Radiology Case Reports 16 (2021) 1138–1143

Available online at www.sciencedirect.com

ScienceDirect

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

Case Report

Superior ophthalmic vein thrombosis secondary to COVID-19: an index case

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ARTICLE INFO

Article history:
Received 9 February 2021
Revised 25 February 2021
Accepted 25 February 2021
Available online 3 March 2021

Keywords:
COVID-19
Thrombosis
Superior ophthalmic vein
Neuroradiology

ABSTRACT

Superior ophthalmic vein thrombosis is a very rare condition, known to have a profound negative impact on vision and eye movement function and is usually associated with orbital infections, inflammation, tumors, or carotid cavernous fistulae. There is an increased risk of arterial and venous thrombosis associated with COVID-19, the presence of which is related to a significantly increased risk of mortality. We report an index case of superior ophthalmic vein thrombosis in a 61-year-old male patient who was diagnosed with COVID-19 pneumonitis and a concomitant saddle pulmonary embolus. He was swiftly treated with low molecular weight heparin which led to the resolution of the thrombosis within 3 weeks. This case highlights the importance of considering this entity in the context of COVID-19 as well as providing prompt treatment to reduce the risk of complications.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARs-COV-2 or COVID-19) is widely reported to be associated with increased risk of thromboembolic disease, likely secondary to hypercoagulability and/or a systemic inflammatory response associated with the infection. Large scale meta-analyses reveal that the pooled odds of mortality in COVID-19 positive patients who develop thromboembolism are 74% higher compared to those who do not [1].

The superior ophthalmic vein (SOV) originates from the superomedial angle of the orbital fossa and courses alongside the superior orbital artery within the intraconal space to ultimately drain into the cavernous sinus. SOV thrombosis is an extremely rare clinical phenomenon with an estimated incidence of 3-4 cases/million/year [2]. Its etiology is broadly categorized into septic and aseptic causes. Orbital cellulitis, sinusitis and septic cavernous sinus thrombosis account for common primary septic causes whereas facial trauma, hypercoagulability, aseptic inflammation, orbital neoplasms, and Tolosa-Hunt syndrome account for the aseptic etiologies [3,4]. The clinical features of SOV thrombosis can include painful proptosis, chemosis, conjunctival swelling, ophthalmoplegia, trismus, and visual disturbance/loss. As such, timely diagnosis and identification of this condition is essential to prevent the profound visual complications and eye movement dysfunction.

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https://doi.org/10.1016/j.radcr.2021.02.063

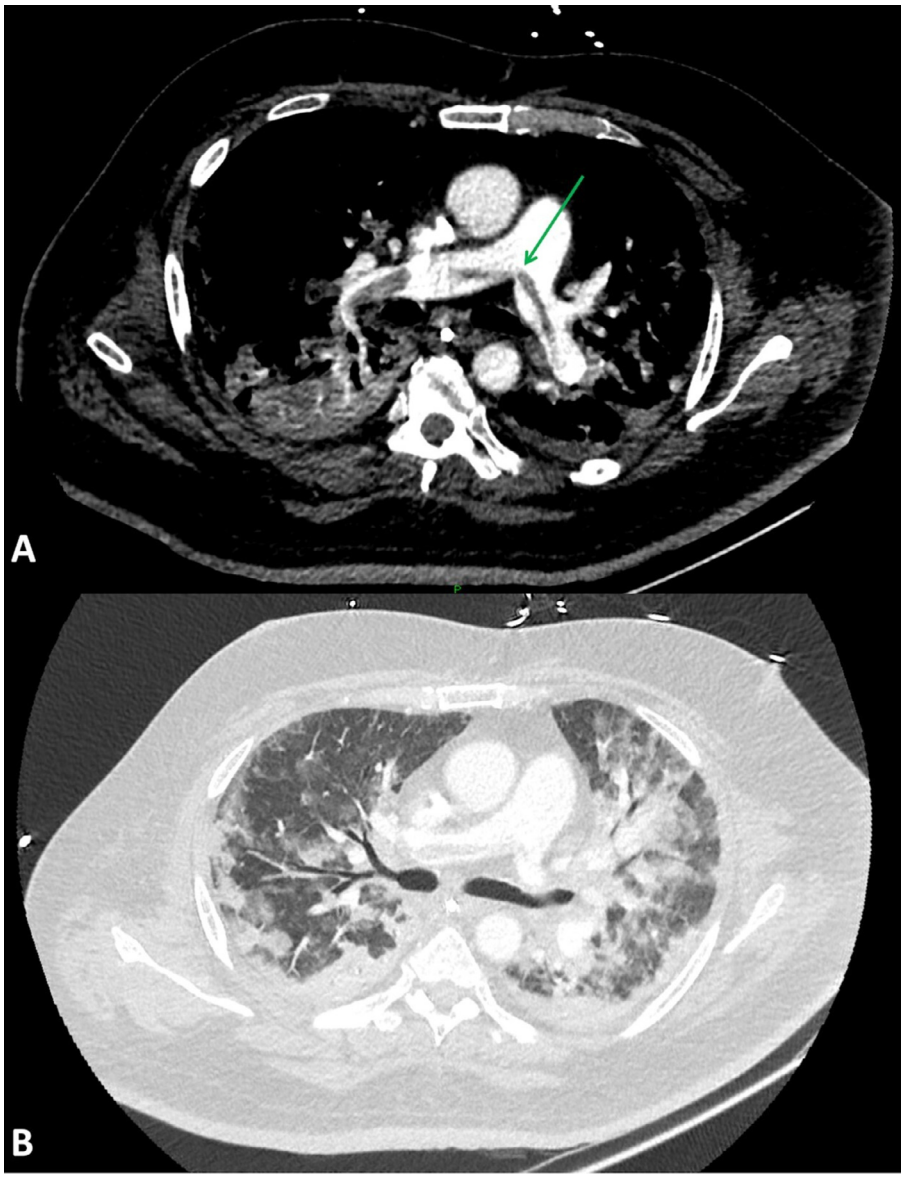

Fig. 1 – CT pulmonary angiogram. (A) Saddle pulmonary embolus (green arrow) with extension into the segmental and subsegmental pulmonary artery branches of the right and left hemithorax. (B) Extensive bilateral ground glass attenuation and patchy consolidation with a peripheral predominance, consistent with COVID-19 pneumonitis.

Herein, we present an index case of SOV thrombosis secondary to COVID-19 pneumonitis and a concomitant saddle pulmonary embolus.

Case report

A 61-year-old man was admitted to hospital with a 1-week history of fever, muscle weakness, and fatigue. His family contacts tested positive for COVID-19. His past medical history included: end-stage renal failure with a renal transplant in 2009 (for which he was immunosuppressed), type 2 diabetes mellitus, cerebrovascular disease, sleep apnea, orthostatic hypotension, benign prostatic hyperplasia (treated with transurethral resection of the prostate in 2009), and recurrent urinary tract infections.

On clinical examination, his temperature was mildly elevated at 37.6°C, his pulse was 112 beats per minute and blood pressure was 111/74. Urinalysis was positive for leucocytes, nitrites, and trace amounts of blood.

He was initially admitted and treated in hospital for urosepsis, but began to develop low oxygen saturations and subsequently tested positive for COVID-19. He therefore received additional treatment with dexamethasone and tocilizumab. Unfortunately, despite 1 week of treatment on the ward, persistently poor oxygen saturations and limited urine output resulted in transfer to the in-

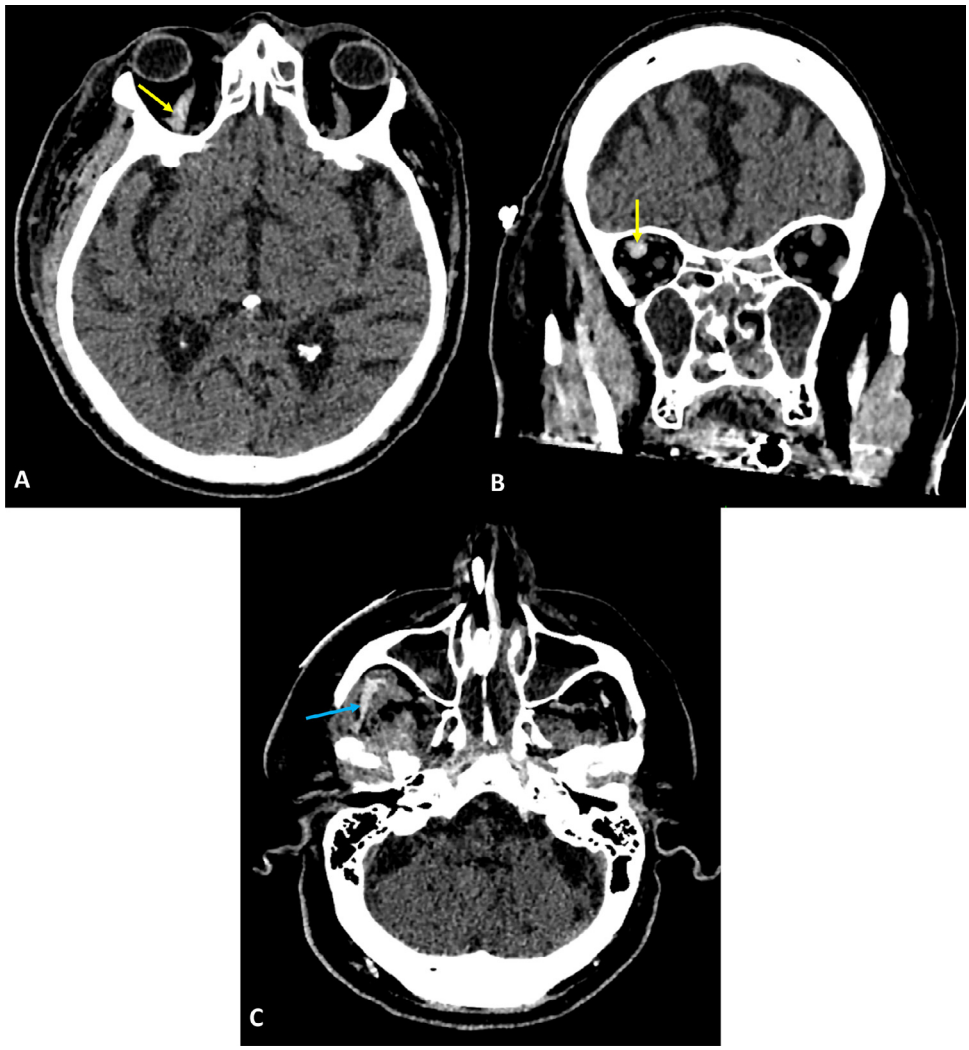

Fig. 2 – (A) Axial and (B) Coronal unenhanced CT head slices demonstrating a dilated asymmetrically hyperdense right SOV (yellow arrows) consistent with acute thrombosis. The left SOV also appears dilated, features of which are suggestive of bilateral CCF. (C) Axial CT image showing asymmetrical hyperdensity within the right masticator space (blue arrow), concerning for acute thrombosis within the right pterygoid venous plexus.

tensive care unit where he was initially intubated and hemodialysed.

Due to persistent fluctuating low oxygen saturations, a computed tomography pulmonary angiogram (CTPA) was performed 5 days following admission to intensive care. This demonstrated a saddle pulmonary embolus with extension into the segmental and subsegmental pulmonary artery branches of the right and left hemithoraces. This was on a background of bilateral ground-glass attenuation and patchy consolidation, consistent with severe COVID-19 pneumonitis (Fig. 1). Treatment with low molecular weight heparin was initiated following this finding.

Three days following a diagnosis of a saddle pulmonary embulus, the patient was incidentally found to have bilateral edematous eyelids. An ophthalmology opinion was sought and an ocular examination revealed bilaterally fixed and constricted pupils (left eye, 2 mm; right eye, 3 mm). No exophthalmos was noted however there was asymmetrical right-sided conjunctival injection and chemosis. Visual acuity was difficult to ascertain at this point since the patient was unconscious and receiving invasive ventilation.

A CT head with orbital imaging was performed which demonstrated an expanded and hyperdense right SOV as well as asymmetrical hyperdensity of the venous structures within the right masticator space. There was also swelling of the right pterygoid muscles and effacement of the fat planes. The findings were consistent with acute thrombosis of the right SOV and the right pterygoid venous plexus (Fig. 2). The left SOV also appeared dilated and this, in addition to the aforementioned findings, raised the suspicion of a bilateral caroticocavernous fistula.

A multidisciplinary team decision was made to treat this abnormality with low molecular weight heparin, which the patient was already receiving for the concomitant pulmonary

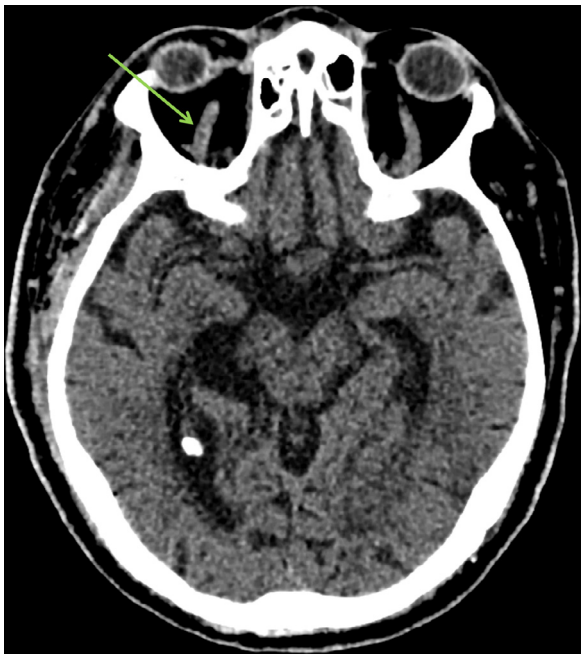

Fig. 3 – Axial CT head slice demonstrating complete resolution of the asymmetrical right SOV hyperdense thrombus (green arrow) following 3 weeks of anticoagulation with LMWH.

embolism. The patient made excellent progress on intensive care and was fortunately extubated 3 weeks following the initial diagnosis of right SOV thrombosis. Repeat interval imaging at this point with a CT head (Fig. 3) and a computed tomography pulmonary angiogram (Fig. 4) demonstrated complete resolution of the right SOV thrombosis and pulmonary embolism, with marked improvement in lung parenchymal appearances. We are pleased to report that the patient has now completely recovered from his illness and there were no residual abnormalities in relation to the SOV thrombosis. He has preserved range of movement in his eyes bilaterally, no diplopia and no deficiency in visual acuity. He is now undergoing speech and language therapy, physiotherapy and rehabilitation to improve his physical function after the prolonged hospital admission with COVID-19.

Discussion

This case report addresses the clinical characteristics of SOV thrombosis and the importance of considering this entity in COVID-19 patients with ocular impairment. To our knowledge, we are the first group to describe SOV thrombosis in a patient with COVID-19 pneumonitis.

COVID-19 is thought to induce a systemic inflammatory response, endothelial dysfunction and a hypercoagulative state which predisposes patients to forming systemic thrombi [5–8]. Proposed molecular and cellular mechanisms include COVID-19 induced pyroptosis, the upregulation of platelet activation, coagulation cascade and proinflammatory cytokines such as interleukin-6 as well as a downregulation of fibrinolysis [6,8]. All of the aforementioned factors are thought to be contributory to the formation of systemic emboli and/or immunothrombosis due to a delicate interplay between the immune system and hemostasis [8]. In our case, the patient also had a concomitant saddle pulmonary embolus which may have directly contributed to the development of SOV thrombosis secondary to distal embolic migration.

Several institutions begin prophylactic anticoagulation in all hospitalized COVID-19 patients, whilst treatment dose anticoagulation is used in confirmed venous thromboembolism, for which there is evidence demonstrating improved clinical outcomes [9]. The attenuation of inflammatory pathways is postulated to have a dampening effect on the development of immunothrombi. Dexamethasone is associated with improved outcomes in hospitalized patients [10] and there is increasing research into the therapeutic utility of anticytokine agents such as tocilizumab (anti-IL6) and anticomplement agents [11]. Further research is required to clarify the optimum management of thrombosis in COVID-19, ensuring that a careful balance is struck between targeting the dysfunctional prothrombotic pathways, without impairing the host immune response against infection.

SOV thrombosis in itself is a very rare entity and infrequently reported in the existing literature [12,13] Its etiology can be categorized into septic and aseptic causes, orbital cellulitis being the most commonly associated condition. [3,14] It can also present either unilaterally or bilaterally and has an association with cavernous sinus thrombosis. The signs and symptoms of SOV thrombosis are usually due to impaired venous drainage from the affected orbit for example, chemosis, painful eye movements, proptosis, eyelid swelling, and visual disturbance [4]. There is considerable overlap and nonspecificity of signs and symptoms when compared to other known ophthalmological conditions, which is why neuroimaging is necessary for a definitive diagnosis. CT or MRI venography are the modalities of choice, however the pathology can also be identified on a noncontrast cross-sectional studies. The primary findings include a dilated SOV with linear filling defects on CT or MRI venography or affected vessel hyperdensity in noncontrast examinations [3].

The management of SOV thrombosis has a focus on identifying and treating the underlying cause. Treatment options include anticoagulation, antibiotics or surgery and there is no definitive consensus and/or guidelines addressing its management. In general, published data suggests that aseptic, post-traumatic or incidental SOV thrombi have been treated with anticoagulation alone whereas septic cases have received additional antibiotics. Incidental and aseptic SOV thrombi are associated with a good prognosis and often respond to conservative/medical management. Septic SOV thrombi, secondary to orbital cellulitis or paranasal sinusitis, have a higher risk of complications such as abscess formation and therefore are likely to require surgical intervention and drainage [3].

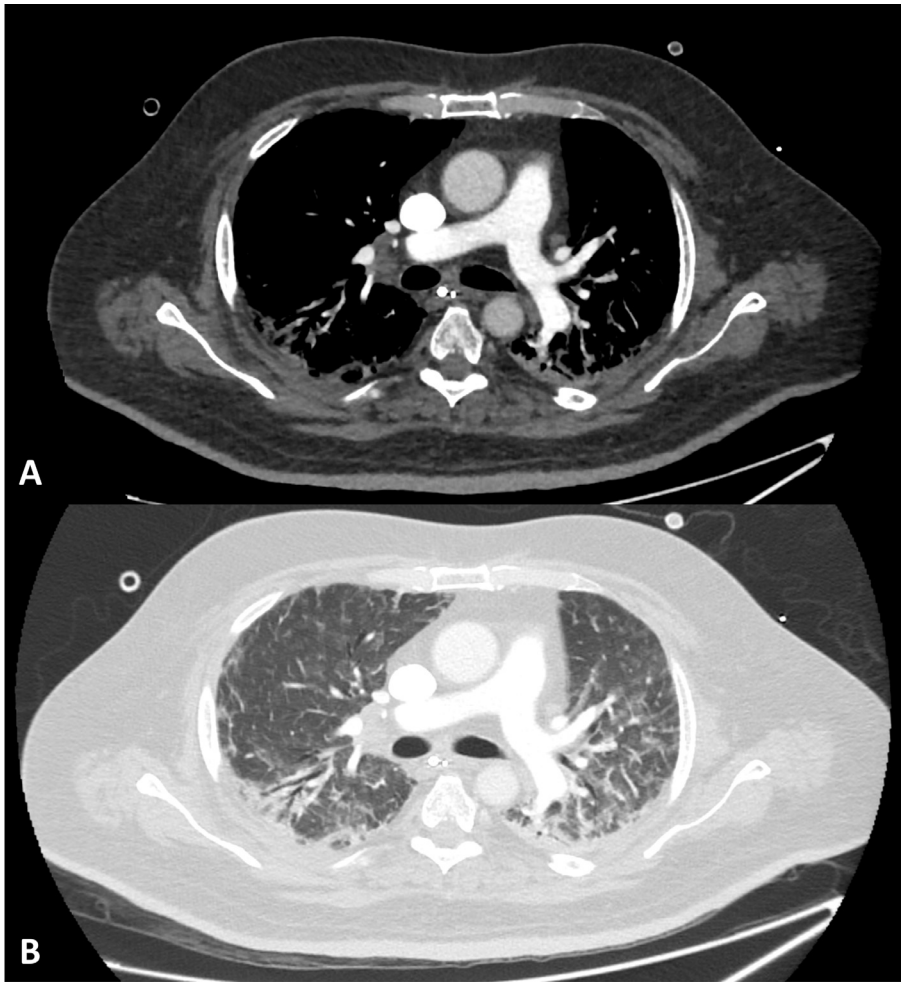

Fig. 4 – CT pulmonary angiogram after 3 weeks. (A) Complete resolution of the saddle pulmonary embolus. (B) Lung parenchymal appearances have markedly improved with mild residual bilateral patchy ground glass attenuation and peripheral consolidation.

Consent statement

The authors of this manuscript have obtained written, informed consent from the patient to write up the case report and for the use of images pertinent to the case. We have ensured anonymity of all clinical and graphical data used.

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