while COVID-19's link to deep venous thrombosis is well established in adults, without cycle time count or a complete thrombophilia workup, the link to head and neck thrombosis in this adolescent patient is theoretical.**

According to the American Academy of Pediatrics, as of July 2022, there have been over 14 million child cases of COVID-19. (10) In adult intensive care unit patients with COVID-19, the incidence of VTE has been estimated to range between 20% and 35%. (11) Hospitalized patients infected with SARS-CoV-2 that did not require intensive care had a rate of VTE of 3.1%, and non-hospitalized patients s had a thrombosis rate of less than 1%. (12) Patients with COVID-19 complicated by VTE have a reported mortality rate of 23%, and an increased odds ratio of death of 2.1 when compared to those without VTE. (13, 14)

While these statistics highlight the clinical significance of VTE and COVID-19 in the adult population, pediatric data suggests decreased incidence of this complication. In critically ill children with COVID-19, the incidence of thrombotic events (including arterial and venous) is 2.1%, with the majority of these children greater than 12 years of age. (15) **While this incidence is a fraction of the adult rate, pediatric thrombosis is a dire prognostic**

indicator, with an in-hospital mortality rate among children with COVID-19 and thrombotic events of 28%. (15)

While several reports have noted sinusitis and VTE in pediatric COVID-19 patients, none reveal thrombosis as extensive as in our patient. Absoud et al describe a 6-year-old male COVID-19 patient with bilateral cavernous sinus thromboses as a complication of sphenoid and ethmoid sinusitis. (16) His initial presentation was of preseptal cellulitis, however after admission and intravenous antibiotics showed no improvement, CT imaging revealed extensive thrombosis. Like our patient, he was treated with intravenous heparin and underwent sphenoidectomy and ethmoidectomy, and his clinical course improved.

Lawrence et al describe a case of OC and cavernous sinus thrombosis in a 17-year-old SARS-CoV-2 positive male. (17) This patient was found to have underlying sinus disease, although to a lesser extent than ours. Turbin et al reported similar cases of OC and COVID-19 in two adolescent males. (18) Patient 1, a 12-year-old, had extensive unilateral sinus disease and a subperiosteal fluid collection treated with superior orbitotomy and irrigation. As in our patient, vancomycin, ceftriaxone, and metronidazole resulted in swift clinical improvement. Patient 2, a 15-year-old male, also presented with periorbital swelling and CT evidence of unilateral sinus opacification, with superior ophthalmic vein thrombophlebitis demonstrated on MRI. His surgical interventions included sinusotomy, total ethmoidectomy, and maxillary antrostomy. Medical treatment included antibiotics (vancomycin, ceftriaxone, and metronidazole), as well as anticoagulation with enoxaparin 2 mg/kg subcutaneously divided twice daily.

Reed et al reported on a 10-year-old COVID-19 positive male that presented with periorbital edema who developed bilateral pansinusitis and left-sided orbital abscess. (19) He was taken for endoscopic sinus surgery and operative abscess drainage. While this patient demonstrated similar sinus and ophthalmologic findings, there was no evidence of thrombosis.

To the best of our knowledge, these cases represent the only documented reports of **adolescent** OC and sinus disease in the **setting of SARS-CoV-2 positivity**. Only 1 of these 3 cases demonstrated evidence of venous thrombosis. **We postulate that her OC and subsequent intracranial abscesses were likely secondary to pansinusitis, with COVID-19 as a potential antecedent infection and contributor to her clinically significant head and neck thromboses.**

In a population-based study examining VTE in Danish children, identifiable triggers were found in 86.6% of cases. These included infection, cardiac disease, and cancer (17.7%, 4.5%, and 2.7% respectively). (20) While our patient had no evidence of malignancy or cardiac disease, she has not been evaluated for thrombophilia as a potential contributing factor, likely because of COVID-19's documented association with thrombosis.

Our patient's blood cultures grew a rare pathogen, *Streptococcus constellatus, which* is a subspecies of *Streptococcus anginosus*, and likely seeded from our patient's OC; the largest case series on this pathogen found a local source of bacteremia 85% of the time. (21) *S. constellatus* is a rare cause of intracranial abscess. (22) While it has been reported as an infectious cause of OC leading to cavernous sinus thrombosis, additional head and neck VTE is not well documented.

Anticoagulation therapy in children is largely based on two large multicenter randomized controlled trials. Both studies featured protocols that initiated oral anticoagulation after five to ten days of parenteral therapy. The EINSTEIN-Jr Phase III study compared rivaroxaban to standard therapy anticoagulation. After three months, more patients taking rivaroxaban had resolution of VTE, while bleeding risk was similar in both groups. (23) Anticoagulant choice should be individualized based on patient risk factors, comorbidities, monitoring, and need for operative or procedural intervention. Our patient was initially anticoagulated with unfractionated

heparin because of her multiple surgeries. She was then transitioned to oral rivaroxaban, similar to the regimens described in the EINSTEIN-Jr study.

Why Should an Emergency Physician Be Aware of This?

Preseptal cellulitis and sinusitis can lead to orbital cellulitis, and in rare instances be further complicated by venous thrombosis of the head and neck, and/or intracranial abscesses. **While OC and subsequent intracranial infection in our patient was likely the result of extensive pansinusitis, the impact of SARS-CoV-2 on the development of additional head and neck thrombosis is potentially contributory**. Clinicians should consider these devastating complications in patients who are not improving as further delays in diagnosis and treatment can lead to severe and potentially deadly consequences.

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Figure legend:

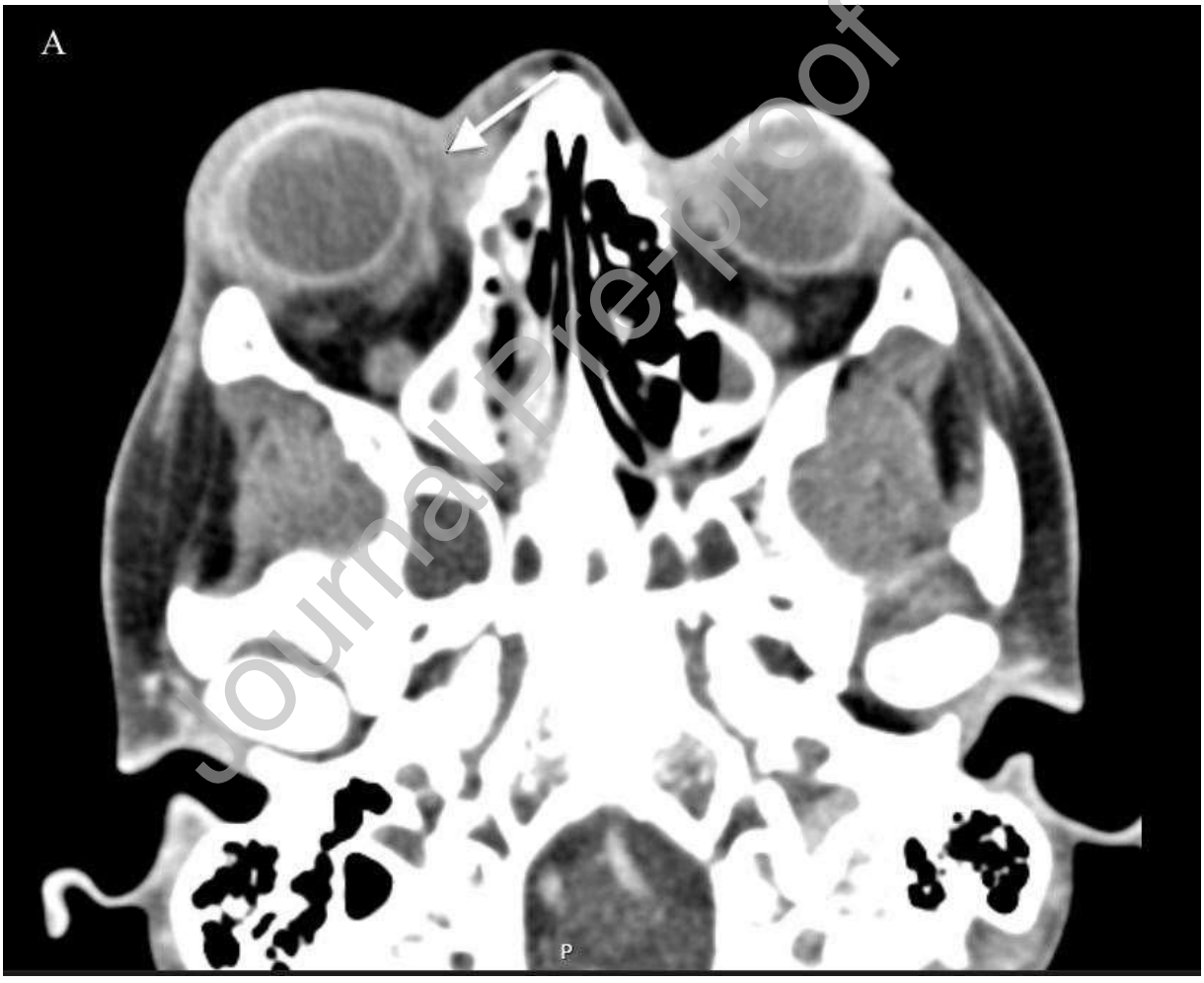


Figure 1

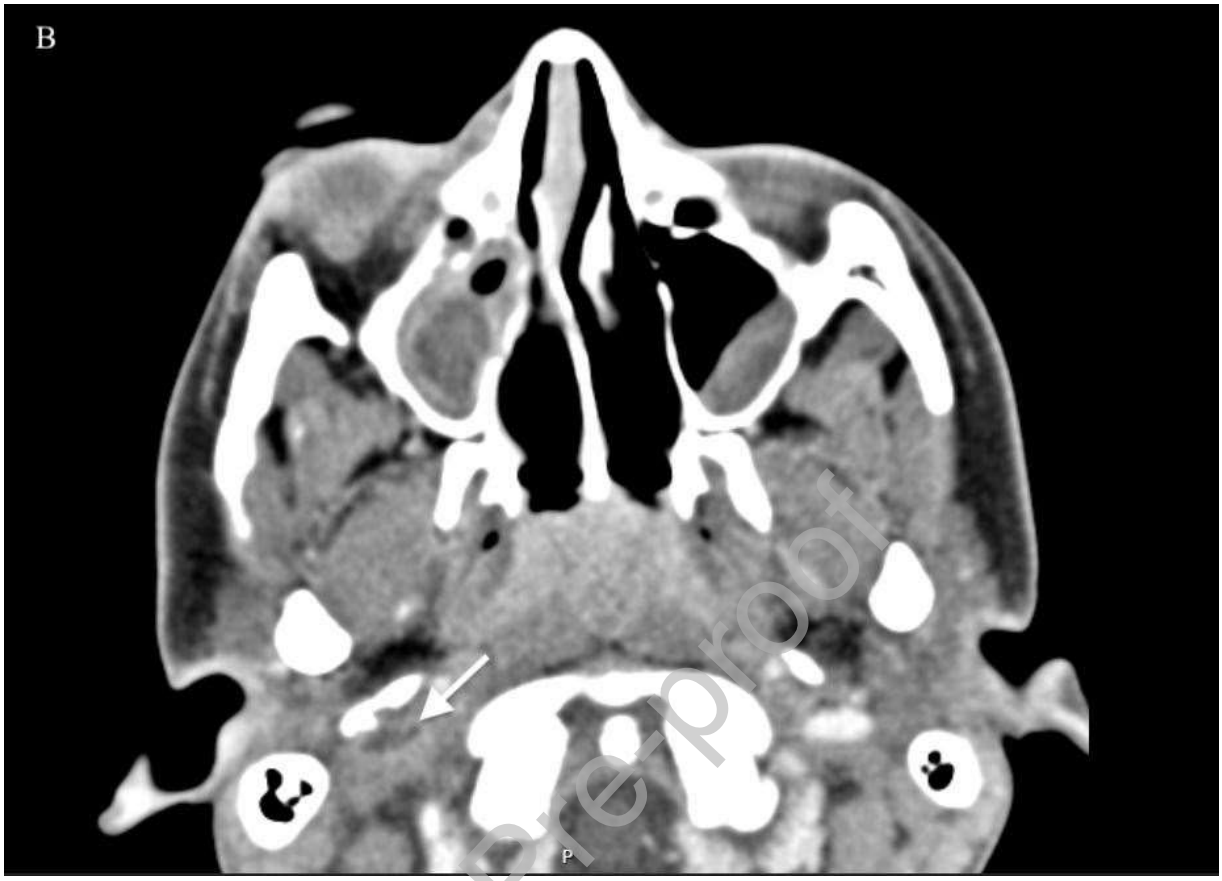
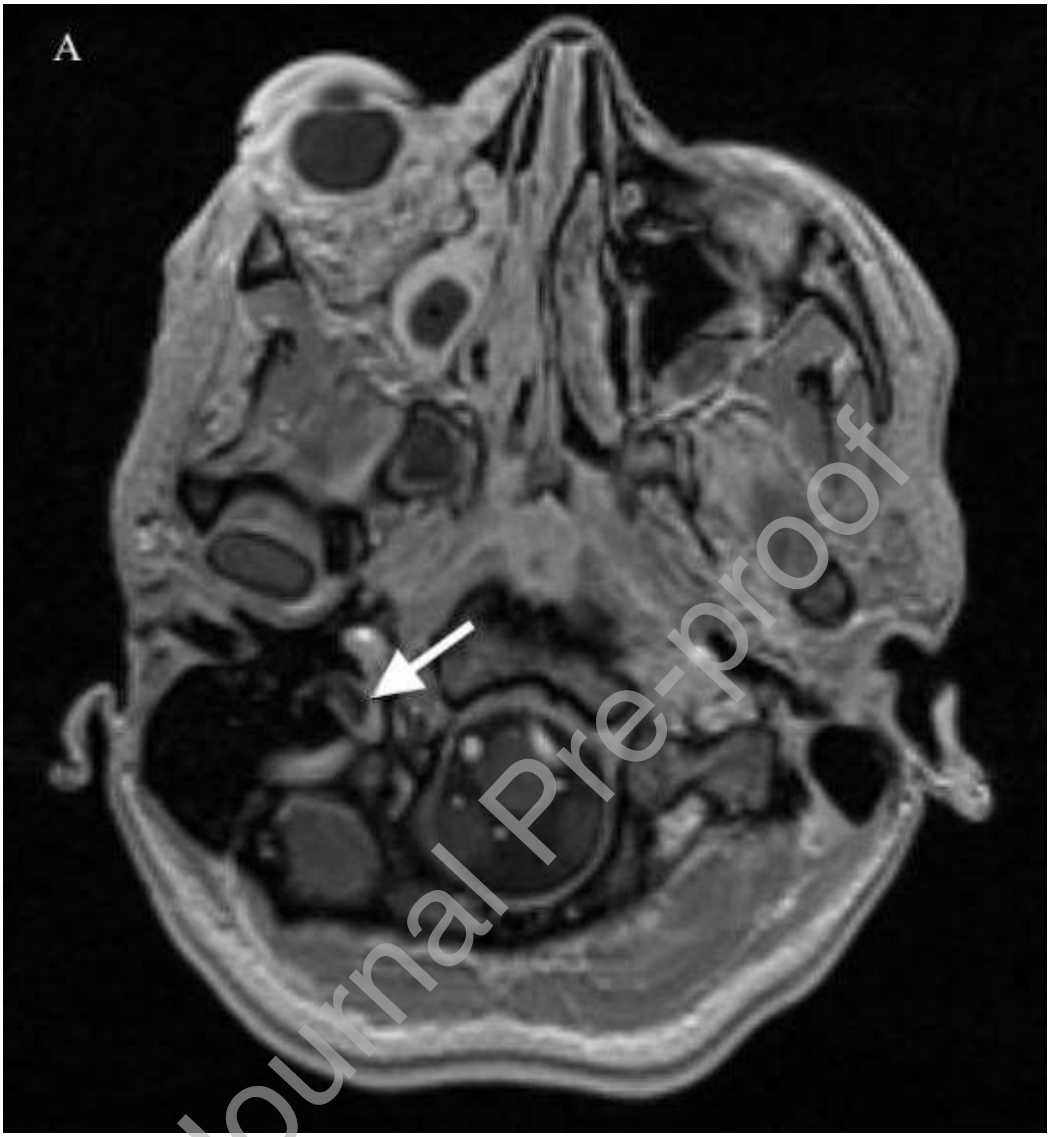
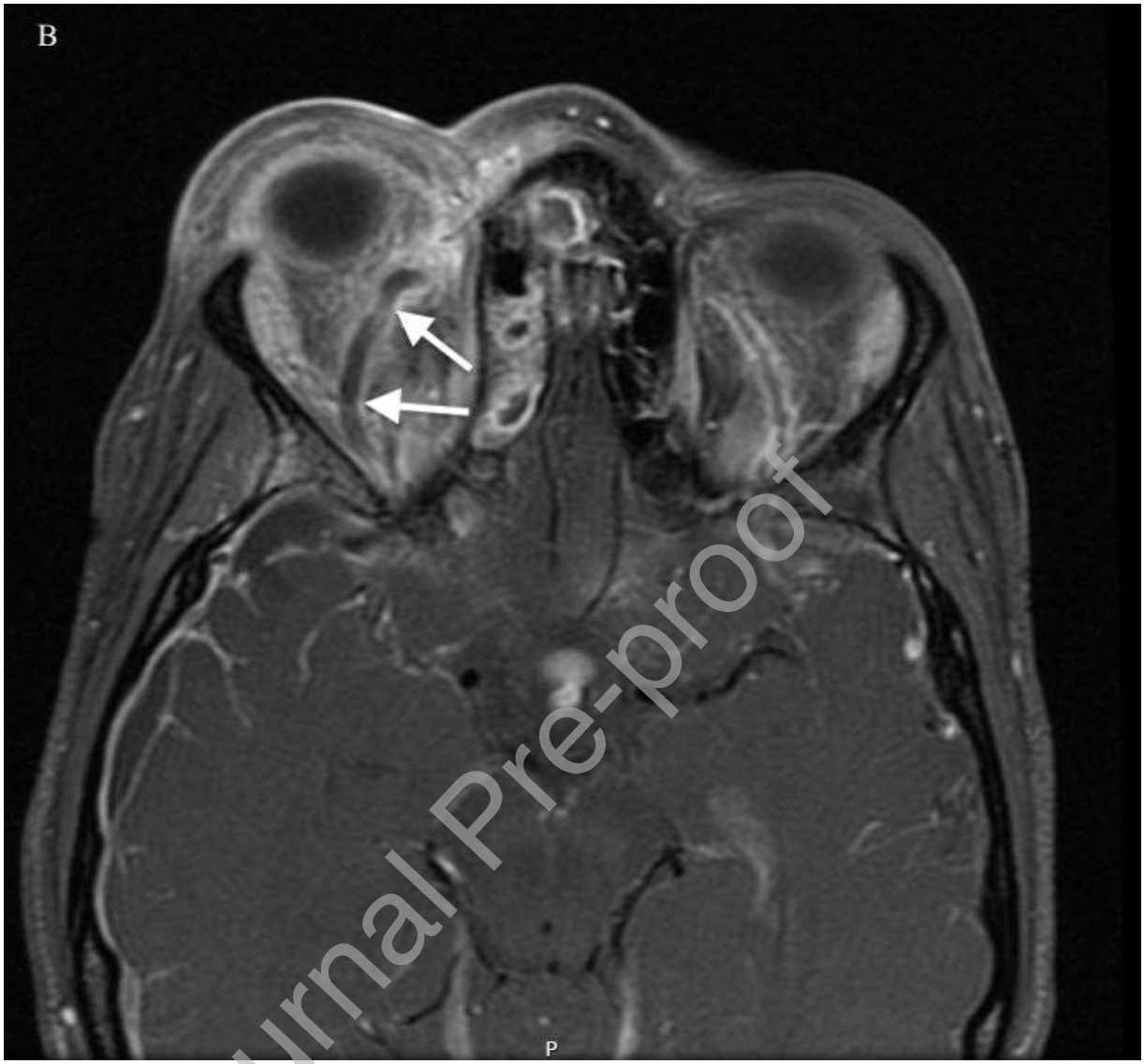
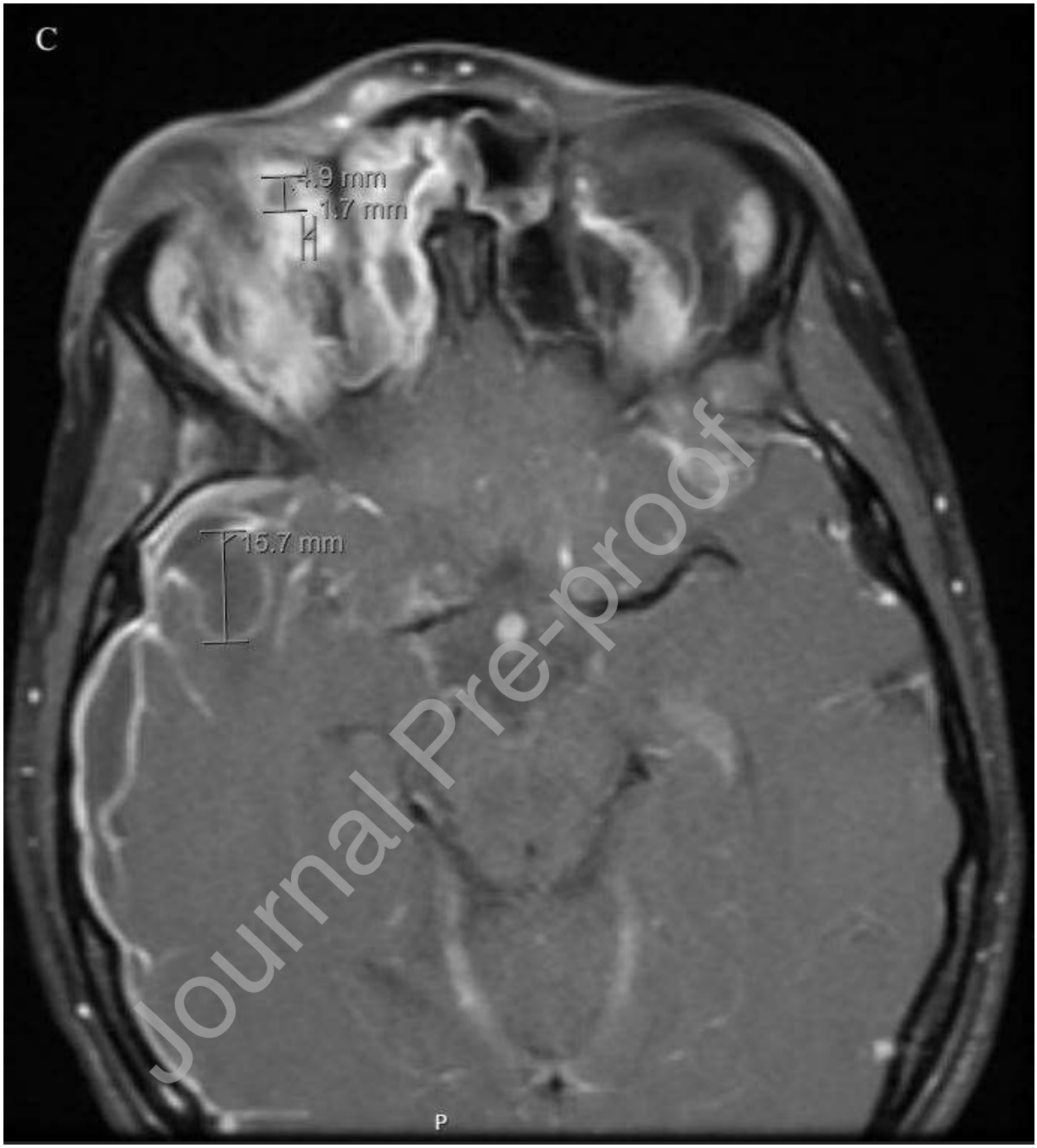


Figure 1: CT orbit with IV contrast showing (A) right orbital cellulitis and proptosis (arrow), and (B) right IJ thrombosis (arrow) with significant bilateral pansinusitis.

Figure 2







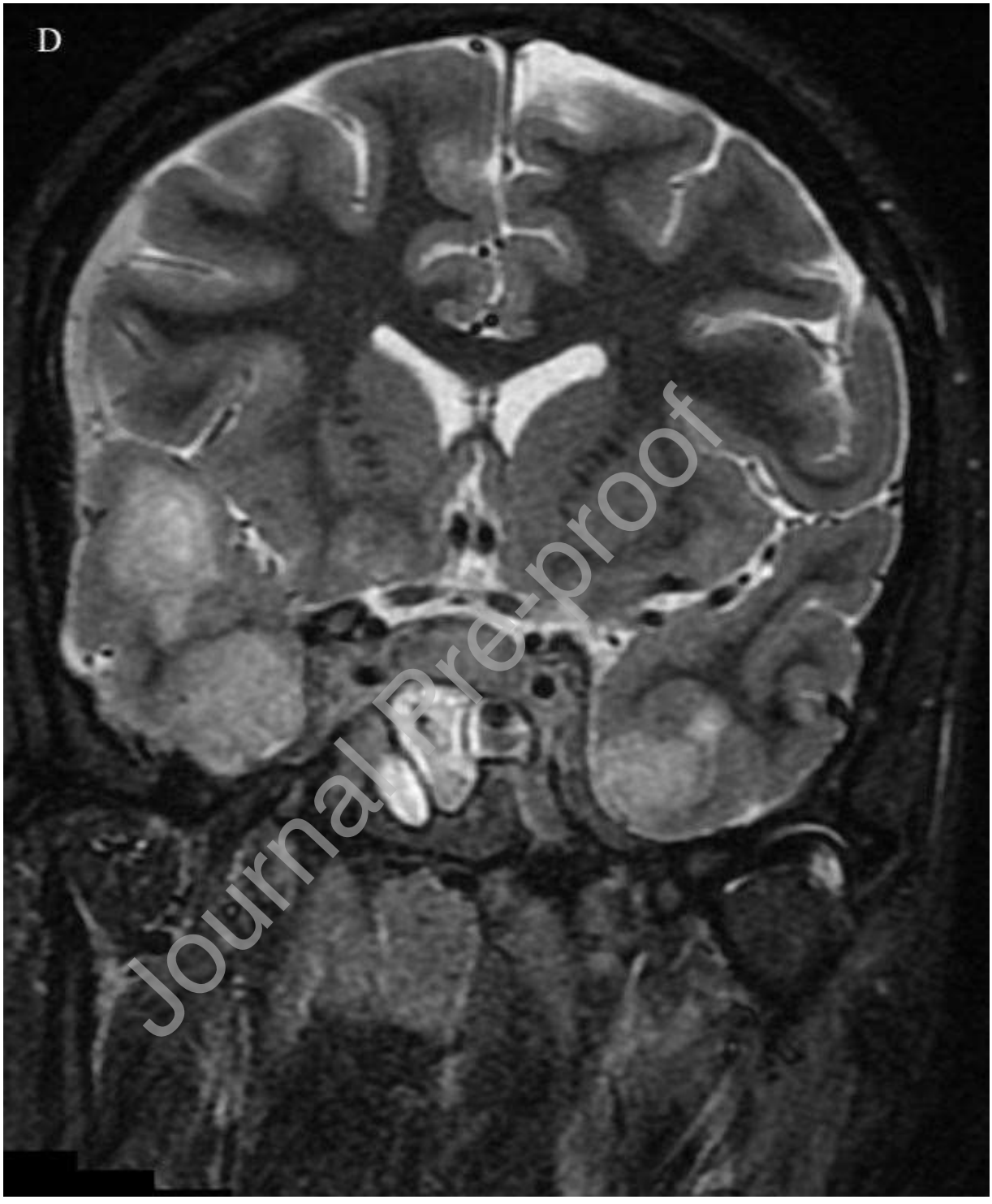


Figure 2: MRI showing (A) IJ thrombosis (arrow), proptosis, and abnormal enhancement of the right periorbital soft tissue, (B) distention of the right superior ophthalmic vein and lack of IV contrast enhancement (arrows) consistent with thrombosis. There is additional cavernous sinus and sigmoid sinus thrombosis, (C) abscesses within the right posterior orbit and right temporal lobe, (D) right temporal lobe abscess, right subdural empyema, bilateral cavernous sinus thrombosis, and small left temporal lobe abscess.