

Congenital infiltrating lipomatosis of the face with hyperplastic mandibular, maxillary and pterygoid bones: case report and a review of literature

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Abstract: Congenital infiltrating lipomatosis of the face (CILF) is a rare lipomatous lesion, commonly seen in childhood, and it is characterized by collections of mature, unencapsulated adipose tissues that infiltrate facial soft and hard tissues. The lesion is seen as an overgrowth of bone and soft tissue and is generally present clinically as slow-growing painless masses. In this case report, we described one case of CILF, which is one of the first cases reported in Ghana and Africa as a whole, along with a literature review on the diagnosis and current treatment strategies.

Keywords: congenital infiltrating lipomatosis of face, facial asymmetry analysis, hemifacial hyperplasia, macrodontism

Introduction

Congenital infiltrating lipomatosis of the face (CILF) is a very rare lipomatous lesion with <60 reported cases in literature.¹⁻³ CILF is nonhereditary and usually seen in childhood, causing unilateral facial skeletal hyperplasia, and it is histologically characterized by collections of mature, unencapsulated adipose tissues that infiltrate facial soft and hard tissues.^{1,4-7} The primary concern in CILF is usually esthetics and the high rate of recurrence after surgical excision, as patients present with normal psychomotor development, and there is no sex predilection.^{7,8} In this case report, we present an additional case of CILF, which is one of the first cases reported in Ghana and Africa as a whole, along with a discussion on the diagnosis and treatment of CILF, with the aim of providing information toward the management of this rare condition.

Case report

A 9-year-old male patient presented with a painless right facial swelling, which had been present since birth and had progressively been increasing in size. Examination revealed facial asymmetry with a right hemifacial swelling spanning from the lower border of the right mandible to the inferior right lower eyelid measuring ~10×15 cm. There was enlargement of the right ear and a bulge on the right parietal scalp. The lesion was soft, non-tender and mobile with hyperpigmentation of the postauricular skin. There was deviation of the lip and nose to the left with obliteration of the right nasolabial sulcus indicating a right facial palsy. Oral examination revealed right-sided lip and tongue enlargement, right palatal bulge, right-sided dental anarchy with anterior open bite and calculus deposition.

Computed tomography (CT) of the head region showed a large lipomatous transformation of the right side of the face, involving the subcutaneous layer and the right

parotid gland, with extension into the right masticator space. The tragus of the right ear also showed lipomatous infiltration. The lesion covered an area of ~13.8×8.5 cm. Evidence of significant hyperplasia of the right mandible was found with the width of the body of the mandible been 1.9 cm, while the contralateral side had a width of up to 0.9 cm. The lateral plate of the right pterygoid bone was also significantly hyperplastic, having a width of up to 0.9 cm compared to 0.2 cm of the contralateral side. The right maxilla was also significantly hyperplastic with a width of up to 2 cm compared to 1 cm on the contralateral side. There was also asymmetry of the face with disorganized dentition on the right side. No other asymmetric parts of the body were involved.

Written informed consent was obtained from the parent to have the case details and accompanying images published.

Discussion

Congenital infiltrating lipomatosis rarely affects the face and has been reported to have a predilection for the trunk and extremities.⁹ The term congenital infiltrating lipomatosis of the face was initially proposed by Slavin et al,⁷ who were the pioneers to report on proliferating and infiltrating lesions of lipocytes that involved only the facial region. The main characteristics of CILF elucidated by Slavin et al included: 1) nonencapsulated tumors containing mature lipocytes; 2) fat infiltration of adjacent muscles and soft tissues; 3) absence of malignant characteristics; 4) absence of lipoblasts; 5) presence of fibrous elements and increased number of nerve bundles and vessels and 6) adjacent bone hypertrophy. CILF is classified under lipoma, and it is distinguished from liposarcoma by the absence of mitosis, lipoblastic proliferation and pleomorphism.⁷ In CILF, mature lipocytes invade into adjacent tissues in the facial region, manifesting as hypertrophy of both hard and soft structures on the affected side of the face and usually presenting clinically as slow-growing painless masses.^{1,4-7} The manifestation is always unilateral, and reported cases that described the site of the facial mass have shown that ~64% occur on the left.¹⁰ In CILF patients who present for treatment at the adult stage, the condition progresses with gradual hyperplasia, while there is extensive hyperplasia in childhood patients (≤1 year of age).¹¹

Several studies have traced the etiology of CILF to postzygotic mutation, as pluripotent cells of embryonic origin are known to precipitate somatic defect under the influence of trauma, muscle metaplasia, hormones and irradiation.¹²⁻¹⁶ This triggers and accelerates the lipomatous change seen in CILF. The postzygotic mutation occurs in the PIK3CA gene in the affected tissues, as PI3K, which is encoded by PIK3CA,

plays a critical role in regulating cell survival, motility, adhesion and proliferation.¹⁷ A study done by Maclellan et al¹⁷ showed that subcutaneous adipose tissue from affected areas of patients with CILF contains somatic activating mutations in PIK3CA. A further study that sought to determine if the overgrowth in subjects with CILF was caused by a postzygotic mutation in only the subcutaneous adipose tissue (one tissue type) or by the presence of mutant cells in each of the subject's overgrown tissues also reported that all tissues (including stroma, adipose, muscle, bone, nerves, etc.) on the side of the face affected with CILF contained PIK3CA mutations.¹⁸

It must however be noted that the same postzygotic mutations have been identified in vascular malformations, cancers and other disorders with overgrowth, collectively termed together with CILF as PIK3CA-related overgrowth spectrum (PROS), hence not surprising that several mosaic disorders are in the differential diagnosis of CILF.¹⁹ Conditions like Parry–Romberg syndrome (progressive hemifacial hyperplasia atrophy) and hemifacial microsomia, which cause contralateral hypoplasia, need to be considered.²⁰ In addition, although hemifacial hyperplasia does not involve mucosal neuromas and mature lipocytic infiltration, it shares common features with CILF and must be noted.^{19,20} In conditions like facial angioma and angiolipoma, cutaneous capillary brush implicated in some patients with CILF has also been found.^{21,22} Lymphangioma has also been associated with diffuse swelling in the facial and neck area, although this is easily resolved with an MRI scan.^{20,22} Encephalocraniocutaneous lipomatosis (ECCL) and proteus syndrome also have infiltrating lipomatosis as a feature. However, CILF unlike proteus syndrome usually presents at birth and does not involve areas outside the head and neck region. ECCL on the other hand manifests in the central nervous system in contrast to CILF.²² Well-differentiated liposarcoma and lipoblastomatosis that involve fat tissue infiltration also need to be ruled out. Liposarcoma is associated with the presence of lipoblastic proliferation and large number of cell mitosis and pleomorphism, with lipoblastomatosis having the presence of fetal adipose tissue, which is absent in the histopathological examination of CILF tissue.^{7,22-24} Facial location, congenital presentation, early eruption of deciduous and permanent teeth, macrodontism, adjacent dentoskeletal manifestations, proliferation of parotid gland on the affected side, macroglossia and specific histological features are possible results for CILF.^{7,23,25-27}

The diagnosis of CILF in our case was based on the patient's medical records, clinicopathological manifestations

and imaging features from CT (Figures 1–5). The CT scan was particularly useful in demonstrating the lipomatous nature of mass, osseous changes and their exact anatomic location and relationship to surrounding structures prior to surgery. Diagnosis of CILF was however confirmed by histopathology. The lesion was histologically characterized by sheets or lobules of mature normal adipocytes infiltrating trabecular bone, muscle fibers and salivary glands.^{28,29}

Bone changes reported in CILF cases include hypertrophy of the skull, hypertrophy of the zygomatic bone, cervical vertebrae, acceleration of dentoskeletal growth, hemimandibular hypertrophy and sclerosis.^{30–33} These changes in bone appear to be associated with periosteal irritation associated with

the overlying mass, regional malformation of mesenchyme affecting bone and soft tissues or increased vascularity.^{30,33,34} Li et al³⁵ in their review of 59 reported cases of CILF noted

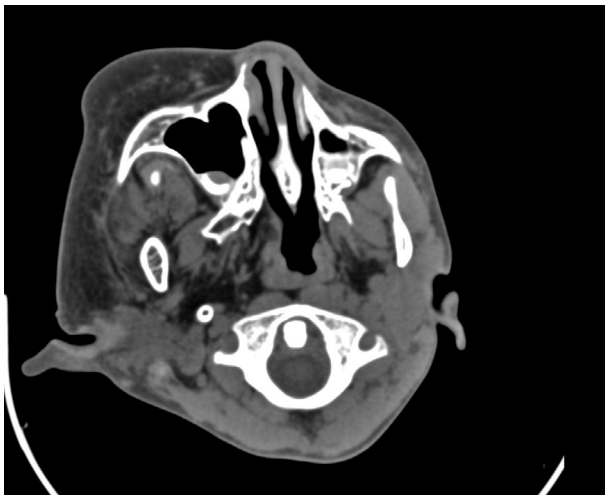


Figure 1 Lipomatous infiltration of the right side of the face, including the parotid gland and masticator space.

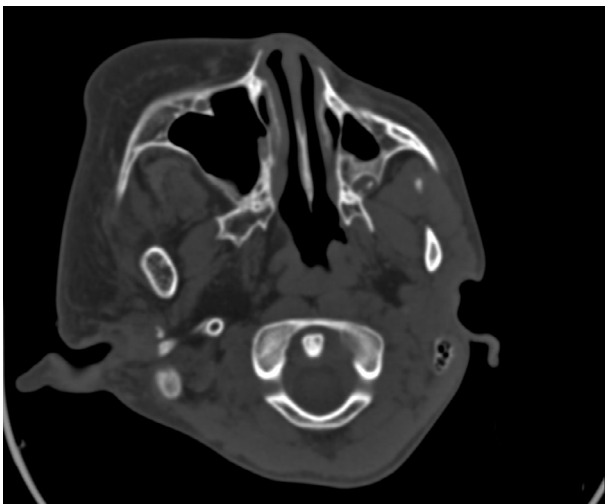


Figure 2 CT scan showing the enlarged pterygoid.
Abbreviation: CT, computed tomography.



Figure 3 CT scan showing the enlarged right mandible.
Abbreviation: CT, computed tomography.



Figure 4 CT scan showing the enlarged maxilla.
Abbreviation: CT, computed tomography.



Figure 5 Volume rendering technique showing radiolucent fat and facial deformity.

that the bony asymmetry appears to increase with age, with the adipose tissue infiltrating into surrounding tissues and causing pterygoid gland and muscles (such as pterygoid plate and masseter and temporalis muscles) involvement, as reported in our cases.

The major concern in the treatment of CILF is the high rate of recurrence after surgical excision although the tumor is benign, with a recent study reporting as high as 79% rate of recurrence.^{1,8,35} As a result, multiple surgeries are needed for cosmetic reasons, and when necessary, osseous reduction operations of the maxilla and mandible are performed.^{21,35,36} Based on the esthetic requirement of the patient, a multidisciplinary approach that involves surgeons, clinicians, dentists, psychologists and geneticists may be ideal.^{22,29,37} The high rate of recurrence may be the result of incomplete resection, as these fatty lesions are histologically benign, and as such, the value of aggressive extirpation needs to be weighed against the facial nerve damage and the likelihood of the resultant deformity.³⁸

Tracy et al in 2013 reported a conservative approach involving targeted chemotherapy and surgical resection in the management of CILF. The use of celecoxib and imatinib

in personalized targeted chemotherapy was associated with improved facial symmetry without evidence of disease progression, thus paving the way for the exploration of this synergistic approach toward the management of this rare condition.⁴¹ Conservative approach has also been reinforced by several authors on the backdrop of the benign nature and critical location of CILF despite the associated high rate of recurrences.^{23,28,39}

A recent study in 2017 by Kalantary et al⁴⁰ proposed a new multistep surgical approach toward the management of CILF. This involves initial debulking to correct the soft tissue asymmetry, followed by orthognathic surgery to correct the skeletal asymmetry, dental problems and associated malocclusion, cautioning however that each patient needs to be evaluated for this additional surgery on the bony level before carrying out this step, and finally bimaxillary procedure and genioplasty. The surgery was successfully performed when the patient was 14 years (after puberty), with no record of clinical recurrence at the time of publication (patient was 18 years then).

In addition, considering the implication of PIK3CA gene mutation in the pathogenic theory of CILF, inhibitors of PI3K, which are currently been used in clinical trials involving cancer patients, may play a role in CILF patients.¹⁷ PI3K inhibitors may therefore be tested for CILF patients in clinical trials in the near future.³⁵

An area of contention in the treatment of CILF is the timing of surgical excision. Slavin et al⁷ in their earlier studies encouraged early aggressive surgery in a bid to improve facial appearance and control the overgrowth. Van Wingerden et al⁴¹ disagreed with this approach on the basis of possible risk to nerve, which is compounded by multiple procedures and the likelihood of recurrence. They however admitted that the postponement of surgery may make the procedure more extensive, along with associated psychosocial issues. They further argued that the delay in surgery lowers the chances of damaging the facial nerve, may require fewer procedures and there will be more mature contralateral cheek for comparison during the procedure. Padwa and Mulliken²¹ also sided with Van Wingerden et al, observing that growth hormone most probably has a role in recurrences and that any effort to reduce the mass before the end of adolescence is bound to fail due to recurrences. Based on our study, we advocate that extensive resection should be delayed as long as possible, with due consideration to psychosocial issues. Elevation of the ptotic upper lip, liposuction and the excision of mucosal neuromas are among the temporary measures that can be taken to improve asymmetry in young patients with minimal risk.²¹

Conclusion

CILF is a rare congenital disorder, histologically characterized by sheets or lobules of mature normal adipocytes infiltrating trabecular bone, muscle fibers and salivary glands. The proximity of vital anatomic structures and the diffuse nature of the disease pose a greater challenge to surgical resection. In this article, we reported an additional case of CILF and did an extensive review of the diagnosis and treatment of the condition, providing information toward the management of this rare disorder.

Disclosure

The authors report no conflicts of interest in this work

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