Journal of Oral Biology and Craniofacial Research 14 (2024) 767–772

Contents lists available at ScienceDirect

Journal of Oral Biology and Craniofacial Research

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

Unravelling the unique case of congenital infiltrating lipomatosis of face with its rare associations—A case report

Ramandeep Singh [a], Aakash Gupta [b,*], Gaurav Shanker Pradhan [c], Arshit Kataria [d]

[a] Department of Radiodiagnosis, All India Institute of Medical Sciences, Bathinda, Punjab, 151001, India
[b] Department of Dentistry, All India Institute of Medical Sciences, Bathinda, Punjab, 151001, India
[c] Department of Radiodiagnosis, Maulana Azad Medical College & Associated Hospitals, New Delhi, 110002, India
[d] Department of ENT, All India Institute of Medical Sciences, Bathinda, Punjab, 151001, India

A B S T R A C T

Congenital infiltrating lipomatosis of facial (CIL-F) is a rare tumour of adipose tissue resulting in a progressive craniofacial deformity with involvement of the underlying bones, muscles and joints. We report a very rare case of CIL-F with left sided temporomandibular joint ankylosis in a young patient who presented with facial swelling and reduced mouth opening. This case highlights the imaging features, differential diagnosis and brief management of CIL-F with special emphasis on CT and MRI findings. Also, some associations of CIL-F such as TMJ ankylosis and extraocular muscle hypertrophy has been described, which has been reported very rarely.

1. Introduction

Congenital infiltrating lipomatosis of the face (CIL-F) is a rare disease characterized by the infiltration of lipocytes into the soft structures of the face.[1] Permeation of lipomatous tissue is observed within the facial muscles, soft tissue, and bones, causing their expansion and ultimately leading to facial asymmetry. The manifestation is almost always unilateral.[2] The facial asymmetry progressively expands on the affected region of face since birth. The disease can either advance swiftly during childhood, leading to significant hyperplasia or can develop gradually over time with patient typically seeking treatment during adulthood. Dental manifestations like macrodontia and precocious tooth eruption have also been encountered. The primary emphasis for these patients is on their overall aesthetic appearance, as their psychomotor development progresses.[3] There is paucity of studies highlighting this anomaly with fewer than 70 case reports.[2,4] The association of CIL-F with bony ankylosis is even rare and to the best of our knowledge only three cases are reported till date.[5,6] Also, we described the ipsilateral hypertrophy of extraocular muscles in this case, which have never been reported. We elaborate the general and radiological aspects in a case of CIL-F associated temporo-mandibular joint (TMJ) ankylosis, where progressive hemifacial hyperplasia and difficulty in mouth opening was unevaluated prior to radiological workup.

2. Patient presentation

A female patient in her 30s reported to the outpatient department with swelling over left region of the face that was present at birth and had been ascending in size causing marked facial disharmony [Fig. 1]. Her chief complaint was difficulty in mouth opening and chewing solid food. She also gave history of fall of multiple maxillary molar teeth 2–3 years ago. No associated history of pain, fever or redness was present with the swelling. On palpation, swelling was doughy, non-pulsatile, poorly marginalised over left side of the face. The overlying skin was normal and no evidence of vascular blanching, cutaneous nevi or stigmata was noted. Cervical lymph nodes were non-palpable. The patient was referred to the Radiology department for evaluation of the facial swelling with a clinical suspicion of lymphangioma or hemangioma.

Frontal and left oblique radiographs of the skull were obtained. However, optimal positioning of the patient could not be done due to the large size of the swelling. The radiographs showed a bony mass in the area of the left temporo-mandibular joint and hypertrophy of the left hemi-mandible. An Orthopantomogram (OPG) was also done which revealed a bony ankylotic mass replacing the normal left temporomandibular joint with non-visualisation of left maxillary molar teeth [Fig. 2].

Contrast enhanced CT scan of the face was performed on a 128 slice MDCT scanner at 90 mAs and 120 KV. The scan revealed a large poorly marginated, nonhomogeneous infiltrative lesion showing fat density;

* Corresponding author.
E-mail addresses: ramandeepsingh1363@gmail.com (R. Singh), guptaaakash95@gmail.com (A. Gupta), drgauravpradhan@gmail.com (G.S. Pradhan), arshitkat1995@gmail.com (A. Kataria).

https://doi.org/10.1016/j.jobcr.2024.10.006
Received 23 February 2024; Received in revised form 5 August 2024; Accepted 13 October 2024

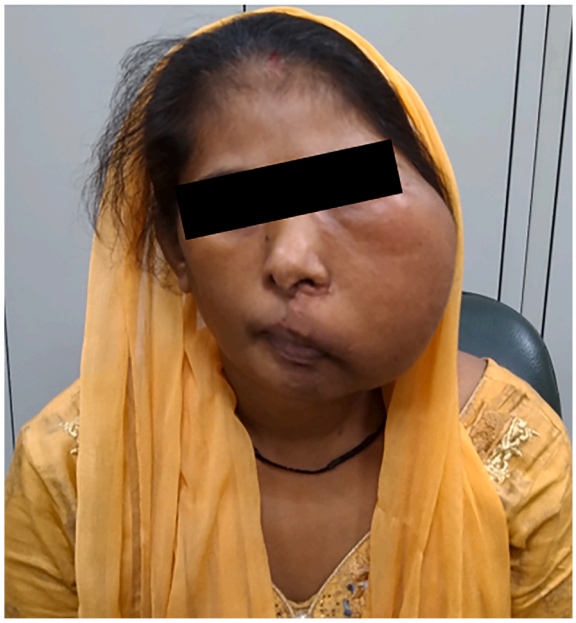

Fig. 1. Photograph of the patient showing swelling over left side of face.

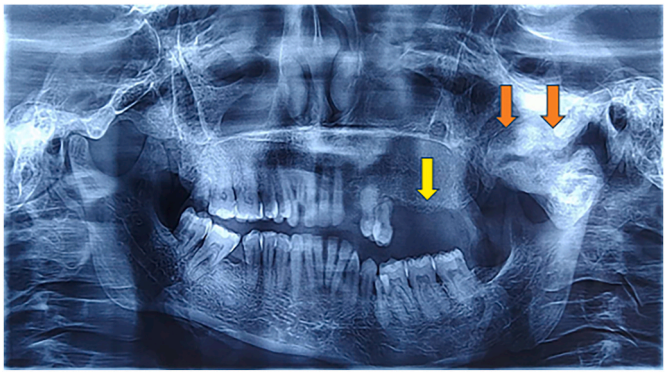

Fig. 2. Orthopantomogram showing an ankylotic bony mass (orange arrows) in the region of left temporomandibular joint with non-visualisation of left maxillary molar teeth (yellow arrows).

predominantly involving the left temporofacial region. Involvement of the masticator space, buccal space, submandibular space, pterygopalatine fossa and retromolar trigone was seen [Fig. 3]. The lesion was also noted to involve the hard palate and soft palate on left side. Left temporalis and masseter muscles showed fatty infiltration. Bony involvement was seen in the form of hypertrophy of zygoma, superior alveolar arch, greater wing of sphenoid and squamous part of temporal bone on left side [Fig. 4]. The articular surfaces of the left temporomandibular joint were fused along with articulation between the left mandibular condyle and the adjacent zygomatic arch suggestive of ankylosis with pseudoarthrosis [Fig. 5]. No calcification or solid component was seen within the lesion. There was also thickening and enhancement of the left infraorbital nerve on left side as compared to the contralateral side.

Further MRI was done to better delineate soft tissue involvement. It showed poorly defined, invasive, nonhomogeneous mass of fat signal in the region corresponding to CT findings. T1/T2 hypointense septae were seen within. The extraocular muscles on the left side also appeared bulky and hyperintense on T2WI, suggesting involvement [Fig. 6]. The lesion was encasing few vessels of left side of face, which were prominent with normal flow void and contrast opacification [Fig. 7]. MRI brain was normal. A final diagnosis of congenital infiltrating lipomatosis of the face was made on the basis of imaging findings. Table 1 shows patient demography, presenting complaint, bony involvement and TMJ ankylosis in published reports of CIL-F.

3. Management and outcome

The patient underwent left temporomandibular joint arthroplasty [Figs. 8 and 9] followed by intensive mouth opening exercises. Histopathological examination of biopsy sample from the swelling showed mature adipocytes without cellular atypia [Fig. 10]. Mouth opening was significantly improved at discharge on day 10. Patient was performing well at one year follow up. She refused the option of excision and cosmetic surgery of the facial swelling, hence no debulking surgery was done.

4. Ethical considerations

This article adhered to all ethical guidelines for conducting research.

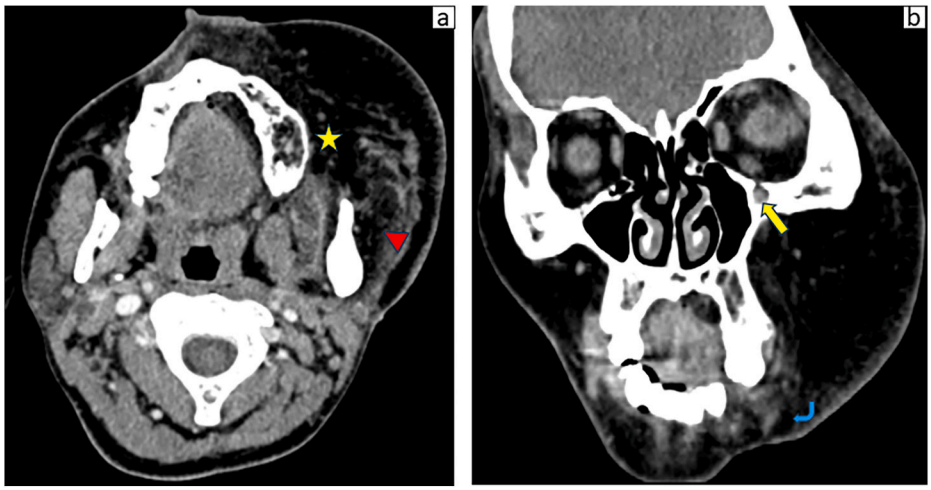

Fig. 3. Axial (a) and coronal (b) CT images (soft-tissue algorithm) depicting a large, poorly marginated, infiltrative lesion of fat density in the left temporofacial region involving the masticator space (triangle), buccal space (star) and submandibular space (elbow arrow). Coronal CT image also shows widening of infraorbital foramen and thickening of the left infraorbital nerve (arrow).

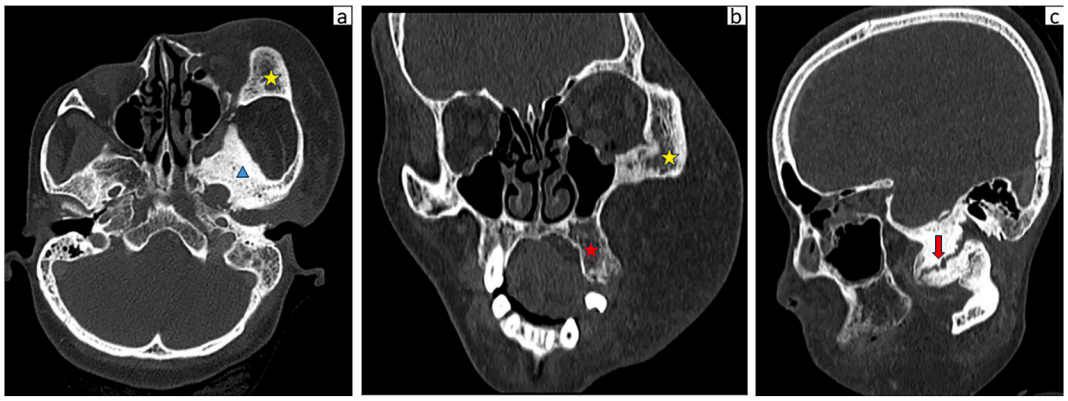

Fig. 4. (a) Axial CT image (bone algorithm) showing hypertrophy of zygoma (yellow star) and greater wing of sphenoid (triangle) on left side. (b) Coronal CT image (bone algorithm) showing fatty infiltration of the superior alveolar arch (red star) on left side and hypertrophy of the left zygoma. (c) Sagittal CT image (bone algorithm) demonstrating bony ankylosis of the left temporomandibular joint with a lucent line inside the fusion area (arrow), no recognizable condyle and fossa are seen.

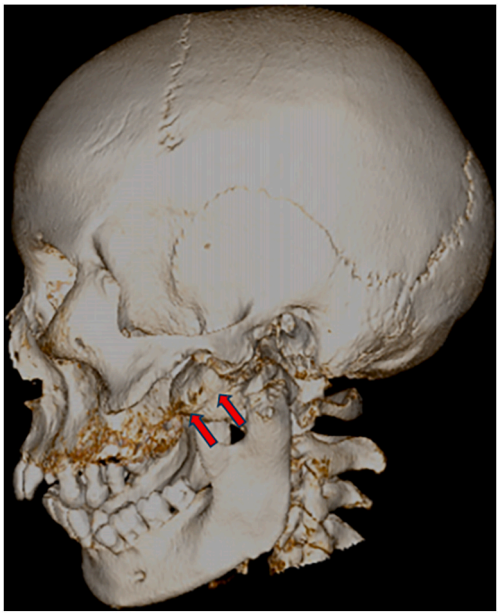

Fig. 5. Three-dimensional volumetric reconstruction image showing fusion of the articular surfaces of the left temporomandibular joint with a bony mass in this region suggesting TMJ ankylosis (arrows).

5. Discussion

Enzinger and Weiss[12] in 1983, defined Lipomatosis as an infiltrative and/or diffuse growth of mature adipose tissue, which can bear resemblance to well-differentiated liposarcoma, leading to potential confusion between the two. However, this description was a generalised term, not specific for involvement of soft structures of the face. Slavin et al.,[1] in same year proposed the term Congenital infiltrating lipomatosis of the face (CIL-F) which is a rare condition that presents as a nonhereditary disease from birth. It is distinguished by the infiltration of mature lipocytes, which have unclear borders, into the adjoining muscles and soft tissues.

Patients usually present with facial disharmony at birth which progresses with the age of person. The causative factor is still unclear though few hypotheses have been proposed. The existing pathogenic hypothesis suggests that there is a somatic mutation occurring in the PIK3CA gene.[13] Additionally, it has been identified in malignancies and impacted tissues from various non-inherited and excessive growth conditions. The PIK3CA gene is essential for regulating several cellular properties such as cell proliferation, adhesion, survival, and motility. Conversely, lipomatous change can be triggered by external factors such as trauma, irradiation, and degenerative processes.

CIL-F is classified as a subtype of lipoma. Non-malignant lipomas are divided into five subgroups[8].

1. Well enclosed lipoma
2. Angiomyolipoma like variants
3. Hamartoma
4. Infiltrating lipoma
5. Lipoma of brown fat

Invasive lipomas mostly occur in 30s of patient's life[8] with involvement of subcutaneous tissues, muscles, and bones. They are referred to as congenital infiltrating lipomatosis when it occurs in infancy or at time of birth and are often seen involving the face.

Histopathologically, these lesions consist of nonencapsulated mature fatty tissue which infiltrate into adjacent muscles, soft tissues and bones. Fibrous elements can also be seen. Characteristically, there is non-presence of lipoblasts and malignant features.

This condition can be recognized on the basis of clinical features and imaging appearance. Simple radiographs are of limited use in the evaluation of CIL – F, and bone hypertrophy, altered status of the teeth and temporo-mandibular joint and swelling of the soft tissue can be observed. Ultrasound with Doppler examination helps to rule out any vascular mass lesion, however, it cannot differentiate the precise extent of the lesion.[2] Cross sectional modalities i.e.; CT scan and MRI are the imaging techniques of preference as they not only find the fat portion of the lesions but also describe their extent, which is important for guiding the appropriate management. CT scan shows a diffuse infiltrating lesion of fat attenuation with involvement of surrounding soft tissues, muscles and bones in exquisite detail. The non-homogeneous appearance of fatty invasion is likely due to intervening fibrous structures.[4]

CT scan is extremely useful in demonstrating the involvement of the articular margins of the temporo-mandibular joint and associated pseudoarthrosis which causes severe restriction in mouth opening in such patients as was seen in our case.[14] CIL-F is known to cause bony expansion due to fatty infiltration, however, it is rare associated with severe restriction of mouth opening due to involvement of the temporo-mandibular joint as was seen in index case.

MRI is superior to CT due to its multiplanar capability and better soft tissue resolution. It not only confirms the fatty type of the lesion but also helps to exclude the possibilities of lymphatic/vascular malformations. It depicts the accurate extent of the lesion. The presence of related signs and symptoms, along with the diagnostic high signal intensity

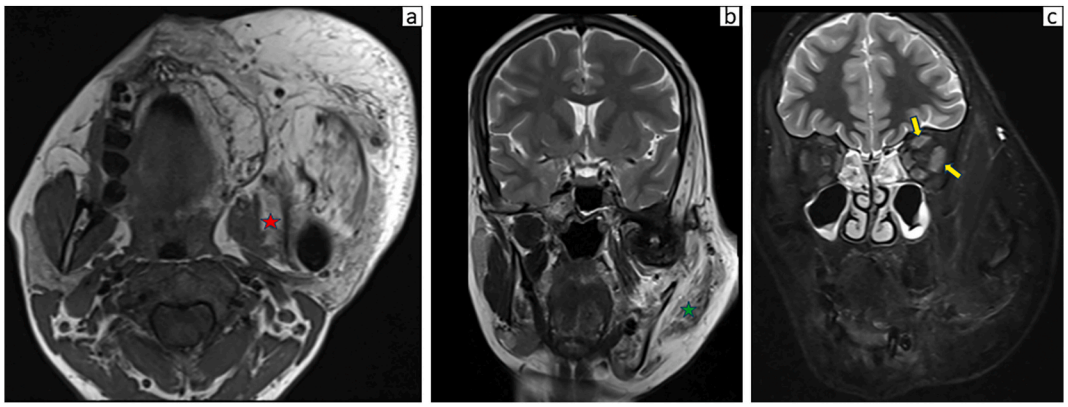

Fig. 6. Axial T1W (a), coronal T2W (b), and coronal STIR (c) images showing an ill-defined lesion with fat-signal intensity involving the superficial and deep planes of the left temporofacial region. Axial T1WI showing involvement of the superior alveolar arch and the palate on the left side. Coronal T2WI showing fatty infiltration of the muscle of mastication on left side, most marked in masseter (green star) and temporalis and also involving the pterygoids (red star). Coronal STIR image revealing hypertrophy of the extraocular muscles (arrows) on left side.

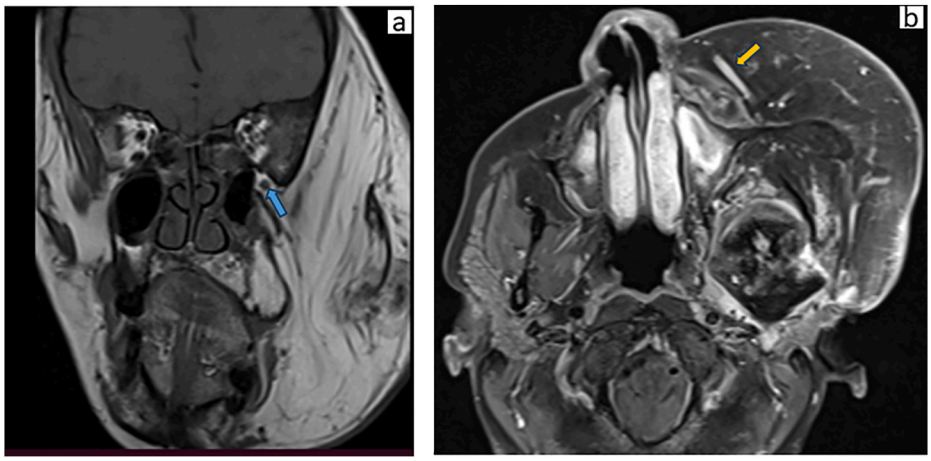

Fig. 7. (a) Coronal T1W image showing thickening of the left infraorbital nerve (blue arrow). (b) Axial T1FS post contrast image showing multiple prominent vascular channels (orange arrow) within the lesion.

Table 1
Bone involvement, TMJ ankylosis and EOM involvement in published cases of congenital infiltrating lipomatosis of the face.

Authors	Age of patient at presentation	Chief complaint	Gender	Bone involvement	TMJ ankylosis	Extraocular muscle involvement	Skull foraminal widening
Rajeswaran et al.[4]	11 years	Diffuse right facial swelling	F	Right frontal, orbital, zygomatic and maxillary bones	Absent	–	–
Kang et al.[7]	25 years	Right facial swelling	M	Maxilla	Absent	–	–
Chen et al.[8]	16 months	Left cheek mass	F	Left zygoma and maxilla	Absent	–	–
Malik et al.[9]	22 years	Diffuse soft swelling over right cheek	M	Right zygomatic arch, mandibular condyle and lateral pterygoid plate	Absent	–	–
Kamal et al.[10]	16 years	Left facial mass	F	Left zygomatic arch	Absent	–	–
Sahai S[11]	53 years	Progressive right facial asymmetry and exophytic right preauricular swelling	F	Ipsilateral Mandibular body, ramus, temporomandibular joint, maxilla, zygomatic bone	Present	–	–
T. Keramidas et al.[5]	49 years	Swelling over right side of the face and trismus	M	Ipsilateral Zygomatic bone, temporomandibular joint, coronoid process	Present	–	–
Gupta R[6]	35 years	Severely restricted mouth opening and right facial swelling	F	Right Maxilla, sphenoid bone	Present	–	Present (ipsilateral foramen ovale, inferior orbital foramen, greater palatine foramen, and sphenopalatine foramen)
This case	34 years	Difficulty in opening mouth and left sided facial swelling	F	Ipsilateral Zygoma, superior alveolar arch, greater wing of sphenoid and squamous part of temporal bone	**Present**	**Present**	**Present** (ipsilateral infraorbital foramen)

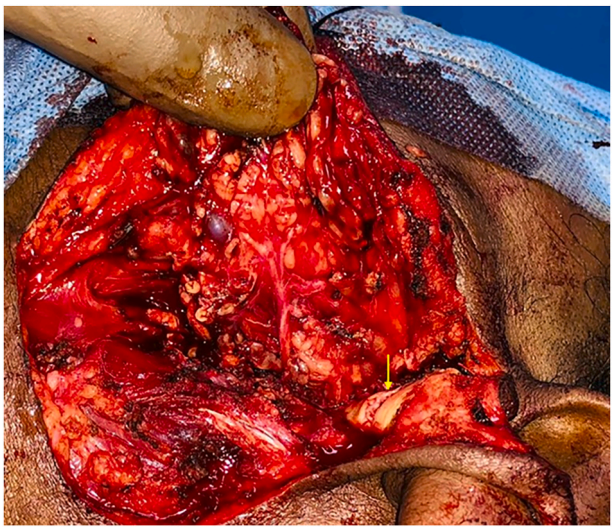

Fig. 8. Intraoperative clinical photo showing the operative field in the left temporo-mandibular region. Bony mass in the TMJ region is clearly visualised (arrow).

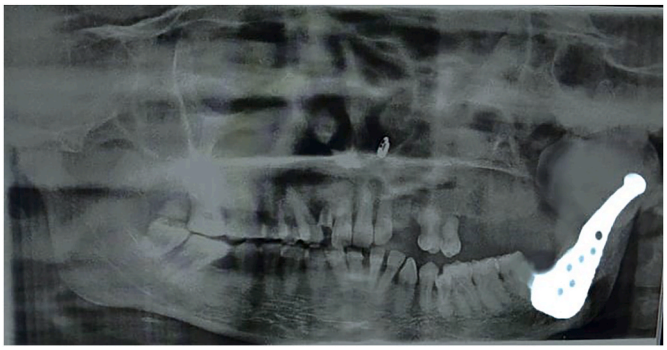

Fig. 9. Post operative orthopantomogram after TMJ arthroplasty.

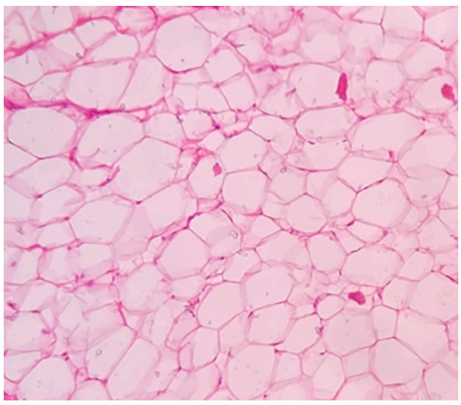

Fig. 10. Light microscope image of the biopsy specimen showing mature adipose tissue.

(resembling fat) of the condition on T1 and T2 weighted images, and the signal drop on fat suppressed pictures in young patients, confirms the diagnosis.[4,15] MRI provides a more comprehensive visualisation of muscle and soft tissue involvement. Biopsy is not essential if relevant findings are present on MRI. MRI may also help to rule out any malignant transformation. At MR imaging, the presence of thick, irregular, enhancing septa and nonfatty soft-tissue mass components raises the concern for liposarcoma rather than benign lipomatosis. However, at times benign lipomatous lesions and the well differentiated liposarcomas may have overlapping MR imaging findings, thus requiring histological evaluation for confirmation.[16] Nevertheless, distinguishing between CIL-F and well-differentiated liposarcomas solely based on MRI features is not consistently dependable.[17]

MRI also helps to detect the associated intracranial anomalies such as ipsilateral hemimegaloencephaly, asymmetric ventricular–sylvian fissure dilatation, arachnoid cyst and cerebellopontine angle lipoma.[18]

The differential diagnosis of CIL-F includes lymphatic/arteriovenous malformations, liposarcomas, Proteus syndrome and encephalocraniocutaneous lipomatosis. Clinico-radiological evaluation is enough to exclude the differentials most of the times; however, differentiation from well differentiated liposarcoma and lipoblastomatosis may require histopathological correlation. Hemangiomas and arteriovenous malformations are compressible lesions and are usually associated with some form of skin stigmata, that allow them to be differentiated clinically. Further, imaging can help to reach the final diagnosis. Based on CT and MRI findings, the lesion in the index case is composed of fatty tissue. Vascular malformations, on the other hand, are predominantly composed of vascular tissue characterized by enhancement and presence of flow voids or phleboliths. Dynamic post contrast MRI can further help in differentiating low vs high flow vascular malformations. Low flow vascular malformation will show lack of early arterial flow and venous shunting in the arterial phase unlike high flow malformations. Absence of these clinical and imaging findings in our case helped to exclude the diagnosis of vascular malformation. Lymphatic malformations are mostly cystic on imaging, hence excluded. Proteus syndrome is rare congenital condition characterized by hyperplasia of tissues from any germinal layer. Patient usually appear normal at birth with progressive development of abnormalities such as hemihypertrophy, macrodactyly, lipoma and vascular malformations in childhood. No such features were seen in our case. Encephalocraniocutaneous lipomatosis is a neurocutaneous syndrome characterized by unilateral lipomas of the scalp and face with ipsilateral cerebral atrophy and lipodermoids of eye. In our case, MRI brain showed normal brain parenchyma, thus excluding the diagnosis of Encephalocraniocutaneous lipomatosis.

Despite being benign tumours, the recurrence rate is exceedingly high following surgical excision. As far as isolated CILF is concerned, post-resection recurrence rate of 62.5 % with an average of 3 debulking procedures per patient has been reported.[7] Since only few cases of CILF with TMJ ankylosis are reported so far, possibility of long-term recurrence of the tumour and the trismus in such cases cannot be ruled out. Out of three previously reported cases, one patient is showing normal mouth opening at two years follow up after Temporomandibular joint arthroplasty.[5] Follow up of other two cases is unknown. In our case, patient refused for any cosmetic surgery as of now. She is kept on follow up and is doing well with normal mouth opening. The clinic-radiological and management findings of our study were correlated with previously report cases of CILF with TMJ ankylosis by Sahai et al.,[11] Keramidas et al.[5] and Gupta et al.[6] Treatment outcomes and follow up in these cases are tabulated (Table 2).

Surgical excision and liposuction are the treatment modalities available for CIL-F. This is done mostly for cosmetic reasons; but in cases of trismus due to associated temporomandibular joint ankylosis, surgical reconstruction is necessary to alleviate the patient symptoms. Future therapy paradigms may allow for a synergistic approach to treat this rare condition, involving both surgical and medical treatments. Patients with CILF may benefit from PI3K inhibitors, which are now being utilized in clinical trials for cancer patients, because the PIK3CA gene mutation is considered as the promising factor in the pathogenesis of CILF.[13] Even though PI3K inhibitors could not cure CILF, it might help to prevent the disease progression or recurrence. Since, these adjuvant treatments are still in pipeline, surgery remains the mainstay of treatment. Proper collection and analysis of the reports of this rare disease are essential to

Table 2
Management, outcome and previous history of debulking in the published cases of congenital infiltrating lipomatosis of the face with TMJ ankylosis.

Authors	Age of patient	Previous debulking surgery	Current Management	Outcome
Sahai S[11]	53 years	No	Debulking, Right hemimandibulectomy with release of the extra-articular TMJ ankylosis	Unknown
T. Keramidas et al.[5]	49 years	Yes (in childhood)	Temporomandibular joint arthroplasty. No debulking	Mouth opening remained in normal range at 2-year follow up.
Gupta R[6]	35 years	Yes (in adolescence)	Surgical excision of ankylosed mass with temporalis muscle interposition. No debulking	Unknown
This case	34 years	No	Temporomandibular joint arthroplasty. No debulking	Mouth opening remained in normal range at 1-year follow up.

learn more about these patients and thereby helping the clinicians to make early diagnosis and appropriate treatment.

6. Conclusion

The importance of early recognition and prompt diagnosis in CIL-F lies in the fact that it is a progressive disorder that leads to permanent disfigurement with significant morbidity in the form of reduced mouth opening due to temporomandibular joint ankylosis. If recognized early, the bony complications of this rare disease can be prevented with corrective surgery. Imaging plays a vital role in ruling out other differential diagnosis, as well as surgical planning and follow up.

Ethical approval

The institutional ethical review board granted a waiver for ethical clearance for this report as no ethical issues were found. An informed and written consent from the next of kin of the patient was taken for the publication of this report.

Ethical clearance

The institutional ethical review board granted a waiver for ethical clearance for this report as no ethical issues were found.

Sources of funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to thank God almighty for his blessings in completion of this task.

References

1. Slavin SA, Baker DC, McCarthy JG, Muffarij A. Congenital infiltrating lipomatosis of the face: clinicopathologic evaluation and treatment. *Plast Reconstr Surg.* 1983;72:158–164.
2. Li Yatong, Chang Guojing, Si Loubin, et al. Congenital infiltrating lipomatosis of the face. Case report and literature review. *Ann Plast Surg.* 2018;80(1):83–89. https://doi.org/10.1097/SAP.0000000000001213.
3. Heymans O, Ronsmans C. Congenital infiltrating lipomatosis of the face. *Eur J Plast Surg.* 2005;28:186–189.
4. Rajeswaran R, Murthy J, Chandrasekharan A, Joseph S. Case report: congenital infiltrating lipomatosis of face. *Indian J Radiol Imag.* 2008;18:306–309.
5. Keramidas T, Lagogiannis G, Vlachou V, Katsikeris N. Congenital infiltrating lipomatosis of the face with associated involvement of the TMJ structures. Case report and review of the literature. *J Cranio-Maxillofacial Surg.* 2012;40(8):750–756. ISSN 1010-5182.
6. Gupta R, Mukul SK, Kumar P, Kumar A. Congenital infiltrating lipomatosis of the face with temporomandibular joint ankylosis. *Natl J Maxillofac Surg.* 2020;11:117–120.
7. Kang N, Ross D, Harrison D. Unilateral hypertrophy of the face associated with infiltrating lipomatosis. *J Oral Maxillofac Surg.* 1998;56:885–887.
8. Chen CM, Lo LJ, Wong HF. Congenital infiltrating lipomatosis of the face: case report and literature review. *Chang Gung Med J.* 2002;25:194–200.
9. Malik A, Jagmohan P, Thukral BB, Khanna G. Rajni. Congenital infiltrating lipomatosis of the face and neck. *Acta Radiol.* 2004;45:556–560.
10. Kamal D, Breton P, Bouletreau P. Congenital infiltrating lipomatosis of the face: report of three cases and review of the literature. *J Cranio-Maxillo-Fac Surg.* 2010;38:610–614.
11. Sahai S, Rajan S, Singh N, Arora H. Congenital infiltrating lipomatosis of the face with exophytic temporomandibular joint ankylosis: a case report and review of the literature. *Dentomaxillofacial Radiol.* 2013;42, 16128745.
12. Enzinger FM, Weiss SW. *Benign Lipomatous Tumors. in: Soft Tissue Tumors.* vol. 199. St Louis, MO: CV Mosby; 1983.
13. Maclellan RA, Luks VL, Vivero MP, et al. PIK3CA activating mutations in facial infiltrating lipomatosis. *Plast Reconstr Surg.* 2014;133:12e–19e.
14. El-Hakim IE, Metwalli SA. Imaging of temporomandibular joint ankylosis. A new radiographic classification. *Dentomaxillofacial Radiol.* 2002;31:19–23.
15. Padwa BL, Mulliken JB. Facial infiltrating lipomatosis. *Plast Reconstr Surg.* 2001;108:1544–1554.
16. Gupta Pushpender, Potti Tommy A, Wuertzer Scott D, Lenchik Leon, Pacholke David A. Spectrum of fat-containing soft-tissue masses at MR imaging: the common, the uncommon, the characteristic, and the sometimes confusing. *Radiographics.* 2016;36(3):753–766. https://doi.org/10.1148/rg.2016150133.
17. Salvatore C, Antonio B, Del Vecchio W, Lanza A, Tartaro G, Giuseppe C. Giant infiltrating lipoma of the face: CT and MR imaging findings. *AJNR Am J Neuroradiol.* 2003;24:283–286.
18. Aydıngöz U, Emir S, Karlı-Oğuz K, Köse G, Büyükpamukçu M. Congenital infiltrating lipomatosis of the face with ipsilateral hemimegalencephaly. *Pediatr Radiol.* 2002;32:106–109.