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Superior ophthalmic vein thrombosis: What radiologist and clinician must know?

Houman Sotoudeh[a,*], Omid Shafaat[b], Noha Aboueldahab[c], Michael Vaphiades[d], Ehsan Sotoudeh[e], Joshua Bernstock[f]

[a] Department of Neuroradiology, University of Alabama at Birmingham (UAB), 619 19th St S, Birmingham, AL, 35294, JTN 333, USA
[b] Department of Radiology and Interventional Neuroradiology, Isfahan University of Medical Sciences, 8174675731 Alzahra Teaching Hospital, Sofeh Blvd, Isfahan, Iran
[c] Department of Neuroradiology, University of Alabama at Birmingham (UAB), 619 19th St S, Birmingham, AL 35294, USA
[d] University of Alabama Birmingham (UAB) Department of Ophthalmology, 700 South 18th Street, Birmingham, AL 35233, USA
[e] Department of Surgery, Iranian Hospital in Dubai, P.O.BOX: 2330, Al-Wasl Road, Dubai 2330, United Arab Emirates
[f] Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School, Hale Building, 60 Fenwood Road, Boston, MA 02115, USA[1]

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ABSTRACT

Purpose: Superior ophthalmic vein thrombosis (SOVT) is an extremely rare condition. Few studies have been published about clinical aspects of this condition. In this study, we have studied the symptoms, underlying etiologies, treatment, pathogenesis and complication of the SOVT and we tried to classify it based on the etiology, treatment, and prognosis.

Methods: We reviewed the patients' data from a tertiary academic referral center. Each patient with SOVT was then reviewed for symptoms associated with SOVT, underlying etiology, treatment protocol, treatment response, complications, possible pathogens, and final outcome.

Results: Twenty-four cases of SOVT were included in this study. Overall, 13 cases were diagnosed as right-sided SOVT, out of which, eight had simultaneous right-sided cavernous sinus thrombosis (CST). Eighteen cases were diagnosed to have left-sided SOVT, out of which, 11 had simultaneous left-sided CST.

Conclusions: The SOVT can be secondary to different mechanisms. The SOVT secondary to trauma, recent surgery and coagulopathy are mostly non-aggressive, and can be managed by conservative therapy and anticoagulation. The SOVT in patients with orbital cellulitis, history of active sinusitis or paranasal sinus surgery are aggressive presenting with acute orbital swelling, abscess and visual loss. This type of SOVT can be complicated by extension to the cavernous sinus and intracranial structures. These patients require urgent antibiotics therapy and sinus surgery. The most severe type of SOVT is caused by mucormycosis which may also extend intracranially resulting in stroke and is often life-threatening.

1. Introduction

Superior ophthalmic vein thrombosis (SOVT) is extremely rare (incidence of 3–4 cases/million/year) but potentially devastating clinical entity [1,2]. The SOVT can be secondary to septic or aseptic causes. Septic causes include orbital cellulitis, paranasal sinusitis, and septic cavernous sinus thrombosis (CST). Aseptic etiologies are secondary to facial trauma or inflammation, spontaneous carotid cavernous fistula (CCF), hypercoagulable states, orbital neoplasm and Tolosa–Hunt syndrome [3–6]. Orbital infections by aerobic or anaerobic organisms are the most common cause of the SOVT. The most common pathogens causing orbital cellulitis are *Staphylococcus aureus* and Streptococcus family [4,6]. Clinically, SOVT manifests with painful ptosis and proptosis, conjunctival congestion and chemosis alone with visual loss which and can be detected on post-contrast computed tomography (CT) or magnetic resonance Imaging (MRI) [1,4–6]. The superior ophthalmic

Abbreviations: SOVT, superior ophthalmic vein thrombosis; CST, cavernous sinus thrombosis; CCF, carotid cavernous fistula; CT, computed tomography; MRI, magnetic resonance Imaging; IRB, institutional review board; SOV, superior ophthalmic vein; SCC, Squamous Cell Carcinoma; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; M, male; F, female; Y, yes; R, right; L, left; N/A, not applicable; B/L, bilateral; UTI, Urinary Tract Infection

* Corresponding author.
E-mail addresses: hsotoudeh@uabmc.edu (H. Sotoudeh), omid.shafaat@yahoo.com (O. Shafaat), naboueldahab@uabmc.edu (N. Aboueldahab), mvaphiades@uabmc.edu (M. Vaphiades), ehsansotoudeh@gmail.com (E. Sotoudeh), jbernstock@partners.org (J. Bernstock).

[1] https://www.brighamandwomens.org/neurosurgery.

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vein originates in the superior inner angle of the orbital cavity and takes a course with superior orbital artery to drain into the cavernous sinus. The SOVT can develop into CST, with involvement of the cranial nerves within the cavernous sinus and intracranial complications [7]. Appropriate and rapid treatment based on the underlying etiology is required to prevent the catastrophic consequences and complications of the SOVT [8]. There is no universal treatment protocol for the SOVT due to its rarity. Most of the published studies in this field are case reports or case series with a limited number of patients. To date, 69 cases of the SOVT have been published in the English literature via Medline search. In this study, we represent a cohort of SOVT cases with attention to risk factors, etiology, treatment, complications, prognosis and outcome. In addition we classify the SOVT based on the underlying etiology and suggest the appropriate therapy in each group. In the cases of septic SOVT we review the microbiology and the underlying causative organisms.

2. Materials and methods

This study was approved by our university review board (IRB No 300001833). The electronic data of our institution were reviewed from 2005 to 2018 for cases with diagnosis of the SOVT. All images were reviewed by one neuroradiologist (HS) with 11 years of experience. Patients with enlargement of the SOV containing filling defect on post-contrast images were included in this study (Figs. 1 and 2). The patients with enlargement or varix of the SOV without internal filling defects were excluded. The CST was considered as a filling defect in the expanded cavernous sinus on post-contrast CT or MR (Fig. 3). For each case, all available images were reviewed documenting orbital complications of SOVT, including extension of the thrombosis to the cavernous sinuses and intracranial structures. For each case, the entire electronic file was reviewed. The demographic data, past medical history, underlying comorbidities, presenting symptoms, treatment and responses, complications, final outcome and mortality related to the SOVT were documented (Figs. 4–8).

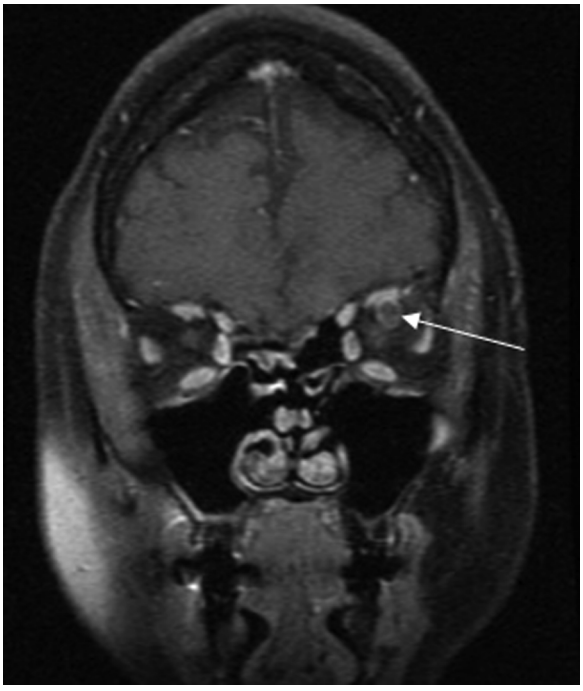

Fig. 1. Coronal post-contrast T1 weighted MRI demonstrates dilation of the left superior ophthalmic vein with internal filling defect. Diagnostic for the left SOVT (arrow).

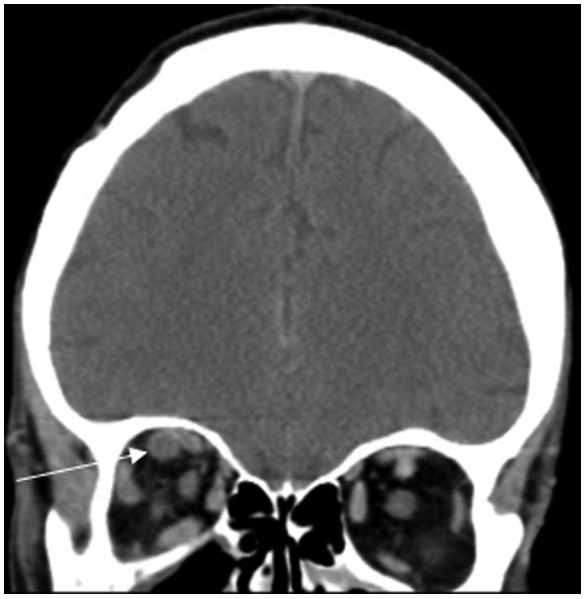

Fig. 2. Coronal post-contrast CT demonstrates dilation of the right superior ophthalmic vein with internal thrombosis consistent with right SOVT (arrow).

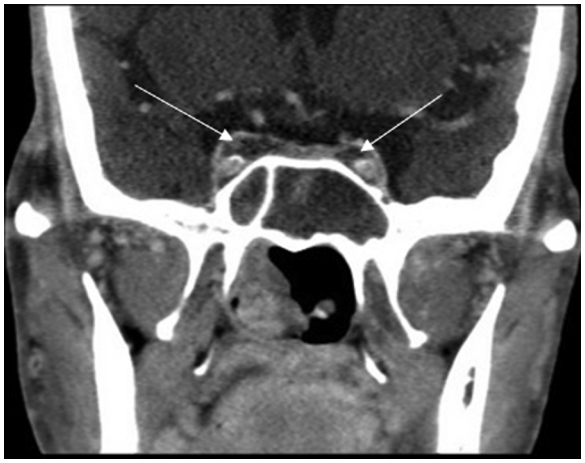

Fig. 3. Coronal post-contrast coronal CT demonstrates expansion of the cavernous sinuses with internal filling defect diagnostic for bilateral cavernous sinus thrombosis (arrows).

3. Results

Over a 13-year period, 24 patients with documented SOVT were included; 13 female and 11 male with a mean age of 56.9 years, (SD = 13.2, range 29–85). Thirteen cases of right-sided SOVT were detected, 8 of which had simultaneous right-sided CST. Eighteen cases of left-sided SOVT were noted, 11 of which had simultaneous left-sided CST. Twelve cases were septic, 9 of which were managed surgically. One case of sinus Squamous Cell Carcinoma (SCC) and SOVT was treated by prednisolone and radiotherapy. One case of CCF did not receive any treatment besides regular follow-up. Three cases of incidentally detected SOVT were treated with Aspirin and Warfarin. Four cases of post-traumatic and two cases of post-surgical SOVT were managed conservatively. One case had long-lasting coagulopathy and received anticoagulation. In eleven cases, all belonging to the septic group, complications were noted. In 10 out of 12 cases of septic SOVT, microbiologic culture results were included. Patients' demographic data, underlying etiologies, past medical histories, symptoms, treatments, complications, pathogens and outcome are presented in Table 1.

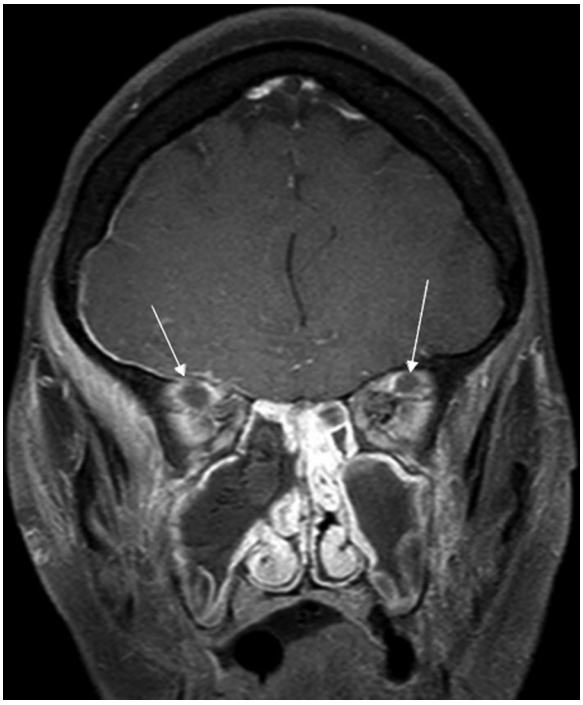

Fig. 4. Coronal post-contrast T1 sequence shows evidence of bilateral SOVT with expansion of veins and lack of enhancement (arrows).The patient is status post functional sinus surgery with persistent sinusitis.

4. Discussion

The SOV is the main draining venous structure in orbit. The SOVT is a rare condition with only 69 cases reported to date [9]. The primary clinical presentation of SOVT is acute painful proptosis, chemosis, conjunctival congestion, and visual loss [10].

The SOVT can be secondary to many underlying etiologies including: infectious (paranasal sinusitis, orbital cellulitis and septic cavernous sinus thrombosis with the extension of the thrombus into the SOV) and aseptic (spontaneous or treated thrombosed CCF, neoplastic invasion of the cavernous sinus and orbit, Tolosa–Hunt syndrome and maxillofacial trauma) [4–6,11]. Many systemic disorders are associated with the SOVT including hypercoagulable states (thrombocytosis, sickle cell trait, hereditary hemorrhagic telangiectasia, antiphospholipid syndrome, use of oral contraceptive pills, and pregnancy). In this study, we detected a case of SOVT because of hypercoagulability state secondary to long lasting elevated factor VIII. Inflammatory diseases (Graves' disease, systemic lupus erythematosus, sarcoidosis, Behçet syndrome, amyloidosis, vasculitis and ulcerative colitis) have been reported to be associated with the SOVT [4–6,12]. We detected SOVT in a case with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) and a case of Sjogren's syndrome. There are several reported cases of SOVT in SLE with and without antiphospholipid syndrome. The SOVT in SLE without antiphospholipid syndrome is attributed to inflammation and SOVT in SLE with the antiphospholipid syndrome is attributed to hypercoagulation [13–15]. There is an association between the systemic malignancies (leukemia, lymphoma, multiple myeloma, lung cancer and amyloidosis) and the SOVT [3–6,16,17]. We also detected a case of breast cancer with SOVT although the patient was complicated by cellulitis.

Regarding the clinical presentation of SOVT, symptoms are secondary to impaired orbital venous drainage including orbital swelling, pain, chemosis, eyelid edema, proptosis, limited ocular motility, with or without fundus findings, and impaired visual acuity [9]. Because of overlap in diagnosis, neuroimaging plays a critical role in the diagnosis of SOVT. The main imaging finding is dilation of the SOV with internal filling defects. Soft tissue stranding around the SOV and within the orbital fat and enlargement of the extraocular muscles are the other imaging findings. Asymmetric dilation of the SOV by itself is not diagnostic for the SOVT. Only about 10% of dilated SOVs are because of the thrombosis [18] which emphasizes the role of contrast imaging.

The SOVT may be unilateral or bilateral and it can be associated with CST. In our study, we had 13 cases of right-sided SOVT and 18 left-sided SOVT. In 13 cases, the cavernous sinus was involved as well. In 6 cases, both SOV and cavernous sinuses were involved.

Among 24 cases, 12 patients had septic SOVT, all of which had evidence of mucosal thickening in paranasal sinuses consistent with either acute or chronic sinusitis. We were able to collect clinical data for 11 of the 12 with 1 case being lost follow-up. This patient had imaging in our institution but decided to leave the hospital without treatment. Since this patient had two complications (optic nerve ischemia and meningitis which were detected on imaging), we decided to include this patient in our study despite the fact that there is no data about treatment and microbiology. In 4 cases, the SOVT was attributed to trauma. In 3 cases SOVT were noted incidentally and without significant orbital symptoms.

4.1. Complications

In three cases (12%), we detected paralysis of cranial nerves, all of which had the simultaneous CST. In two patients (8%) the SOVT was complicated by septic thrombosis of internal jugular veins (Lemierre's

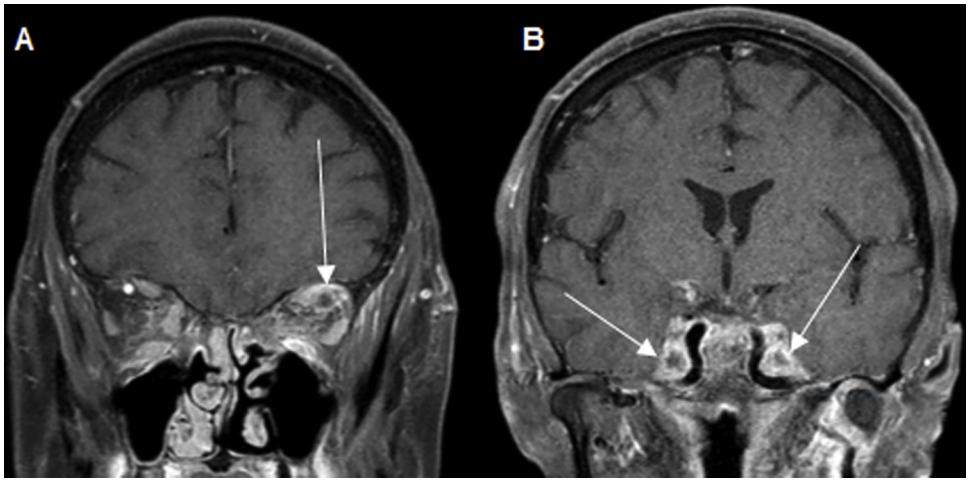

Fig. 5. Coronal post-contrast T1 show left SOVT (arrow A) with thrombosis of bilateral cavernous sinuses (arrow B).

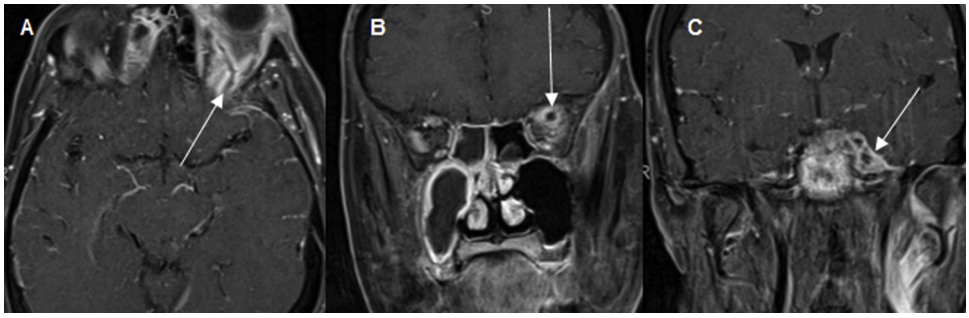

Fig. 6. Axial and coronal post-contrast T1 show left sided SOVT (arrows A and B) with extension to left cavernous sinus (arrow C). Evidence of left orbital cellulitis is also noted.

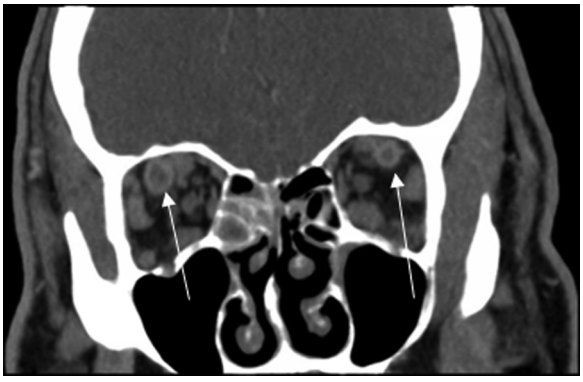

Fig. 7. Coronal post-contrast CT shows bilateral SOVT with venous dilation and lack of enhancement (arrows).

syndrome) both had CST as well. The Lemierre's syndrome has never been reported as a complication of SOVT before. The SOVT was complicated by acute cerebral hemispheric infarction and death in one patient, which was because of mucormycosis infection and reveals the mortality rate of SOVT to be 4% in the presented cohort. Optic nerve infarction was seen in one case (4%) diagnosed by imaging. In three cases, the SOVT was complicated by intracranial infection (subdural empyema, ventriculitis and temporal lobe abscess) revealing 16% chance of intracranial involvement (including the mucormycosis patient).

Orbital cellulitis is the most prevalent underlying etiology for SOVT and was detected in 50% of our patients. The orbital cellulitis is more common in the pediatric population [19]. The infectious etiologies are commonly bacterial or polymicrobial, often including aerobic and anaerobic bacteria, less commonly fungal or mycobacteria. The most common bacteria causing orbital cellulitis are Staphylococcus aureus and Streptococci family. The non-spore-forming anaerobes Aeromonas hydrophila, Pseudomonas aeruginosa, and *Eikenella corrodens* are rare. Mucormycosis and Aspergillus are rare causes of the orbital cellulitis [20].

Most cases of paranasal sinusitis are due to viral infections with few secondary bacterial infections [21]. The Rhinoviruses, influenza/parainfluenza viruses are the most common causes of paranasal sinusitis. The most common bacterial causes of acute purulent sinusitis are Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and *Streptococcus pyogenes*. In chronic paranasal sinusitis, the most common isolated bacteria are staphylococcus aureus and anaerobic bacteria (Prevotella and Porphyromonas, Fusobacterium and Peptostreptococcus spp). *Pseudomonas aeruginosa* and other aerobic and facultative gram-negative rods can be seen in immunocompromised patients. Fungi and *Pseudomonas aeruginosa* are common pathogens in neutropenic patients [22].

In our study, 12 patients had septic SOVT, among them the bacteriologic data of 10 cases are available. In 4, the infection was polymicrobial. The most common pathogens in our study were: *Staphylococcus aureus* (methicillin sensitive and resistant), B-hemolytic Streptococcus, Pseudomonas aeruginosa, Coagulase-negative Staphylococci, Staphylococcus Epidermis, Staphylococcus Intermedius, Mucormycosis, Streptococcus viridans, and *Streptococcus constellatus*. In our cohort the microbiology of the septic SOVT was different than the acute sinusitis or even orbital cellulitis and has overlap with common bacteria causing chronic sinusitis.

4.2. Treatment

Treatment of the SOVT depends on the underlying etiology and includes anticoagulation, antibiotics and surgery. In our study, the patients with post-traumatic, incidental and aseptic SOVTs were treated by anticoagulation without antibiotics. Treatment response in these

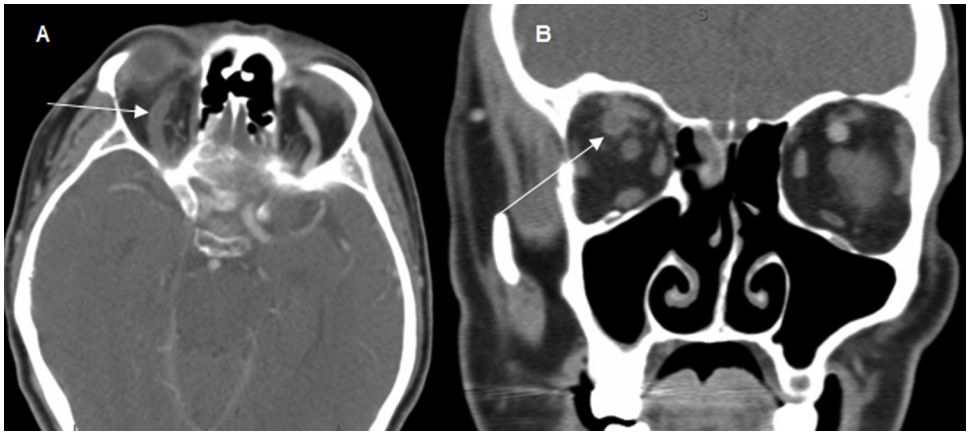

Fig. 8. Axial and coronal post-contrast CT show right SOVT with dilation and lack of enhancement (arrows A and B).

Table 1
Patient's demographic data, underlying etiologies, past medical histories, symptoms, treatments, complications, microbiology and outcomes. M: Male; F: Female; Y: Yes; R: Right; L: Left; N/A: Not applicable, B/L: Bilateral, SCC: Squamous Cell Carcinoma, CCF: carotid-cavernous fistula, SLE: Systemic lupus erythematosus, RA: Rheumatoid arthritis, SOVT: Superior ophthalmic vein thrombosis, CST: Cavernous sinus thrombosis, UTI: Urinary Tract Infection.

Case	Underlying etiology	Past medical history	Sex	Age	Symptoms	Thrombosis	Surgical treatment	Medical treatment	Complications	Pathogen in case of infection
1	Chronic sinusitis (Fig. 4)	SLE, RA, hypertension, depression, anxiety, drug abuse	F	46	Head ache and R eye swelling, altered mental status	B/L SOVT, B/L CST	Endoscopic B/L frontal, ethmoidal, maxillary and sphenoidal sinusotomy	Dexamethasone, vancomycin, ceftriaxone, metronidazole	Subdural empyema and meningitis	Methicillin-sensitive Staphylococcus aureus, rare E. coli, few Staph epidermis
2	SCC of L maxillary sinus	SCC L maxillary sinus T4bN2MX status post chemo-radiation (cisplatin and taxotere)	M	53	L facial swelling, L eye vision loss	LSOVT and LCST	No	Dexamethasone and radiation	No	N/A
3	Motor vehicle collision	Hypertension, diabetes, gastroesophageal reflux and diabetic retinopathy	M	53	Head trauma	B/L SOVT and B/L CST	No	Aspirin	No	N/A
4	R anterior skull base meningioma status post resection	Otherwise healthy	M	50	No Orbital Symptom	RSOVT and RCST	No	Aspirin	No	N/A
5	B/L Indirect CCF Status Post Arterial Embolization	Anorexia related to nausea	F	78	L eye swelling	LSOVT and B/L CST	No	No	No	N/A
6	B/L orbital cellulitis and meningitis	No data	F	68	B/L orbital swelling	B/LSOVT and B/L CST	No data	No data	R optic nerve infarct and meningitis on imaging	No data
7	Motor vehicle collision with L globe tearing status post-surgery and repair complicated by L orbital cellulitis	Atrial fibrillation, coronary artery disease, hypothyroidism	F	79	L eye swelling	LSOVT	No	Bacitracin, polymyxin B, prednisolone	No	No culture performed
8	L eye cellulitis	Congenital R blindness, history of sinus surgery	M	29	Headache, L eye swelling and pain, L sided vision loss	LSOVT	L orbital decompression, L sinusotomy	Vancomycin, piperacillin/tazobactam, dexamethasone, enoxaparin, coumadin, prednisone	Diminished L vision and orbital abscess	B-hemolytic Streptococcus
9	Incidentally Noted SOVT on Brain CT done for Altered Mental Status	Advanced Dementia, Active Urinary Tract Infection (UTI), Benign prostate Hypertrophy (BPH), Hypothyroidism	M	85	No orbital symptom	LSOVT	No	Aspirin, heparin, ceftriaxone (for UTI)	No	N/A
10	Acute sinusitis with orbital cellulitis	Chronic Sinusitis	F	70	L eye swelling	LSOVT	L frontal, ethmoidal, maxillary, and sphenoid sinusotomy. L anterior orbitotomy with drainage of two sub periosteal abscesses	Amoxicillin, cephalexin, ciprofloxacin	Myositis of L medial and superior rectus muscles and orbital abscess	Pseudomonas aeruginosa
11	Head trauma	Otherwise healthy	M	45	No eye symptom	RSOVT	No	Bacitracin, polymyxin B, and enoxaparin	No	N/A
12	Incidentally noted SOVT during work up for carotid artery stenosis	Carotid stenosis, coronary artery disease status post CABG	F	49	No eye symptom	RSOVT	No	Aspirin	No	N/A
13	L sphenoidal sinusitis, L orbital cellulitis (Fig. 5)	Chronic sinusitis, diabetes mellitus	F	68	Headache	LSOVT and B/L CST	Functional endoscopic sinus surgery (FESS) with revision sphenoidectomy	Vancomycin, piperacillin-tazobactam, coumadin, Enoxaparin	L internal jugular vein thrombosis, B/L abducens nerve palsy	coagulase-negative staphylococci
14	R orbital cellulitis	Breast cancer	F	63	R eye swelling	B/L SOVT and B/L CST	R orbital abscess drainage, R maxillary and sphenoidal sinusotomy	Ceftriaxone, cefepime, vancomycin, metronidazole, amphotericin B	L temporal lobe abscess and abscess	Staphylococcus aureus
15	L orbital cellulitis (Fig. 6)	Chronic sinusitis	F	54	L eye swelling	LSOVT and LCST	Endoscopic B/L pan-sinusotomy	amoxicillin/clavulanate, clindamycin, levofloxacin,	Septic thrombophlebitis from transverse sinus to	

(*continued on next page*)

Table 1 (*continued*)

Case	Underlying etiology	Past medical history	Sex	Age	Symptoms	Thrombosis	Surgical treatment	Medical treatment	Complications	Pathogen in case of infection
								ceftriaxone, vancomycin, metronidazole, amphotericin B, enoxaparin, heparin, warfarin, dexamethasone	internal jugular vein and skull base osteomyelitis	Staphylococcus epidermis, Staphylococcus intermedius
16	Hyper coagulation. Persistently elevated factor VIII Level. Coagulation work-up is otherwise negative	Hypertension, asthma, history of deep vein thrombosis 20 years ago	F	56	L visual loss	LSOVT	No	Heparin, Enoxaparin, Coumadin		N/A
17	Sinusitis and L eye cellulitis	History of functional endoscopic sinus surgery (FESS), diabetes mellitus, hypertension	M	42	L eye swelling	LSOVT and LCST	No	Clindamycin, Vancomycin, Piperacillin-Tazobactam, Amphotericin B	L hemispheric infarction and death	Mucormycosis
18	Assault by knife with subdural hematoma	Otherwise healthy	M	53	Trauma	LSOVT	L parietal craniotomy. Evacuation of subdural hematoma. Debridement of skull fracture.	Ceftriaxone	No	N/A
19	Incidentally noted SOVT by MRI For migraine	Sjogren's syndrome, hypothyroidism	F	51	No orbital symptom	B/L SOVT	No	Warfarin	No	N/A
20	Acute sinusitis	Cocaine abuse, cirrhosis, diabetes mellitus	M	58	R eye swelling	B/L SOVT and B/L CST	Drainage of orbital abscess, R frontal, ethmoidal, maxillary and Sphenoidal Sinusotomy	Amphotericin B, vancomycin, heparin	Sepsis secondary to acute sinusitis	Methicillin-Resistant Staphylococcus aureus (MRSA)
21	Maxillofacial fractures status post orbital reconstruction	Otherwise healthy	F	39	Trauma	RSOVT	No	Enoxaparin	No	N/A
22	B/L orbital cellulitis (Fig. 7)	Allergic fungal sinusitis, chronic headache, hypertension, gout	M	52	L eye swelling followed by R eye swelling	B/L SOVT and B/L CST	B/L maxillary antrostomy, ethmoidal and sphenoidal sinusotomy	Vancomycin, amoxicillin-clavulanate	B/L cranial Nerve 3^{rd},4^{th} and 6^{th} paralysis and orbital abscess	Staphylococcus epidermidis, Streptococcus viridans. No Fungus Isolated
23	Motor vehicle collision	Depression, hypertension	F	65	Facial ecchymosis	RSOVT	No	Enoxaparin	No	N/A
24	Acute R ethmoidal and sphenoidal sinusitis (Fig. 8)	Hypertension, chronic sinusitis, prior stoke, narcolepsy, nephrolithiasis and benign prostate hypertrophy	M	61	R proptosis, opthalmoplegia and lethargy	RSOVT and B/L CST	Functional endoscopic sinus surgery, ventriculostomy	Cefepime, enoxaparin, dexamethasone, intrathecal tobramycin	L 6^{th} nerve palsy, ventriculitis	Streptococcus intermedius, Streptococcus constellatus, Staphylococcus epidermidis and Pseudomonas aeruginosa.

groups were appropriate and no complication was noted. All of the septic SOVTs cases were treated with antibiotics. The septic SOVTs with orbital abscess required surgical drainage. From 12 cases of septic SOVT data, 11 cases were available; all of which received antibiotics, and 9 cases underwent sinus and orbital surgery.

4.3. Limitations

Our study is limited because it is retrospective. One patient was lost to follow-up, and microbiologic results of all septic SOVT were not available. In addition, we tried to follow the patients regarding the final visual accuracy and any permanent visual defect after treatment of SOVT, but the ophthalmologic data was not available in all patients. Despite the above-mentioned limitations, based on our knowledge, our study includes the largest published patient population of the SOVT to date.

5. Conclusion

The SOVT is a rare condition with many underlying etiologies. Its symptoms overlap with the orbital cellulitis, and post-contrast CT and MRI is critical for diagnosis. The treatment and prognosis of the SOVT depend on the underlying etiology. Based on underlying etiology, SOVT can be classified into different categories including:

A.) Incidental SOVT (good prognosis, usually self-limited and treated by anticoagulation)
B.) Post-traumatic and post-surgical SOVT (usually good prognosis which is treated by anticoagulation)
C.) Septic SOVT (secondary to paranasal sinusitis, orbital cellulitis or a history of paranasal sinus surgery with aggressive behavior, different organisms in comparison to the usual cause of acute sinusitis with a high risk of complication which requires specific antibiotics, anticoagulation and surgery)
D.) Aseptic SOVT (secondary to inflammatory-autoimmune diseases, coagulopathy, CCF and direct tumor invasion, usually requiring treatment for the underlying condition in association with anticoagulation).
E.) The CT and MR imaging studies are vital to the correct diagnosis and management of patients with SOVT. Evidence of sinusitis or a history of functional sinus surgery is critical to the diagnosis of septic SOVT. The antibiotic therapy of the septic SOVT must cover the Staphylococcus (including the Methicillin-Resistant Staphylococcus aureus), Pseudomonas, Streptococcus, and mucormycosis families.

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None.

Author contributions

HS, OS, and NA contributed conception and design of the study; HS organized the database; HS, OS, NA, and ES wrote the first draft of the manuscript; MV wrote sections of the manuscript. All authors contributed to manuscript revision, read and approved the submitted version.

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