International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2020): 7.803

Varied Aetiology of Orbital Cellulitis at Tertiary Care Center in India during COVID-19 Pandemic: A Case Series

Goswami Urmish V, Prajapati Kamini M, Ravani Swati A, Parmar Rutvi

Abstract: ***Purpose: To study the cases of Orbital Cellulitis presenting to tertiary care centre with varied aetiologies during the COVID-19 lockdown in India. Design: Cross Sectional study. Methods: Cases presenting with features of orbital cellulitis at M & J Institute of Ophthalmology during COVID-19 related lockdown (23rd March 2020 - 30th June 2020) were studied with respect to the aetiology, signs, symptoms, past history, different clinical presentations, treatments, investigations and associated complications. Results: A total 21 cases of Orbital cellulitis were identified including 19 males and 2 females (9.5:1). The median age was 47 years (3-71 years). Average duration of onset of symptoms before presenting at hospital was around 34 days (4-60 days). 13 had Infective, 6 had Neoplastic, 1 had Traumatic and 1 had Vascular as well as Infective etiology. 9 patients had Orbital mucormycosis as the cause of Infective aetiology. 19 (90%) had unilateral and 2(10%) had bilateral presentation. Conclusions: Our study highlights the abnormally increased incidence of orbital cellulitis during COVID-19 pandemic restrictions. Orbital mucor infection was the most common aetiology in COVID-19 positive patients. Most can be managed effectively by parental antibiotics, anti-fungals and if there is poor response with medical therapy, surgical treatment may be sought. Role of steroid is emerging however it might be the culprit behind the development of orbital mucormycosis especially in patients with COVID-19 infection. More future studies are required to establish the exact relation between COVID-19 infection and Orbital mucormycosis.***

Keywords: Orbital cellulitis, COVID-19, Corona Virus, Lockdown, Mucormycosis

1. Introduction

Orbital cellulitis is a purulent inflammation of the cellular tissues of the orbit [1]. Based on the involvement of structures and soft tissues, anterior or posterior to orbital septum anatomically are divided into; Preseptal cellulitis (anterior to the septum) and Orbital cellulitis (posterior to the septum). Although Orbital cellulitis is less common, careful clinical and radiological evaluation is required to differentiate it from preseptal cellulitis. Clinical symptoms and signs referring to orbital cavity involvement and Orbitalcellulitisare; proptosis, decreased visual acuity, conjunctival chemosis, relative afferent pupillary defect, pain on eye movements, limitation of ocular motility resulting in diplopia [2].

There are three main sources for orbital infection; (a) Secondary extension from Peri-orbital structures for e.g. sinusitis, dacryocystitis, dental infection, skin infection, fasciitis, eyelid pathologies, (b) Direct inoculation of microorganisms following penetrating trauma and surgery, (c) Hematogenous dissemination for e.g. sepsis, distant infected site [1].

The most common cause of Orbital cellulitis is a secondary extension from paranasal sinusitis especially ethmoid sinus[3].

Sub-periosteal abscess formation is mostly seen at the medial wall of orbit due to thin paper like bone of the ethmoid sinus and loose adherence to the periosteum. The inferior orbital wall adjacent to the maxillary sinus is also susceptible. There are no sinuses adjacent to the lateral wall.

The superior wall adjacent to the frontal sinus is thicker than the medial and inferior but superior wall infection may extend to the brain resulting in intracranial spread [4].

Orbital cellulitis is an ophthalmic emergency, which may be associated with life-threatening complications like, meningitis, epidural and subdural empyema, intracranial abscess, cerebral venous thrombosis and may complicate into death of an individual [2].

Other complications like loss of vision due to compressive optic neuropathy, artery and vein occlusion may occur [1, 2]. That is why for early diagnosis and treatment radiological imaging is necessary.

The Classical triad of fever, headache, and focal deficit is present in less than 50% cases. Headache, usually dull and poorly localized can be present in more than 70% of the cases and because of its nonspecific nature might be the cause of diagnostic delays [5].

The most common bacteria are Staphylococcus and Streptococcus in adults, and in children, Haemophilus Influenzae[6].

Timely diagnosis and early treatment reduces morbidity and mortality. The purpose of this study is to evaluate and compare the etiology, radiological findings, treatment and complications related to it, especially during the COVID-19 pandemic when more number of cases are presenting with Orbital cellulitis.

2. Materials and Methods

Cases presenting with features suggestive of orbital cellulitis at M & J Western Regional Institute of Ophthalmology during COVID-19 related lockdown (23rd March 2020 - 30th June 2020) were studied with respect to the aetiology, signs, symptoms, past history, different clinical presentations, treatments, investigations and associated complications. The study was conducted in accordance with

the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board and Ethics Committee.

The patients were explained regarding the study and written consent was taken. Then visual acuity was assessed on Snellen and Jaeger chart. The best corrected visual acuity was assessed. Eye movements and associated symptoms like pain were examined. It was followed by measurement of intra-ocular pressure by non-contact tonometry, anterior segment evaluation by slit lamp bio-microscopy, posterior segment evaluation with the help of direct and indirect ophthalmoscope. In cases presenting with media opacity or for the purpose of diagnosis Ultrasound B scan examination was done. Appropriate radiological investigations like CT scan and MRI of brain with orbits were done. MR Venogram was done in patients suspected of cerebral venous thrombosis. All routine blood tests were done including blood & pus culture. Available ocular specimens were sent for microbiological examinations.

Associated systemic features like fever with chills, malaise, and pain were documented. COVID-19 positive patients were treated in a separate facility under the guidance of Physicians, ENT surgeons, Anaesthetists and Ophthalmologists. Biopsy and endoscopic debridement of associated fungal infections (e.g. Mucor) were performed by ENT surgeons.

3. Results

Incidence

A total 21 cases of Orbital cellulitis were identified who were admitted in our hospitals. There were 19 males and 2females giving gender ratio of male to female as 9.5:1. The median age was 47years (3-71years). Mean duration of onset of symptoms before presenting at hospital was around 34± 8.44 days at 95% Confidence Interval.

Presentation and Aetiology

All patients presented with Swelling of lids with mean duration of onset of symptoms of34 days. 12 patients (57%) had fever at presentation and pain in eyes were presenting complaints in 15 patients (71%). 12 patients (57%) had preceding upper respiratory tract infection, history of sinusitis was present in 10 patients (47.6%). 13 patients had Infective, 6 patients had Neoplastic, 1 Patient had Traumatic and 1 patient had Vascular as well as Infective etiology. A total of 9 patients had orbital mucormycosis as a cause of infective aetiology. 19 patients (90%) had unilateral presentation and 2(10%) had bilateral presentation and 13 patients (68%) had right side involvement among unilateral involvement and 6(32%) had left sided involvement.

All patients had lid edema, conjunctival congestion and proptosis at presentation but 19 had ophthalmoplegia and 11 had pus discharge at presentation (Table 1). 2 had involvement of Both eyes. 7 were positive for COVID-19 RTPCR test. 12 had Diabetes mellitus and 5 had hypertension, 5 had both as co-morbidities. 1 male child developed brain abscess and hydrocephalus due to intracranial extension of infection and required ventricular shunt surgery. The mean leucocyte count was 14121 ± 3430/cumm at 95% Confidence Interval with polymorphs of 68%. The mean ESR was 28.2 ± 12.728 mm at 95% Confidence Interval. Only 3 (14%) showed any organism on microbiological culture, 2 were positive on blood culture and 1 was positive on local pus culture. Biopsy was positive for Mucor infection in 9 patients. (Table 2). All patients underwent CT scan, 15 additionally required MRI, revealing ethmoid sinus involvement in 15 patients, 1 showed dacryoadenitis, 6 had intracranial extension, 5 had cavernous sinus thrombosis and 10 required some sort of surgical intervention. (Table 3)

Table 1: Summary of Results

Parameters	
Total No. of cases	21
No. of pediatric cases	5
No. of adult cases	16
Predisposing factors	Sinusitis
	Prolonged steroids use
	Trauma
	Co-morbidities
	Adjacent local infections
Etiology	1. Infective
	(i) Bacterial - Methicillin sensitive staph. epidermidis, klebsiella pneumoniae
	(ii) Fungal - Orbital Mucormycosis, Candida Albicans
	(iii) Viral
	2. Neoplastic
	(i) Primary Orbital Retinoblastoma
	(ii) Spindle cell carcinoma
	(iii) Neuroblastoma
	(iv) Metastasis from Carcinoma Palate
	(v) Poorly differentiated Neuroendocrine tumor
	(vi) Poorly differentiated carcinoma
	3. Vascular - Sickle Cell Anemia
Parameters	
COVID-19 Positive patients	7
Supplemental Oxygen Requirement	6
Requirement of ICU admission	3
Average duration of symptoms	34 days
Culture Positivity	20%
Associated complications	Retrobulbar abscess - 4
	Lid abscess - 5
	Scleral abscess - 2
	Panophthalmitis - 6
	Retinal detachment - 3
	Cavernous sinus thrombosis - 6
	Bone abscess - 1
	Septicemia - 1
	Brain abscess - 1
Surgical interventions	FESS - 9
	Tarsorraphy - 2
	Endoscopic debridement - 7
	Endoscopic decompression - 3
	Exenteration - 4
	Evisceration - 1
	Maxillectomy - 1
	Ventricular Shunt Surgery - 1

Table 2: Organisms Isolated

Organism Isolated	
Mucor	9
Candida Albicans	1
Methicillin sensitive staphylococcus epidermidis	1
klebsiella pneumoniae	1

Table 3: Presentation of Orbital Cellulitis

Presentation of Orbital Cellulitis	
Clinical Description	Number (%)
Lid swelling	21 (100%)
conjunctival congestion	21 (100%)
Fever	12 (57%)
Orbital pain	15 (71%)
proptosis	21 (100%)
pus discharge	11 (52%)
Ophthalmoplegia	19 (90%)
Visual acuity changes	19 (95%)

4. Management and Outcome

The patients were managed by a multidisciplinary team of Physicians, ENT specialists and Ophthalmologists. All were started on injectable antibiotics on admission. 3rd generation cephalosporin and vancomycin with or without metronidazole were used in 15 patients (71%) and in 9 patients (43%) inj. Amphotericin B was started. COVID positive patients were managed in a separate facility under guidance of Physicians, ENT specialist and pulmonologists. Topical antibiotic eyedrops along with lubricants were given. They were also given oral/injectable ibuprofen or paracetamol for pain relief. The mean duration of injectable antibiotics was 10 ±5 days. Sinus surgery and abscess drainage was required in 4 (19%) by ENT specialists.5 required Exenteration and 2 required maxillectomy surgery for Orbital mucormycosis. 1 had ventricular shunt surgery required for hydrocephalus. 2 required tarsorraphy for unable to close eyelids completely due to proptosis. All were given antibiotic eye drops and lubricants during treatment. Mucormycosis patients were given Liposomal amphotericin B 1mg/kg for 14 days and syrup posaconazole 800 mg per day in four divided doses. Mean duration for hospitalisation was 20 ± 5 days. 9 had previous use of corticosteroids and immunomodulators as per COVID-19 treatment guidelines [7] and subsequently developed Orbital cellulitis. Higher morbidity and mortality was seen in COVID-19 positive patients.

5. Discussion

The higher incidence of orbital cellulitis in our country may be related to tropical climate, late presentation and high humidity in coastal areas. Like other studies, our studies documented high vulnerability of orbital cellulitis in male patients and especially in co-morbid patients. M:F ratio was9.5 although reason for same is obscure. Our median age was 47 years. (3-71year). Mortality was found higher in patients with COVID-19 infection (2 out of 7). Mucor was the main culprit for orbital cellulitis in COVID-19 Positive patients. Our study showed mean duration of onset of symptoms before presenting at hospital of 34 days (4-60days) which is significantly higher; which might be due to lockdown restrictions related to COVID-19 pandemic.

Although we had relatively small number of patients from our outpatient department due to COVID-19 restrictions, the occurrence of orbital cellulitis might be due to late presentation, associated COVID-19 infection and previous treatment with steroids and immunomodulators. In our study 50% of patients had previous upper respiratory tract infection. Patients diagnosed with COVID-19 infections were treated in dedicated COVID-19 facility separate from our ophthalmology wards. The development of orbital cellulitis in these patients might be due to use of corticosteroids and immunomodulators (e.g. Sarilumab, tocilizumab, siltuximab). Future studies are required in this direction to rule out the association.16 cases out of 21 cases in which we did CT and/or MRI showed evidence of ethmoid sinusitis. In 9 patients features suggestive of Orbital mucormycosis were present. We did not find any history suggestive of recurrent orbital cellulitis.1 patient had history of primary immunodeficiency syndrome. In a study by Murphy C et al had 47% similar antecedent illness and 87% showed sinus disease[8]. Various previous studies suggest the inherent vulnerability of this infection in primary immunodeficiency syndromes [9]. We had 1 patient with history of Carcinoma of hard palate and 1 person had history of lymphoma which lead to subsequent metastasis and occurrence of Orbital cellulitis. One patient had history of dacryoadenitis which predisposes to local spill of infection and subsequent development of orbital cellulitis.

The common organisms in orbital cellulitis are staphylococcus, streptococcus and H.influenza[6]. Prior to Hemophilus influenza B vaccination, this was the most common cause of orbital cellulitis in children and had propensity to spread to meninges and cause cavernous sinus thrombosis [10]. We had sent blood cultures in 15 patients and local swabs in all patients however only 3patients (14%) grew organism, 2 on blood culture and 1 in local swab culture. 1 patient had candida albicans infection, 1 patient had kelbsiella pneumoniae, 1 patient had methicillin sensitive staphylococcus epidermis. On ENT reference and endoscopic biopsy, in 9 patients septate fungal elements were seen on KOH preparation.

Cannon P et al in their study from a tertiary care centre proved that Orbital cellulitis can be successfully treated with oral Ciprofloxacin and Clindamycin in children and adult. Both these oral antibiotics have good oral bioavailability comparable to intravenous preparations and also give broad spectrum cover to gram negative and gram positive organisms [11].Oral antibiotics decrease the cost of treatment, less disruption of treatment and prevention of complications due to intravenous therapy and cannulation. If Methicllin resistant Staphylococcus aureus (MRSA) is suspected or culture proven, Vancomycin or Teicoplanin needs to be added.

Surgical intervention is not usually required unless there is ophthalmoplegia with frank Orbital abscess, frontal sinusitis (Pott Puffy tumor), intracranial complication, large sub-periosteal abscess, abscess volume > 5% of orbital volume or poor response to antibiotics in 48 hours. Garcia et al have shown that medical management alone may be sufficient in age, 9 years old with subperiosteal abscess [12, 13].

Large abscess may require combined external and sinus drainage. Most can be managed with parental antibiotics therapy and followed by oral antibiotics. Cases with biopsy proven Orbital Mucormycosis were managed with intravenous Amphotericin B preparation [14] and 7 patients required surgical intervention.

Corticosteroid use has been controversial, although encouraging results of its use are forthcoming in the treatment of orbital abscess. Pushkar N et al in a prospective study from India used adjuvant oral Prednisolone at 1.5 mg/kg/day for 3 days, 1 mg/kg/day for another 3 days followed by tapering over 1-2 weeks demonstrated early resolution of orbital edema, chemosis, early return of vision and movement and decrease in overall use of intravenous antibiotics and hospital stay [15].Davies BW et al in their study used oral Prednisolone as adjuvant when CRP was ≤ 4 mg/dl for 7 days at 1 mg/kg and showed early discharge from the hospital [16].These studies have not been able to clarify on dosage of corticosteroid, days of starting of steroid, exact use of biomarker to start steroid and total duration of steroids. Future prospective studies are required before same can be recommended. In our study patients with COVID-19 infections were given intravenous Methylprednisolone 2 mg/kg for an average period of 20 days with or without use of immunomodulators and antiviral agents (e.g. Remdesivir, Fevipiravir).

There are very few studies done on Orbital cellulitis during ongoing COVID-19 pandemic. Especially to know the association between orbital mucormycosis and COVID-19 infection. Whether it is due to use of steroid or other immunomodulators, or because of the virus itself.

Currently even more number of cases are presenting with orbital mucor infection in patients of corona virus infection during the Second Wave of COVID-19 in India.

Our study has several limitations. Due to ongoing COVID-19 pandemic and travelling restrictions, many of the patients presented in late stages and had associated complications. Method of culture collection is not specified hence it's possible that anaerobes and mixed infections might have been missed.

6. Conclusion

Our study highlights the unusually increased incidence of orbital cellulitis during COVID-19 pandemic restrictions. Orbital mucor infection was the most common aetiology in COVID-19 positive patients. Most can be managed effectively by parental antibiotics, anti-fungals and if there is poor response with medical therapy, surgical treatment may be sought. Role of steroid is emerging however it might be the culprit behind the development of orbital mucormycosis especially in patients with COVID-19 infection. More future studies are required to establish the exact relation between COVID-19 infection and Orbital mucormycosis.

Source of funding: Nil

Conflict of interest: Nil

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