International Journal of Otolaryngology Research

ISSN Print: 2664-6455
ISSN Online: 2664-6463
Impact Factor: RJIF 5.44
IJOR 2023; 5(2): 28-34
www.otolaryngologyjournal.in
Received: 03-06-2023
Accepted: 11-07-2023

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Magnetic resonance and computed tomographic findings in acute invasive fungal rhino sinusitis during COVID-19 pandemic

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DOI: https://doi.org/10.33545/26646455.2023.v5.i2a.28

Abstract
Background: AIFR occurs secondary to the increased immunocompromised cases during COVID 19 pandemics. We aimed to study the CT and MRI findings in AIFR during COVID 19 pandemics.
Methods: A retrospective study was performed on 50 cases having the history of COVID 19 infection aged from 24 to 85 years old, both sexes, with AIFR and renal failure, poorly controlled type 1diabetes mellitus and malnutrition. All patients were subjected to CT scans, and MRI.
Results: Extra sinus soft tissue infiltration was pterygopalatine infiltration in 48 (96%) patients, anterior periantral fat and posterior periantral fat in 8 (16%) patients, nasolacrimal duct and lacrimal sac in 4 (8%) patients, orbital fat (medial/inferior) in 16 (32%) patients, nasal septal mucosal ulcer in 17 (34%) patients. Intracranial extension was subdual in 18 (36%) patients, epidural in 18 (36%) patients and brain parenchymal in 22 (44%) patients. vascular complications were venous thrombosis in 20 (40%) patients, arterial thrombosis in 1 (2%) patient and both arterial and venous thrombosis in 2 (4%) patients. Cavernous sinus involvement was in 23 (46%) patients, cranial nerve affection was in fourteen (28%) cases and bone dehiscence/abscess was in 22 (44%) patients.
Conclusions: CT and MRI results of AIFRS showed great variations starting from thickened mucosa of the paranasal sinuses, reaching orbital and intracranial extension with vascular thrombosis in addition to neuro-invasion. The distinctive mark inflammatory tissue infiltration into the pterygopalatine fossa and facial soft tissue might happen before the appearance of the mucosal disease.

Keywords: MRI, CT, Invasive Fungal Rhino Sinusitis, COVID-19

Introduction
Acute invasive fungal rhinosinusitis (AIFR) is essentially manifested by fungal infiltration of the mucosal tissue in the nasal cavity along with the paranasal sinuses. Numerous fungal species were detected in cases suffering AIFR such as Aspergillus and Mucoraceae that are considered the commonest pathogens [1]. Indeed, it is highly destructive and serious form of the disease. It necessitates rapid diagnosis and management; if not, the mortality rates might reach fifty to eighty percent [2].
The disease results essentially due to immunosuppression. The vast majority of cases with AIFR are actually in a state of poor health and are anticipated to have poor prognosis due to the underlying pathology. The increased numbers of cases suffering AIFR recently are suggested to result from the increased numbers of immunocompromised cases especially during COVID 19 pandemics. Renal failure, uncontrolled T1DM and malnutritional state are of the predisposing factors for developing AIFR. Aggressive surgical debridement and IV antimycotic treatment are the 2 essential arms of therapy [3].
computed tomography (CT) is used to evaluate patients with suspected AIFR; CT might detect staging of the disease and might participate in diagnostic delay if it's carried out without nasal endoscopic assessment [4].
CT of the sinuses shows hollow air-filled spaces within the facial bones surrounding the nasal cavity. Osseous erosion and bony destruction are obvious signs of the disease in CT indicating AIFR. To assess the sinuses along with the neighbouring structures, CT is carried out at intervals of less than 3 mm, in axial as well as coronal planes [5].

Of note, MRI is indicated in cases at risk because of underestimated disease in addition to nonspecific findings on CT as it helps better differentiation of soft tissue elements within the sinuses [6].
In addition MRI is specific for evaluation of focal sites with loss of contrast enhancement (LoCE) of the mucosal layer of the sinuses that's ideally detected to enhance using gadolinium or iodinated contrasts [7].
The aim of the work is to study CT and MRI findings in AIFR (Retrospective study) during COVID 19 pandemics.

Patients and Methods

This retrospective study was conducted on 50 patients 24 - 85 y of age, both gender, with clinical criteria of Patients with AIFR with history of COVID 19 infection [Immunocompromised patients with marked neutropenia (Fulminant invasive sinusitis or neutropenic sinusitis)] (Cases suffering hematological malignancies, cases subjected to systemic chemotherapy, systemic corticosteroid treatment, bone marrow transplant, immunosuppression treatment for organ transplant, and AIDS) and renal failure, poorly controlled type 1diabetes mellitus and malnutrition.
The study was carried out following approval from the Ethical Committee Tanta University Hospitals, Egypt. An informed written consent was taken from the patient or the their relatives.

Exclusion criteria was Non COVID 19 AIFR
All cases underwent

- Demographic data taking.
- History taking.
- Clinical assessment.
- The COVID-19 infection was classified based on WHO guidelines: mild, moderate, and severe.
- CT scans (GE Optima).
- MRI (GE SIGNA™).
- All radiographic along with clinical materials were retrospectively assessed.
- Each CT and MRI were assessed for thickened nasal cavity mucosa and soft tissues, thickened sinus mucoperiosteum, osseous erosion, extra sinus extension (orbital and intracranial invasions), thickened soft tissue of the face, thickened retro nasal fat pad thickening, and unilaterally versus bilaterally affection.
- Comorbidity in COVID-19 cases suffering invasive fungal rhinosinusitis [No comorbidity, Comorbidities (DM (known, newly diagnosed, and not diabetic), hypertension, COPD, CKD, hematological malignancy D, and hepatic)].
- Extra-sinus soft tissue infiltration in COVID-19 cases suffering AIFRS [Pterygopalatine infiltration, anterior peri-antral fat, posterior peri-antral fat, nasolacrimal duct, lacrimal sac, orbital fat (medial/inferior), and nasal septal mucosal ulcer]
- Extension beyond the sinus to the intra-cranium [Intracranial infection (Subdual, Epidural, and Brain parenchymal), cavernous sinus involvement, other vascular complications (thrombosis in arteries or veins, or both) affection of the cranial nerves and bone dehiscence/abscess].

Statistical analysis

Statistical analysis was carried out using SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and SD. Qualitative variables were presented as frequency and percentage (%).

Results

The range age of the studied cases was 24- 85 y with a mean value (± SD) of 55.34 (±20.34) years. Sex was male in 30 (60%) patients, female in 20 (40%) patients. Regarding clinical presentation, 46 (92%) patients had facial pain or loss of sensation, 35 (70%) patients had visual loss, 23 (46%) patients had facial skin infarction/ulceration, 22 (44%) patients had nasal congestion epistaxis and cavernous sinus thrombosis, 14 (28%) patients had cranial nerve involvement and 6 (12%) patients had Conscious level. 37 (74%) patients had comorbidity. DM was known in 40 (80%) patients, newly diagnosed in 8 (16%) patients and 1 was not diabetic in 2 (4%) patients. Hypertension in 26 (52%) patients, COPD in eleven (22%) cases, CKD in 9 (18%) cases, hematologic malignancy in 2 (4%) patients and in 2 (4%) patients was hepatic. (Table 1)

Table 1: Demographic data, clinical presentation and comorbidity of the studied cases

		N=50
Age (years)		**55.3 ± 20.34**
Sex	Male	30 (60%)
	Female	20 (40%)
Facial pain or lost sensation		46 (92%)
Lost vision		35 (70%)
Infarcted and/or ulcerated skin in the Face		23 (46%)
Nasal congestion &bleeding		22 (44%)
Cavernous sinus thrombus		22 (44%)
affection of the Cranial nerves		14 (28%)
Conscious level		6 (12%)
	Comorbidity	37 (74%)
	No comorbidity	13 (26%)
Diabetes Mellitus	Known	40 (80%)
	Recently diagnosed	8 (16%)
	Non-diabetics	2 (4%)
Hypertension		23 (52%)
COPD		11 (22%)
Chronic kidney disease		9 (18%)
Hematologic malignancy		2 (4%)
Hepatic		2 (4%)

Data are presented as mean ± SD and number (%). COPD: Chronic obstructive pulmonary disease.

Pre-operative imaging was CT only in 33 (66%) patients, MRI only in 4 (8%) patients and CT and MRI in 13 (26%) patients. The surgical approach was external debridement in 19 (38%) patients, endoscopic in 16 (32%) patients and was combined in 13 (26%) patients. 2 (4%) patients passed away before surgery. Surgical serious decision was maxillectomy in 5 (10%) cases and orbital exenteration in 13 (26%) cases. (Table 2)

Table 2: Pre-operative imaging, surgical approach and surgical serious of the studied patients

		N=50
Pre-operative imaging	CT alone	33 (66%)
	MRI alone	4 (8%)
	Combined CT & MRI	13 (26%)
Surgical approach	External debridement	19 (38%)
	Endoscopic	16 (32%)
	Combined	13 (26%)
	Passed away before surgery	2 (4%)
Surgical serious decision	Maxillectomy	5 (10%)
	Orbital exenteration	13 (26%)

Data are presented as number (%).

All patients received systemic antifungal infection. The pathogen was Aspergillus fumigatus in 12 (24%) patients and was Mucormycosis in 38 (76%) patients. Mortality was 17 (34%) of the studied patients. (Table 3)

Table 3: Systemic antifungal and outcome of the studied patients

		N=50
Systemic anti-mycotic		**50 (100%)**
Pathogen	Aspergillus fumigatus	12 (24%)
	Mucormycosis	38 (76%)
Outcomes		
Survivors		33 (66%)
Death		17 (34%)

Data are presented as number (%).

Extra sinus soft tissue infiltration was pterygopalatine infiltration in 48 (96%) patients, anterior periantral fat and posterior periantral fat in 8 (16%) patients, nasolacrimal duct and lacrimal sac in 4 (8%) patients, orbital fat (medial/inferior) in 16 (32%) patients, nasal septal mucosal ulcer in 17 (34%) patients. Intracranial extension was subdual in 18 (36%) patients, epidural in 18 (36%) patients and brain parenchymal in 22 (44%) patients. vascular complications were venous thrombosis in 20 (40%) patients, arterial thrombosis in 1 (2%) patient and both arterial and venous thrombosis in 2 (4%) patients. Cavernous sinus involvement was in 23 (46%) patients, affection of the cranial nerves was in 14 (28%) cases and bone dehiscence/abscess was in 22 (44%) patients. (Table 5)

Table 4: Extra sinus infiltrations of the soft tissues and extension beyond the sinus to the intracranial of the studied patients

		N=50
Pterygopalatine infiltration		48 (96%)
Anterior periantral fat		8 (16%)
Posterior periantral fat		8 (16%)
Nasolacrimal duct		4 (8%)
Lacrimal sac		4 (8%)
Orbital fat (medial/inferior)		16 (32%)
Nasal septal mucosal ulcer		17 (34%)
Intracranial extension	Subdual	18 (36%)
	Epidural	18 (36%)
	Brain parenchymal	22 (44%)
Vascular complications	Venous thrombosis	20 (40%)
	Arterial thrombosis	1 (2%)
	Both arterial and venous thrombosis	2 (4%)
Cavernous sinus involvement		23 (46%)
Affection of the Cranial nerves		14 (28%)
Bone dehiscence/abscess		22 (44%)

Data are presented as number (%).

Example of cases are shown in (Fig 1: Fig 4).

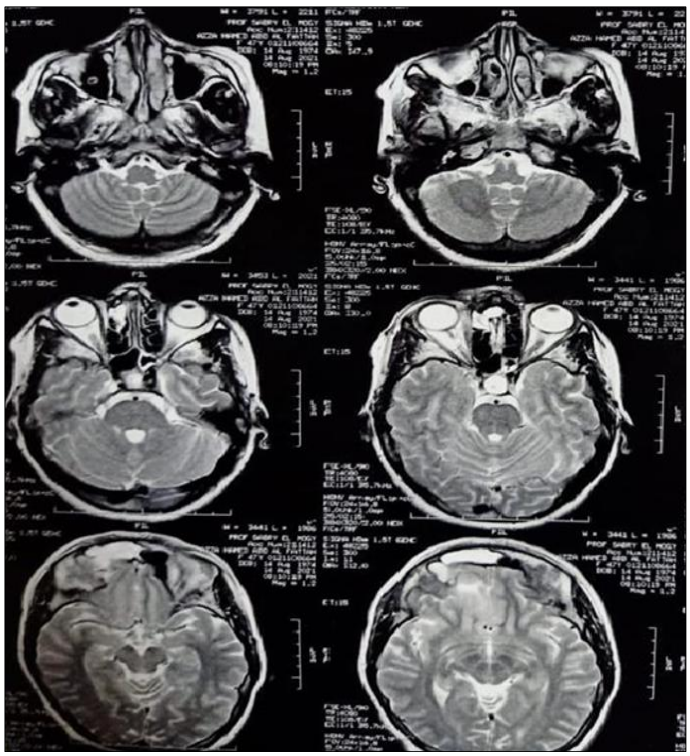

Fig 1: a male cases aged 75- y with DM presented with facial tingling following 17 days of COVID-19 infection. Axial T2 weighted MRI at level of nasopharynx showing high signal / hyperintense lesion in the Rt frontal lobe

Fig 2: A female case aged 65 y presented with Rt facial pain for ten days following 2 weeks of COVID-19 infection with poorly controlled DM. A Coronal CT imaging shows Opacified right osteomeatal unit, with Polypoidal mucosal thickening and subtotal Opacification of the Rt maxillary sinus, mild Polypoidal mucosal thickened right frontal recess

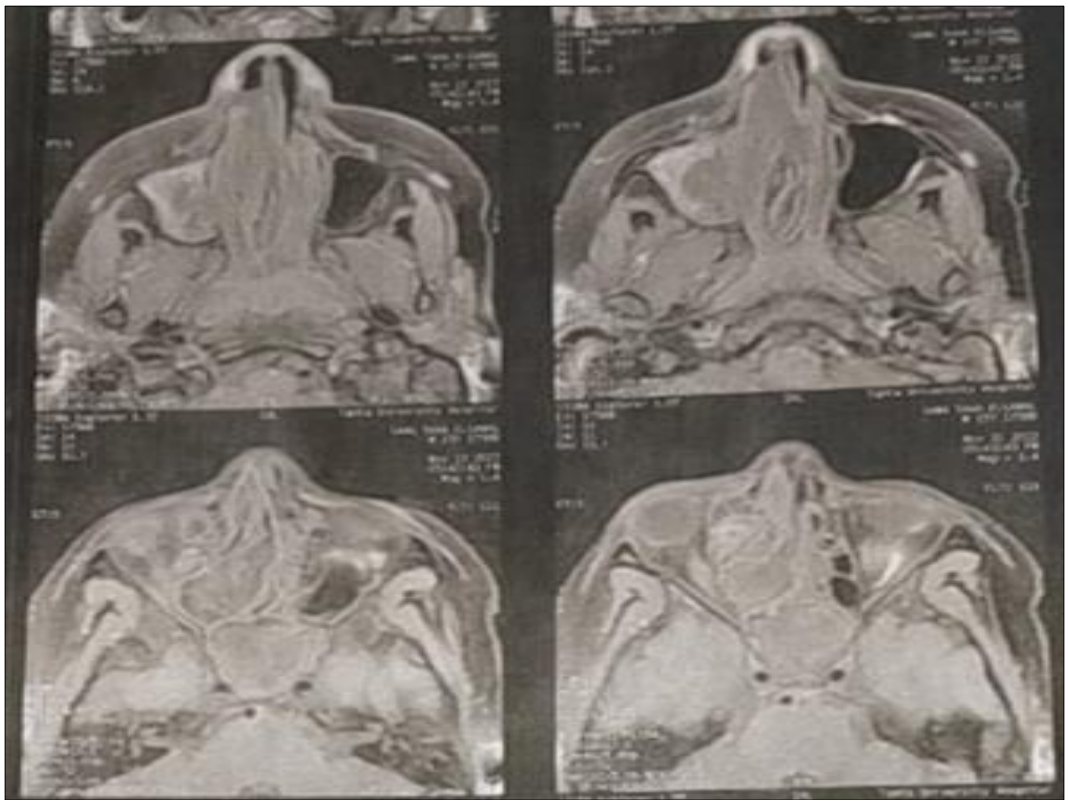

Fig 3: A male aged 70 y suffering from lost vision, complete ophthalmoplegia, severe headache and right facial gangrene following four weeks of COVID-19 infection with poorly controlled DM. Axial (A) T1, (B) T2 weighted MRI at level of nasopharynx showing a lesion occupying RT maxillary sinus, RT ant., post. Ethmoid sinus, sphenoid sinus and compressing the nasal septum

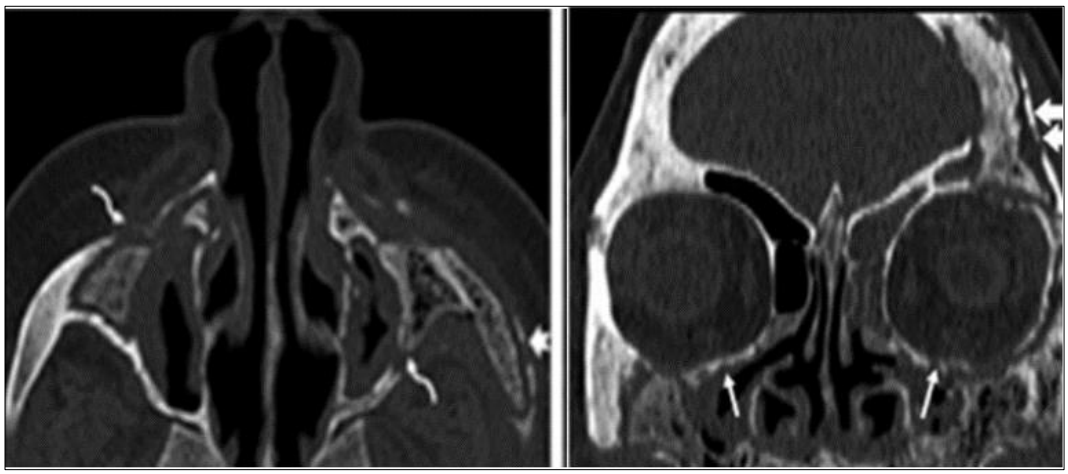

Fig 4: A female aged 50 y with poorly controlled hyperglycaemia and post-COVID-19 infection with 2-weeks duration. Axial and coronal reformatted CT imaging demonstrates bony erosions of the wall of both maxillary sinuses, left zygomatic bone, left frontal bone, floor of bilateral orbits

Discussion

The COVID-19 pandemic is still a challenge globally. Pathophysiological characteristics of COVID-19 that might enable secondary fungal infection, a propensity to produce respiratory infections, might elevate the susceptibility to invasive fungal rhinosinusitis [8, 9]. Furthermore, the immune dysregulation accompanying COVID-19, with decreased T lymphocytes, CD4+T, and CD8+T cell count, could change the inherent immunity [10].

In the current study, regarding clinical presentation, 92% of the patients had facial pain or loss of sensation, 70% of the patients had visual loss, 46% of the patients had facial skin infarction/ulceration, 44% of the patients had nasal congestion epistaxis and cavernous sinus thrombosis, 28% of the patients had cranial nerve involvement and 12% of the patients had Conscious level. Such findings came in harmony with Shaban *et al*. [11] since they observed that regarding clinical presentation, pain in the face or lost sensations was in 92.6% of the patients, visual loss was in 70.4% of the patients, infarcted/ulcerated facial skin was in 46.3% of the patients, nasal congestion epistaxis was in 40.7% of the patients, cavernous sinus thrombosis was in 40.7% of the patients, cranial nerve involvement was in 25.9% of the patients, conscious level was in 11.1% of the patients.

In the present study, regarding pre-operative imaging, CT was only in 66% of the patients, MRI only in 8% of the cases and CT and MRI in 26% of the cases. Our results came in line with Shaban *et al*. [11] who observed that pre-operative imaging showed that, CT only was in 68.5% of the patients MRI only was in 7.4% of the patients, CT and MRI was in 24.1% of the patients.

In the current study, the surgical approach was external debridement in 38% of cases, endoscopic in 32% of the cases and combined in 26% of the cases. 4% of cases passed away before surgery. The current findings are similar to Shaban *et al*. [11] as they demonstrated surgical debridement was carried out for fifty-two/fifty-four cases; 37.2 percent of cases carried out external debridement, 37 percent carried out endoscopic debridement, and 24.1% had combined open and endoscopic debridement, 2 cases died before operation.

This was against Turner *et al*. [12] results since they reported external debridement for 37.2 percent of cases, endoscopic debridement in thirty seven percent of patients and combination of both for 24.1% of the patients.

In the current study, surgical serious decision was maxillectomy in 10% of cases and orbital exenteration in 26% of the patients. In agreement with our study, Shaban *et al*. [11] observed that regarding beyond endoscopic debridement, maxillectomy was carried out in 9.3% of the patients and orbital exenteration in 24.1% of the cases.

This is contradictory with Malleshappa *et al*. [13] they documented that the recruited cases suffering AIFS prospectively were subjected to clinic radiological evaluation then bilateral FESS and debridement of involved tissues. They recorded partial/total maxillectomy in 29.4% of the patients, orbital exenteration in 7.8% of cases and craniotomy in 2% of cases.

In the current study, all cases received systemic antifungal infection. The pathogen was aspergillus fumigatus in 24% of the patients and was mucormycosis in 76% of the patients.

Our results are comparable to Shaban *et al*. [11] who observed that systemic antimycotics were administered to fifty cases on diagnosis and were continued post-operatively. Mucor species was the highest isolated type (77.8 percent) then Aspergillus fumigatus (22.2 percent). In the present study, death rate of AIFS disease was 34% of the studied patients. In agreement with our study, Elmokadem *et al*. [14] found that mortality rate of AIFS disease was 32%. These findings are in coherence with Shaban *et al*. [11] who observed that the overall deaths in the AIFS disease group were 40.7 percent.

In the present study, 74% of patients had comorbidity. DM was known in 80% of the patients, newly diagnosed in 16% of cases and 4% of cases were not diabetic. HTN in 52% of the patients, COPD in 22% of the patients, CKD in 18% of the patients, hematologic malignancy in 4% of cases and in 4% of cases was hepatic. Poorly controlled diabetes is considered an established risk factor for developing fungal infection as hyperglycaemia, DKA, and disturbed metabolism are a preferred environment for fungal multiplication [15]. In harmony with our finding, Elmokadem *et al*. [10] found the most prevalent comorbidities in the studied individuals were diabetes 60percent, followed by hyertension 28percent, cardiac disease 8%, chronic kidney disease4%.

In the present study, extra sinus soft tissue infiltration was pterygopalatine infiltration in 96% of the patients, anterior & posterior peri-antral fats in 16% of patients, nasolacrimal ducts as well as lacrimal sac in 8% of patients, orbital fat (medial/inferior) in 32% of the patients, nasal septal mucosal ulcer in 34% of the patients. These findings are similar to Shaban *et al*. [11] as they observed that AIFR have very strong correlation with affection of the pterygopalatine fossa (90.7). Interestingly, infiltration of pterygopalatine fossa (90.7percent) occurs before radio logically significant opacifcation of mucosa sinuses, nasal cavity and nasopharynx (39.9 percent).

Khullar *et al*. [4] reviewed numerous imaging signs which can detect earlier invasion in COVID associated mucormycosis and found emphysema or ulcers of the nasal mucosa is one of the early imaging characters of COVID associated mucormycosis. Periantral soft tissues as well as soft tissues in the pterygopalatine fossae are pivotal imaging signs indicating extra sinus invasion. Infection in pterygopalatine fossae might result in multidirectional widespread and is a crucial site to be check.

The CT finding can be detected as hypodense opacification of the sinus, in contrast to chronic fungal infection in which the sinus is hyperdensed because of the building-up of mineral rich waste products of the fungi. The cross-sectional imaging criteria of AIFR accompanying COVID-19 infection don't distinguish from findings documented as regard AIFR accompanied by other risk factors [16]. Such findings are comparable to study of Middlebrooks *et al*. [17].

In the present study, regarding extended infection beyond the sinuses to the intracranial structures of the studied patients, intracranial extension was subdual in 36% of cases, epidural in 36% of cases and brain parenchymal in 44% of cases. Our results came in line with Shaban *et al*. [11] who observed that nasal septal ulceration was reported in 31.5%. Orbital involvement in 29.6%, intracranial affection (epi & sub-dural abscesses, thrombosis of veins or arteries, cavernous sinus affection, and intra parenchymal extension, and affection of the cranial nerves have been documented in fourteen cases; 2nd and 5th cranial nerves were the most affected directly or via neuro-invasion.

In the present study, there was nasal extension in twelve cases (forty-eight percent), in addition the nasal septum was involved in five cases (twenty percent). 24 cases had unilateral orbitally extended infection, and one patient had bilateral affection. Vascular complications were venous thrombosis in 40% of the patients, arterial thrombosis in 2% of the patients and both arterial and venous thrombosis in 4% of the patients. Cavernous sinus involvement was in 46% of the patients, cranial nerve involvement was in 28% of the patients and bone dehiscence/abscess was in 44% of the patients. The current study findings came in consistent with Shaban *et al*. [11] who observed the extent of mucosal opacifcation of sinuses along with the nasal cavity and nasopharynx showed relative poor sensitivity and specifcity. Extra sinus soft tissues affection revealed strong correlation with affection of the pterygopalatine fossa. The mucosal opacifcation was weakly correlated with the infiltration. Unilateral predominance was determined. One case had AIFR bilaterally with a potentially dominant disease on the left aspect.

Gaviani *et al*. [18] exhibited that despite fungal cerebritis showed heterogeneous foci of limited diffusion, fungal brain abscesses showed limited diffusion centrally comparable to what occur in the bacterial abscess yet with histological criteria of acute or chronic inflammatory reaction and necrosis instead of suppuration. They suggested that despite the heterogeneous limited diffusion observe in fungal cerebritis may be considered sites for cellular infiltration and multifocal infarctions, limited diffusion observed in the central part of fungal brain abscesses may be due to highly proteinaceous fluid in addition to cellular infiltrate. Also, Safder *et al*. [19] revealed limited diffusion of the infarction sinonasal mucosa in cases suffering mucormycosis.

Limitations: the current study findings is limited since it's a single institutional one. It was a retrospective study with the possibility of missing some related data. Cases selectivity bias might occur because of the rapid nature of the disease as well as the unfavourable prognosis. There was no control group for comparison. Ultimately, the availability of long-term clinical findings was finite. International longitudinal studies are of great significance for in the future.

Conclusions

CT and MRI results of AIFRS showed great variations starting from thickened mucosa of the paranasal sinuses, reaching orbital and intracranial extension with vascular thrombosis in addition to neuro-invasion. The distinctive mark inflammatory tissue infiltration into the pterygopalatine fossa and facial soft tissue might happen before the appearance of the mucosal disease.

Financial support and sponsorship

Nil.

Conflict of Interest

Authors declared no conflict of interest.

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How to Cite This Article
El Ashmawy AM, Safan ME, EL Badry AM, Ebeid K. Magnetic resonance and computed tomographic findings in acute invasive fungal rhino sinusitis during COVID-19 pandemic. International Journal of Otolaryngology Research 2023; 5(2): 28-34.