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Case Series

Skull base osteomyelitis in acute invasive fungal rhinosinusitis-A case series

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Abstract

Skull base osteomyelitis (SBO) is an uncommon but a life-threatening condition seen as a complication of otologic, sinonasal, deep face or dental infections in the debilitated, uncontrolled diabetic and immunocompromised patients. The infection spreads from pneumatized spaces or soft tissues to the osseous skull base with the multiple foramina and the traversing neurovascular bundles forming important pathways of disease spread. We present a case series of MR imaging in fungal SBO, which was seen as a complication of acute invasive fungal rhinosinusitis during the COVID-19 pandemic, along with pictorial depiction of skull base anatomy and the various pathways of disease spread.

Keywords: Skull Base osteomyelitis, Fungal osteomyelitis, COVID-19 associated mucormycosis (CAM), Skull base imaging

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1. Introduction

Skull base osteomyelitis (SBO) is an uncommon but a life-threatening condition seen as a complication of otologic, sinonasal or dental infections, most often in debilitated patients, in those with uncontrolled diabetes and in immunocompromised patients, where the infection spreads from the adjacent pneumatised spaces or soft tissue into the osseous skull base.[1-4]

During the COVID-19 pandemic, there was a significant surge in the incidence of acute invasive fungal rhinosinusitis (AIFRS) in patients affected with COVID-19 infection, also known as COVID-19 associated mucormycosis (CAM).[5-6] Factors such as complex host microbe immune system reaction in COVID-19 infection, together with uncontrolled diabetes and systemic corticosteroid treatment, were found to be the main associated and possible contributory factors.[7-10] Contrast MRI (CE MRI) at presentation and on follow up demonstrated skull base osteomyelitis as a complication in some of these patients.[7-8]

This case series is a retrospective analysis of skull base osteomyelitis developing as a complication of COVID-19 associated AIFRS in single tertiary care multispecialty Hospital in India.

1.1. Skull base anatomy

The skull base refers to the floor of cranial cavity, separating the intracranial structures from the oro-naso- facial region and the suprahyoid neck spaces. It is formed by parts of ethmoid, frontal, sphenoid, paired parietal, paired temporal and the occipital bone (**Figure 1** a).

The anterior skull base is mainly formed by the frontal and ethmoid bones and part of the planum sphenoidale (**Figure 1** b). It separates the anterior cranial fossa from the paranasal sinuses and orbits. The middle or central skull base is predominantly formed by the sphenoid bone, together with the squamous and petrous parts of the temporal bones, and bound laterally by the parietal bones (**Figure 1** b). The posterior skull base is predominantly formed by the occipital

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bone with contributions from temporal and sphenoid bones anteriorly (**Figure 1** b).[3,4,11]

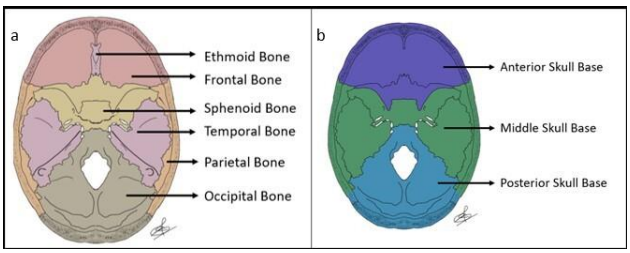

Figure 1: Bones forming the skull base and compartments

1.2. Foramina and pathways of disease spread in the skull base

Cribriform plate of the ethmoid bone in the anterior skull base transmits the olfactory nerves from the nasal mucosa and forms an important pathway for disease spread from the sinonasal region. The sphenoid bone, which forms a major part of the central skull base has 4 components–paired lesser wings, paired greater wings, paired pterygoid processes and the unpaired central body (**Figure 2**).

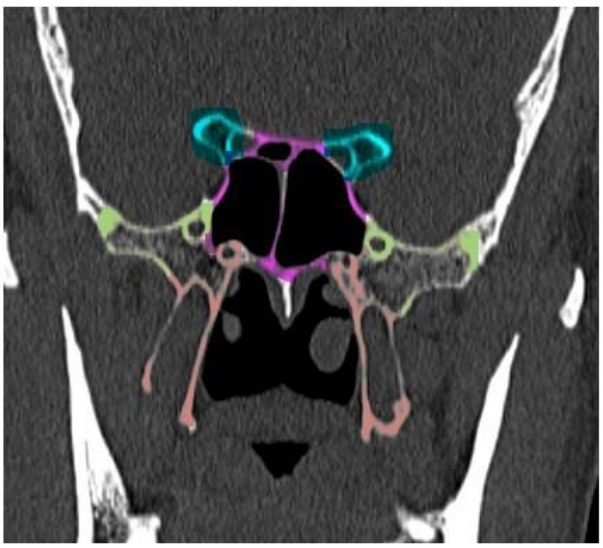

Figure 2: Coronal CT image of the central skull base in bone window depicting the parts of sphenoid bone: Aqua Blue: Lesser Wing, Light Green: Greater wing, Orange: Pterygoid process, Pink: Body

The orbital apex and the cavernous sinus form important pathways of disease spread between the orbit and the middle cranial fossa.[12]

The pterygopalatine fossa is an important anatomic space containing the maxillary division of the trigeminal nerve (V–2), the pterygopalatine ganglion and the maxillary artery. It lies posterior to the maxilla and anterior to the pterygoid process, caudal to the sphenoid bone. Through multiple fissures and foramina, it communicates with the orbit, the nasal cavity and nasopharynx, masticator space and infratemporal fossa, oral cavity and palate and the middle cranial fossa (**Figure 3**). Its location and its multiple communication pathways make it one of the important crossroads for disease transmission from the orbit, nasal and oral cavities, and deep fascial planes of the face to the skull base and the middle cranial fossa.

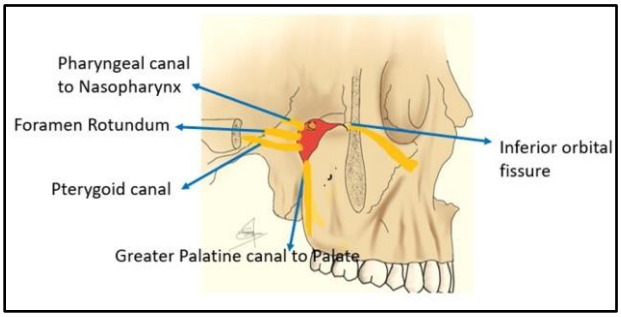

Figure 3: The Pterygopalatine fossa (in red) in the Sagittal Plane; communicates with the orbit anteriorly, the palate and oral cavity caudally and with the middle cranial fossa posteriorly

Figure 4: a,b: The Pterygopalatine fossa(in red) in the axial planes at the level of (a). Vidian canal (yellow line) and (b). Foramen Rotundum (purple line). The Sphenopalatine foramen (green line) connects it to the nasal cavity, the pterygomaxillary fissure (blue line) to the infratemporal fossa and the inferior orbital fissure (pink line) to the orbit

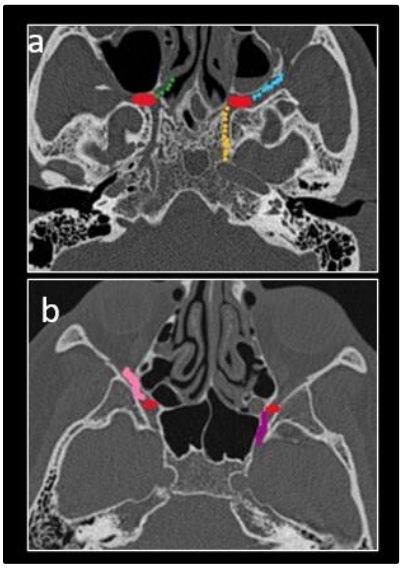

Figure 4: a and **b** depict the CT anatomy of the pterygopalatine fossa and its connections in the axial plane.

1.3. Skull base osteomyelitis (SBO)

SBO is of 2 types, typical and atypical, depending on the source of infection and route of spread.[13-14]

Typical SBO: This arises as a complication of otitis externa where uncontrolled infection leads to the spread of the disease from the soft tissue to the temporal bone.

Atypical SBO or central SBO: This kind of osteomyelitis has a predilection for the central skull base, involving the sphenoid bone and clivus without any precipitating otologic infection. It can be idiopathic or secondary to regional infection of the sinuses, the deep face or the oral cavity.[13]

In the routine clinical scenario, SBO can be a diagnostic challenge to the clinician, requiring high index of clinical suspicion together with corroborative imaging findings and a positive microbiological profile.[11]

1.3. SBO as a complication of COVID-19 associated AIFRS

Fungal rhinosinusitis can be acute or chronic, invasive or non-invasive.[15-17] AIFRS, which was seen in association with COVID-19 pandemic, is the most rapidly progressing form of fungal sinusitis, often with a fulminant course spanning over a few days to weeks.[15-17]

Angioinvasion leads to rapid spread across intact bony walls from the nasal cavity to the orbits, retro-maxillary and premaxillary tissue, pterygopalatine fossa, cavernous sinus, and infratemporal fossa. Development of intracranial complications such as meningitis, cerebritis, infarcts and abscesses are seen early in the course of the disease.

Bony skull base involvement is generally identified late in the disease, as was in our study, which may be explained by the angio-invasive nature and perineural spread which precede bony destruction and because patients with AIFRS might succumb to the disease before SBO occurs.[2,8,18]

CE-MRI is the imaging modality of choice in evaluation of fungal SBO in AIFRS since it is superior to CT for evaluating the extent of soft-tissue involvement, marrow involvement and associated intracranial complications especially in the absence of frank bony destruction.[15,19] CT has an additional contributory role in evaluation of the extent of bone destruction later in the course of the disease.

2. Materials and Methods

At our centre, a retrospective analysis of data showed that a total of 88 patients diagnosed with COVID-19 associated AIFRS had undergone in-house contrast enhanced MR imaging on Philips MR Systems Ingenia S, 1.5 Tesla, Release 5.7, between March and June 2021.[19] out of these 88 patients had developed SBO.

Institutional review board approval was waived as this was a retrospective analysis of the existing data. All the images were analysed independently by two radiologists, each with an experience of over 9 years in head and neck imaging. A combination of MRI sequences including T2, T2-FS or STIR, DWI, T1 and post contrast T1-FS were used to detect the presence of skull base osteomyelitis, to evaluate the disease extent and to detect the presence of tissue devitalization (necrosis), which is a major feature in acute invasive fungal infection caused by the angioinvasive nature of the disease, leading to infarcts and tissue necrosis.[13,20]

3. Results and Imaging Findings

Table1 gives the demographic details of the patients with SBO in our center. All the patients with SBO had sinonasal mucosal necrosis and involvement of the pterygopalatine fossa.

Table 1: Clinical details, demographics and imaging findings

Total number of patients with SBO		**N=19**
Number of males		15
Number of females		4
Diabetes		19
SBO detection on imaging from the time of disease onset:		
Between 6 to 12 weeks		17
3 weeks		1
Unclear		1
Sinonasal mucosal necrosis with devitalization		19
Pterygopalatine fossa involvement		15
Cavernous sinus involvement		12
Microbiology		Mucor= 11
		Aspergillus=4
		No growth=4

Table 2 enlists the major imaging features and the organism in all the 19 patients with SBO

Table 2: major imaging features and organism in all the 19 patients with SBO.

S. No	**Age/ Sex**	**Sinuses Involved**	**Orbit /Side**	**Cav Sinus/ Side**	**Part of Skull Base Involved**	**Associated Intracranial Complications**	**Org**
1.	63/F	All sinuses	Yes B/L	Rt cav sinus thr	MCF	Meningitis Rt temporal lobe abscess	Muc
2.	52/M	All sinuses	Yes Lt	Lt cav sinus thr	MCF and ACF	B/L frontal lobe cerebritis Lt ICA territory infarcts	Muc

3.	57/M	All sinuses	Yes Rt	No	MCF	Meningitis Rt Temporal cerebritis Rt trigeminal nerve inflammation Rt caudate nucleus infarct	Muc
4.	68/F	All sinuses	Yes B/L	Rt cav sinus thr	MCF	Clivus necrosis with retro-clival soft tissue encasing basilar artery, Perineural spread, Posterior circulation infarcts	Muc
5.	58/M	All sinuses	Yes Lt	No	MCF	Meningitis, Bilateral mandibular nerve perineural spread	Asp
6	46/M	B/L Max, Lt Fr, Eth, Sph	Yes Lt	Lt cav sinus thr	MCF	Lt frontal lobe cerebritis Extension of lt optic neuritis to optic chiasm	Asp
7.	37/M	Lt Max, Eth, Sph	No	No	MCF	None	Asp
8.	65/F	B/L Max, Lt Eth, Sph	Yes Lt	No	MCF	None	NG
9.	45/M	All sinuses	Yes Rt	No	MCF	None	Muc
10.	56/M	B/F Max, Rt Fr, Eth, Sph	Yes Rt	No	MCF	None	Muc
11.	38/M	All sinuses	Yes Lt	No	MCF	None	Muc
12.	48/M	B/L Eth, Sph, Rt Max	No	No	MCF	None	NG
13	60/M	All sinuses	Yes Lt	Lt Cav Sinus thr	MCF	LT ICA arteritis with embolic infarcts, Lt temporal lobe cerebritis	Muc
14	65/F	All sinuses	Yes Rt	No	MCF	Meningitis	Muc
15	48/M	All sinuses	Yes Lt	Lt Cav Sinus thr	MCF and ACF	Meningitis Lt frontal lobe abscess Lt ICA thrombosis with infarct	NG
16	65/M	All sinuses	Yes Rt	No	MCF	Meningitis Rt temporal lobe abscess	Muc
17	32/M	All sinuses	Yes Rt	Rt Cav Sinus thr	MCF	Meningitis Rt temporal lobe cerebritis Rt ICA thrombosis with infarcts	Asp
18	74/M	All sinuses	No	Lt Cav Sinus thr	MCF	Meningitis B/L frontal cerebritis Lt ICA thrombosis with infarcts Lt trigeminal nerve inflammation	Muc
19	38/M	B/L Fr and Eth	No	No	ACF	None	NG

M- Male, F- Female, B/L- Bilateral , Rt- Right, Lt- Left, MCF- Middle cranial fossa, ACF- Anterior cranial fossa, Max- Maxillary sinus, Eth- Ethmoid sinus, Fr- Frontal sinus, Sph- Sphenoid sinus, ICA- Internal Carotid artery, Cav- Cavernous sinus, Thr- Thrombosis, Org- organism, Muc- Mucorales, Asp- Aspergillus, NG- No growth

Note:

**Pterygopalatine fossa involvement was seen in all the 19 patients with SBO*

**All the involved sinuses showed mucosal necrosis*

Key imaging findings on MRI in SBO as a complication of COVID-19 related AIFRS:

1. Osteomyelitis of the bone marrow: loss of normal fat signal in the marrow space of the skull base bones, seen as T1 hypo intensity, T2 and STIR hyperintensity and heterogeneous post contrast enhancement. (**Figure 5** b,e)
2. Soft tissue involvement: Inflammation, edema and phlegmon, seen as heterogenous T2 hyperintensity and heterogeneous enhancement on T1-weighted fat-saturated contrast-enhanced sequence in an infiltrating soft tissue at the skull base in contiguity

from the orbital apex, sinonasal region or deep facial planes. (**Figure 5** c,f)

3. Necrosis and devitalization of the soft tissue and marrow. This presented on imaging as sheet like areas of non-enhancing tissue of heterogenous signal with peripheral rim enhancement[6,15]

    a. (**Figure 6** b,g; **Figure 7** c,d; **Figure 8** a,d)
    b. The associated complications that were seen on imaging in patients with SBO were:

4. Orbital involvement in the form of cellulitis, necrosis, optic nerve involvement (**Figure 5** d; **Figure 7** b,f). Meningitis characterised by thickening and enhancement of pachymeninges and/or leptomeninges (**Figure 7** h; **Figure 10** b,d)
5. Cerebritis, predominantly in contiguity with the involved meninges and skull base (**Figure 5** a, **Figure 6** e,f; **Figure 7** a)
6. Involvement of cavernous sinus and the cavernous segment of ICA (**Figure 6** c,d)
7. Cerebral infarcts (**Figure 7** g, **Figure 8** e,f) and abscess, either from temporal evolution of cerebritis or infarcts (**Figure 5**)
8. Perineural disease spread (**Figure 7** e; **Figure 9**)

The above findings were frequently associated with but were also seen in patients without SBO due to direct intracranial spread from angioinvasion.

2.1. Case 1

63/ F - Post sinonasal debridement with complaints of headache.

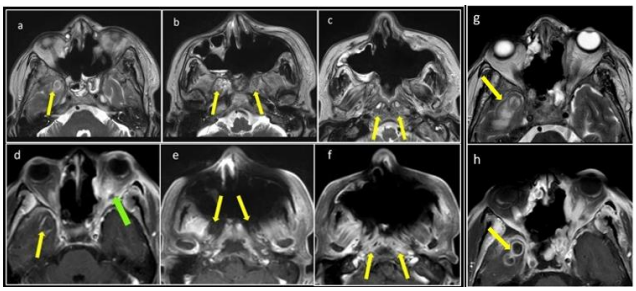

Figure 5: (a-f) Axial T2W and T1 post contrast images demonstrate: Right temporal lobe cerebritis (**a, d**), bilateral sphenoid wing osteomyelitis (b, e), diffuse enhancement of the soft tissue at skull base and pre vertebral space with abscess in the longus capitis**(c, f).** Also seen is left orbital cellulitis with proptosis (green arrow in d)., (**g,h**) Follow-up CE MRI in the same patient ,after 2 weeks, showed disease progression , but development of right temporal lobe abscess

2.2. Case 2:

52/M, Post sinonasal debridement for AIFRS.

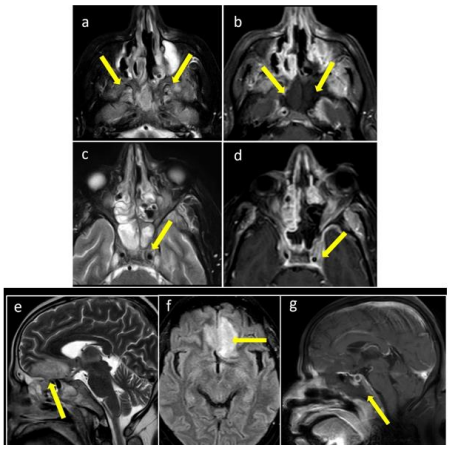

Figure 6: *(a-d) Axial T2-FS and T1 Post contrast images demonstrate: bilateral pterygopalatine fossa involvement and Central SBO with osteonecrosis (a,b), left cavernous sinus involvement with left cavernous ICA wall thickening(c ,d).*(e-g) Sagittal T2W, Axial FLAIR and Sagittal T1 post contrast images in the same patient: Contiguous extension of disease from ethmoid sinus across the cribriform plate to the frontal lobes (e,f) and necrosis of the clivus presenting as complete loss of enhancement (g).

2.3. Case 3

57/M with facial pain and headache. **Figure 7** (a-d) Coronal T2W (a, b) and Axial T1 post contrast (c, d) - extensive osteonecrosis of the right pterygoid bone and sphenoid wing, necrotic tissue in Rt pterygopalatine fossa, masticator space, temporal fossa. Severe Rt orbital cellulitis (green arrow) and Rt temporal lobe signal changes (blue arrow).

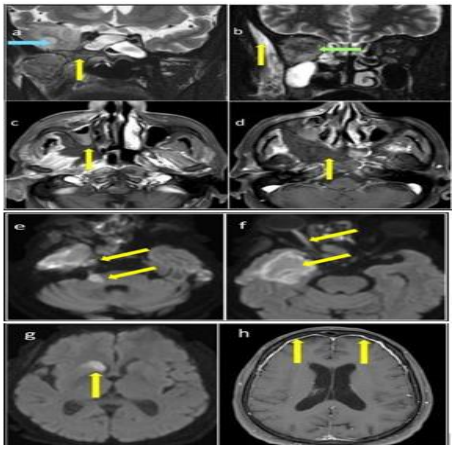

Figure 7: (e,f): Axial DWI in the same patient: restricted diffusion along the course of right trigeminal nerve and infarct in the pons at its root exit zone (yellow arrows in e). Also seen are Rt posterior ischemic optic neuropathy and Rt temporal lobe cerebritis (yellow arrows in f). (g, h) Follow up imaging in the same patient: DWI (g) and T1 post contrast (h) images demonstrate infarct in the right caudate nucleus as a complication and diffuse pachymeningeal enhancement.

2.4. Case 4

68/F: SBO involving the sphenoid sinus walls and clivus with osteonecrosis.

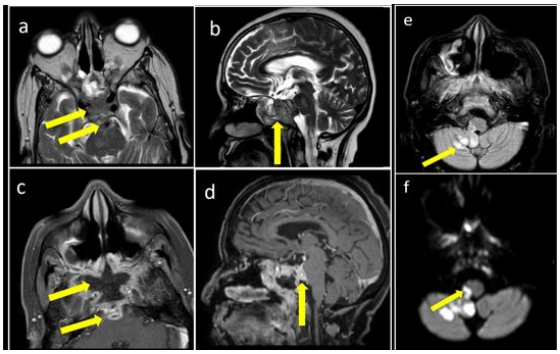

Figure 8: (a-d) Axial and sagittal T2W (a,b), axial and sagittal T1 post contrast (c,d) images demonstrate retroclival soft tissue indenting on the pons and encasing the basilar artery. (e,f) Follow up imaging after 4 days: Axial FLAIR (e) and DWI (f) images show development of infarcts in the cerebellum and medulla.

2.5. Case 5

58/M, post sino-nasal debridement.

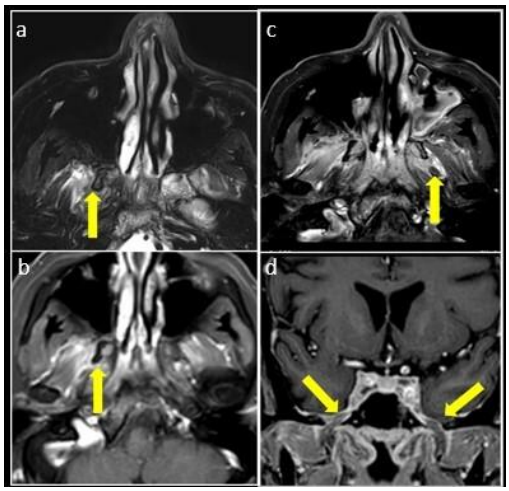

Figure 9: Osteonecrosis of the right Pterygoid bone (yellow arrows in **a, b**), Perineural enhancement along bilateral mandibular divisions of trigeminal nerves across the foramen ovale (yellow arrows in **c, d**)

2.6. Case 6

46/M with poorly controlled diabetes.

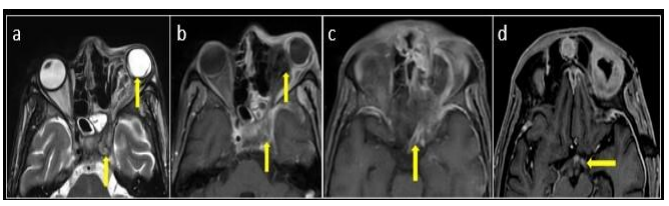

Figure 10: Left orbital abscess with deformed globe and optic nerve necrosis (a,b). Extension of perineural enhancement to the optic chiasm (c) and, on follow up imaging, to the optic tract (d). Also seen are left cavernous sinus thrombosis and left Cavernous ICA thrombosis (a,b) and left temporal lobe meningeal involvement (b-d).

4. Discussion

While typical SBO arising secondary to bacterial otological infections is the more common type, atypical SBO involving the central skull base was the dominant presentation in our case series of fungal osteomyelitis.[13] The diagnosis of SBO is usually delayed and requires biopsy for confirmation in addition to imaging findings as the destructive appearance can often mimic skull base malignancy.[3] In our case series, the high incidence of Acute invasive fungal rhinosinusitis in the background of Covid-19 infection led to a high index of clinical suspicion in the presence of any sinonasal symptoms, prompting early imaging. Skull base osteomyelitis was detected as a complication, often presenting late in the disease beyond 4 weeks.[8] Contrast enhanced MRI, being superior to CT in early detection of invasive disease, was the imaging modality of choice.[9]

The presence of altered marrow signal in the bones of the skull base are detected much earlier than CT, which takes longer to manifest the findings of bone erosion.[13,18]

The spread of disease to the skull base in our patients was mostly by direct contiguous extension from the adjacent sino-nasal cavity, pterygopalatine fossa and cavernous sinuses. But additional pathways of perineural and vascular spread were also noted.

4.1. Pathways of spread of sinonasal infection to skull base in our cases

Involvement of one or more of the following areas was invariably seen in patients with AIFRS who had skull base involvement, indicating the pathways for contiguous as well as non-contiguous (perineural and vascular) spread:

1. Pterygopalatine fossa with or without infratemporal fossa (**Figure 6** a,b)
2. Orbital apex (**Figure 10**)
3. Cavernous sinus (**Figure 6**c,d; **Figure 10** a,b)
4. Cribriform plate, Frontal sinus (**Figure 6** e,f)
5. Sphenoid sinus (**Figure 8** a-d)

5. Conclusion

Skull base osteomyelitis is a dreaded condition with high morbidity and contrast enhanced MRI plays a major role in diagnosis, in defining the extent of the disease, detecting associated complications and in follow-up imaging.

Incidence of AIFRS showed a significant increase during the 2nd wave of COVID-19 pandemic; SBO was seen as a complication generally beyond the 4th week of disease despite treatment. Patients with early involvement of the pterygopalatine fossa, orbital apex and the cavernous sinus

are at high risk of developing SBO and intracranial complications due to contiguous, perineural and vascular spread.

Contrast enhanced MRI is superior to CT in the early detection of SBO as the marrow signal changes and the adjacent soft tissue changes are detected before bone erosion becomes evident on CT. Intracranial complications such as meningitis, vascular complications, cerebritis and abscesses are often seen as associations.

6. Source of Funding

None.

7. Conflict of Interest

None.

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