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# Congenital Infiltrating Lipomatosis of the Face Case Report and Literature Review

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**Rationale:** Congenital infiltrating lipomatosis of the face (CILF) is a rare disorder characterized by collections of nonencapsulated mature lipocytes that infiltrate surrounding tissues. In this article, we would report a new case of CILF, which may be one of the first few cases reported in China.

Patient Concerns: An 8-year-old boy presented with a hyperplasia of subcutaneous tissue of his left face, which had been gradually progressing since birth, resulting in a marked facial asymmetry. Then he underwent an operation of resection of the subcutaneous mass, and the postoperative pathological analysis reported a mature adipose tissue.

**Diagnoses and Outcomes:** The diagnosis of CILF was finally made according to a comprehensive consideration of the patient's situation. We then searched different databases for studies that had investigated CILF, reviewed those literatures, and gave our summaries for such a rare disease.

Lessons: Congenital infiltrating lipomatosis of the face is an extremely rare disease. There is so much unknown about it, and the gradual progress and recurrence make it even harder to cure. Besides, the psychological impact on such patients must be considered. Thus, a proper collection and analysis of the reports of such a disease are very important.

Key Words: congenital infiltrating lipomatosis of the face,

hyperplasia of facial subcutaneous tissue, gradual progress, macrodontism

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**C** ongenital infiltrating lipomatosis of the face (CILF) is a very rare disorder in which mature lipocytes invade into adjacent tissues in the facial region.<sup>1-4</sup> The manifestation is always unilateral, with hypertrophy of both soft and hard structures on the affected side of the face. Congenital infiltrating lipomatosis of the face is a nonhereditary disease. The gradual enlargement of the affected side of the face and the resulting facial asymmetry are crucial features (100%). Besides, macrodontism, early eruption of deciduous and permanent teeth, hypertrophy of bones, macroglossia, and the proliferation of parotid gland on the affected side are all possible results.<sup>1-4</sup> In our study, we would like to report a new case of CILF, which is one of the first few cases reported

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in China. Because CILF is very rare, we hope that our report and review of literatures will give more suggestions for the diagnosis and treatment of this disease.

## CASE REPORT

An 8-year-old boy was admitted to our hospital in December 2016, having suffered from a hyperplasia of subcutaneous tissue of his left face since birth. At that time, the upper boundary of the left cheek enlargement was his left arcus zygomaticus, the lower boundary was his left mandibula, the inner boundary was the left side of his nose and mouth, and the outer boundary was the vertical line of the outer corner of his left eye (Fig. 1A). He came from a full-term pregnancy of nonconsanguineous parents. The prenatal history was normal, and his mother denied any press or injury during the stage of labor, and there were no asphyxia, pathological jaundice, or other neonatal diseases. Developmental milestones were normal. The swelling gradually progressed in size, resulting in an asymmetry of the face, and there were no any diagnosis or treatment. When he presented to us, the 4 boundaries of the mass were almost the same as born, except for the inner boundary, which progressed to the midline of the boy's nose and mouth (Fig. 1B). During the whole course of the disease, the patient denied any discomforts, including fever, pain, hypoesthesia, weakened muscular strength, obnubilation, or unconsciousness. Moreover, there was no early eruption of deciduous or permanent teeth on the left side.

The past, personal, and family history of the patient were all clear. The physical examination showed an enlargement of the left face, measured approximately  $10 \times 7$  cm. The midline of the face moved right, whereas the left nasolabial fold was lighter, and the left palpebral fissure was smaller than that of right (Fig. 1C). However, there was nothing special of the left facial mass compared with the right face. The color and texture of the skin were normal, and the pain was negative. The cranial nerves examination also presented no positive results. The sense, muscular strength, and muscular movement of the left face were all as normal as that of right.

The blood examination of this patient showed nothing special, as well as the ultrasound and electromyography test results. The 3-dimension computed tomography (CT) examination reported a symmetrical skull without any malformation or asymmetry externally. However, an abnormal big left upper canine could be seen, which led to an absence of the left upper lateral incisor, and a dislocation of the left upper incisor (Fig. 2A). The teeth CT examination also reported those relatively bigger left teeth, which conformed the performance of macrodontism (Fig. 2B). Besides, bone asymmetry of maxillary alveolar ridge was also shown (Fig. 2B). The magnetic resonance imaging (MRI) examination reported a hyperplasia of the subcutaneous tissue of the left face. According to the density and characters of the mass, we guessed it as subcutaneous lipomatosis

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FIGURE 1. The schematic diagram of the 4 boundaries of the patient's left cheek enlargement when he was born (A) and when presented to us (B), showing the progress of CILF and photos before surgery (C).

(Fig. 2C). Thus, an admitting diagnosis of subcutaneous tissue accumulation of the left maxillofacial region, lipomatosis probability was made.

The patient underwent a surgical treatment of subcutaneous lipectomy of the left maxillofacial lipomatosis on December 13, 2016. During the operation, we saw some big fat granules under the patient's skin, and his buccal fat pad was very thick (Fig. 3A). The postoperative pathological analysis reported the mass as mature fat tissue without any capsule (Fig. 3B). Therefore, we made the final diagnosis as subcutaneous lipomatosis of the left maxillofacial region comprehensively, and CILF was the most possible cause.

The patient and his family gave their informed consent for the treatment and inclusion in this study, after having been provided with all the necessary information. His outward appearance had certainly improved after the surgical treatment, and the postoperative MRI examination showed the same result (Fig. 3C). During a 6-month follow-up, there were no signs of disease recurrence or metastasis. A long-term follow-up will be done, to get more information about this rare disease.

## DISCUSSION

#### **CILF and Differential Diagnosis**

Congenital infiltrating lipomatosis of the face is also called facial infiltrating lipomatosis. It is a congenital, nonhereditary disease, which was first described by Slavin et al<sup>5</sup> in 1983. Congenital infiltrating lipomatosis of the face is a very rare disorder, which is characterized by a collection of lipocytes with ill-defined borders that infiltrates surrounding muscles and soft tissues. Patients are presented with facial asymmetry at birth that evolves as the patient grows.

The etiology of CILF remains unknown. Originally, Donati et al<sup>6</sup> considered the relationship between CILF and cytomegalovirus infection, and they reported such a case. Among the subsequent reports, only 1 case fitted this hypothesis, with anticytomegalovirus IgG positive and IgM negative.<sup>7</sup> Couto et al<sup>8</sup> proved that neovascularization does not play a potential role in the pathogenesis of CILF. Capra et al<sup>9</sup> reported a deletion of chromosome 1q24.3q31.1 in a girl with pituitary deficiency and CILF. The current pathogenic theory was a somatic mutation



FIGURE 2. The preoperative image examinations of the patient, including the 3-dimension reconstruction of the CT scan of the skull, with an arrow pointing the abnormal big left upper canine (A), the CT scan of the teeth (B), and the MRI examination (C).

in the *PIK3CA* gene in the affected tissues,<sup>10</sup> which is also detected in cancers and affected tissues from other nonheritable and overgrowth disorders. PIK3, encoded by PIK3CA, plays a crucial role in regulating cell proliferation, adhesion, survival, and motility. External environmental conditions, including irradiation, trauma, and degenerative processes with fatty transformation, could trigger and accelerate the lipomatous change.

Our diagnosis of CILF was based on the patient's medical history, clinical manifestations, and imaging features. The ill-defined fatty tissue could be detected by ultrasound, CT scan, and MRI, with infiltration into surrounding tissues, and no abnormal vascularity could be detected inside the lesions.

Histopathological analysis of the excised specimens could show the diffuse, nonencapsulated mature adipocytes variably infiltrated into submucosa, dermis, skeletal muscle, parotid, and minor salivary glands, with an increased number of small vessels and nerves. Neither lipoblasts nor signs of malignancy could be found. However, in our case, we did not resect any tissues except for adipose mass. Thus, our pathological reports only showed a mature fat tissue.

The differential diagnoses included encephalocraniocutaneous lipomatosis and Proteus syndrome. Encephalocraniocutaneous lipomatosis is characterized by lipomas of the scalp and central nervous system, as well as focal alopecia.<sup>10</sup> Proteus syndrome is characterized by vascular malformations, lipomas, hyperpigmentation, and several types of nevi. Cutaneous lesions of Proteus syndrome tend to appear over time, the diagnosis may be delayed until late infancy, childhood, or even adulthood.<sup>11</sup> According to the clinicopathological manifestations in our case, both of these 2 syndromes were eliminated. Moreover, other diseases, such as hemangioma and lymphangioma, were easily obsoleted by postoperative pathological diagnosis.



**FIGURE 3.** The intraoperative and postoperative findings: big fat granules under the skin and thick buccal fat pad (A); the pathological analysis showed a mature fat tissue (B); preoperative and postoperative photos and MRI examination results showed an obviously improved outward appearance as well as a more symmetrical face (C).

## TABLE 1. Case Reports of CILF

Case	Author and Year	Sex	Age at First Clinic	Site	Hypertrophy of Bones	Macrodontism and Early Eruption Of Deciduous And Permanent Teeth On The Affected Side	Muscle Involved	Surgery	Recurrence
1	Slavin et al (1983)	М	2	R	N	N	Y	Y	Y
2		F	9	R	Y. Zyg	N	Y	Ŷ	N
3		F	2	R	N	N	N	v	v
4	DeRosa et al (1987)	M	53	T	V. Zvg Max	N	N	v	v
5	Dertosa et al (1967)	F	9	I	V. Max	N	N	v	v
6		F	23	P	V: Man	N	N	v	V
7	Van Wingerden et al	M	1.5	R	N N	N	N	Y	N
8	MacMillan et al	F	36	L	Y: Zyg, Max	Ν	Ν	Y	Y
0	(1990)	м		т	V	N	N	V	N
9	Donati et al $(1990)$	IVI E	15	L	ľ N	IN N	IN N	Y N	IN N
10	Batainen et al (1996)	r M	15	L	N	N	N N	Y	IN N
11	Kang et al (1998)	M	25	ĸ	Y: Zyg, Max	N	N	Ŷ	Ŷ
12	Bouletreau et al (2000)	F	22	L	Y: Max, Man	Y	Ŷ	Y	Y
13	Unal et al (2000)	М	2	L	Ν	Ν	Y	Y	Y
14		F	0.2	L	Ν	Ν	Ν	N	—
15		F	1.5	R	Ν	Ν	N	Y	Y
16–28	Padwa et al (2001)	M=8 F=5	12.4		Y: Zyg, Max, Man	Y	Ν	Y	Y
29	Aydíngöz et al (2002)	М	0.25	L	Ν	Ν	Ν	Ν	
30	Chen et al (2002)	F		L	Y	Ν	Ν	Y	Y
31	Unal et al (2002)	F	2	L	Ν	Ν	Ν	Y	Ν
32	Malik et al (2004)	М	22	R	Y: Zyg, Max, Man	Y	Y	Y	Y
33–36	Haloi et al (2006)	_			Ν	Ν	Ν	Ν	
37	Rajeswaran et al (2008)	F	11	R	Y: Zyg, Max	Ν	Υ	Υ	—
38	Pires Fraga et al (2008)	М	2	L	Ν	Ν	Y	Y	Y
39	Alkan et al (2009)	М	1.5	L	Ν	Y	Y	Y	Ν
40	Maruyama et al (2010)	М	4	R	N	N	N	N	
41	Kim et al $(2010)$	F	3.5	L	Y. Man	Ν	Y	Y	Y
42	Kamal et al $(2010)$	F	18	ī	V· Zvg	N	N	v	v
43	Tunia et al (2010)	M	2	L	Y. Max	N	Y	N	
44	Singh et al (2011)	F	27	I.	V· Zvg	N	N	v	v
45	Balaii et al (2012)	M	3	L	V. Zvg Max Man	N	v	v	V
46	Keramidas et al (2012)	M	49	R	V	N	v	v	v
47	Mahadevappa et al	M	0.75	R	N	Y	Y	Y	N
48	Talamanca et al (2012)	М	0.5	L	Y. Zvo Max	Ν	Y	Y	
49	Sahai et al (2013)	F	54	R	Y: Zyg, Max	N	v	v	v
50	Capra et al $(2013)$	F		R	V	N	v	N	
51	Tracy et al (2013)	F	15	T	V· Zva	N	v	N	
52	Sup at al $(2013)$	I E	15	I	V. Zug May Man	V	v	N	V
52 53	Sull et al (2015)	Г Г	8	L P	1. Lyg, Iviax, Iviali	í V	ı V		I V
55 54		r F	0	л т	I. Lyg, Max	í V	I V	I V	I V
J4 55		r F	10	L T	I. Lyg, Wax	Ι Ν	I V	I V	I V
55 56	DIG	r F	23 17	L	1: Zyg, Max, Man	IN NT	Ϋ́ Υ	Y V	Ŷ
30 57	D'Souza et al (2014)	F M	1/	L	Y: Zyg	IN N	Y V	Y	Ŷ
51	Santana-Kamirez et al (2014)	IVI	0.4	L	IN	IN	Ŷ	IN	

Continued next page

Case	Author and Year	Sex	Age at First Clinic	Site	Hypertrophy of Bones	Macrodontism and Early Eruption Of Deciduous And Permanent Teeth On The Affected Side	Muscle Involved	Surgery	Recurrence
58	Shenoy et al (2015)	М	6	L	Y: Max	Ν	Y	Ν	
59	This case	М	8	L	Y	Ν	Ν	Y	
Total		M = 27, F = 28	Average 11.9	R = 15, L = 27	Y = 69.49%	Y = 33.90%	Y = 40.68%	Y = 77.97%	Y = 62.71%

However, the term lipomatosis implies multiple lipomas, which are not a component of CILF. Thus, *adiposis* may be a better word to describe the proliferation of adipose cells and the accumulation of mature fat tissue. Because CILF is very rare, more data and discussion are needed to give a more accurate description about the disease.

### **Review of Literatures**

To investigate more about CILF, the PubMed, Embase, and Science Citation Index databases were systematically searched until January, 2017. The key words used were "lipomatosis," "face/facial," "infiltrating," and "congenital." The citation lists associated with all of the studies retrieved were used to identify other potentially relevant publications. The reference lists were also checked, including case and review publications. The search results were then screened according to the following inclusion criteria: (1) any form of publications focused on facial asymmetry at birth, with or without cutaneous, subcutaneous, skeletal, sarcous, and neurological clinical manifestations; and (2) presentation of sufficient data, including clinical characteristics and histopathological detection. Studies were excluded if they met the following criteria: (1) were not published in English; and (2) duplicated data from the same sample of patients.

The systematic search yielded a total of 59 patients including the 1 reported in this article.<sup>1,2,4–7,9,12–36</sup> The male-to-female ratio was 1:1.037, with no sex differences. All of those patients were presented with facial soft tissue mass, which was nonpulsatile, noncompressible, ill-defined, and facial asymmetry (100%). Among them, 42 cases described the site of the facial mass, 64% of which were on the left. The lesions could range from infraorbital rim, along the inferior mandibular border and lateral border of the nose, to the lower lip, even the ear and neck (2 cases, 3%) of the affected side (Table 1).

Forty-one cases (69%) showed ipsilateral hypertrophy of the underlying facial skeleton, among which 24 cases (67%) of zygoma, 23 cases (64%) of maxilla, and 11 cases (31%) of mandibule were involved. Bony asymmetry seemed to increase with age. Adipose tissue infiltrated into surrounding tissues, which caused muscles (24 cases, 41%; such as masseters, pterygoid plate, and temporalis muscles) and parotid glands involvement (22 cases, 37%). Oral malformation was also described. Macroglossia was involved in 19 cases (32%). Nineteen cases (32%) exhibited early eruption of deciduous and permanent teeth on the affected side. Thirteen cases (22%) were presented with teeth missing, and 11 cases (19%) exhibited macrodontism. Intracranial abnormality was reported in 10 cases (17%), which presented as unilateral hemimegalencephaly, which showed hypertrophy of cerebral hemisphere, unilateral diffuse pachygyria, thickening of gray matter, enlargement of lateral hemi-ventricle, and 2 high-signal intensities in the white matter. Pigmented nevi was observed in 4 cases (7%) (Table 1).

There were no abnormal results of ophthalmological and buccal neurological examinations, and no vascular problems reported. Since the hemihypertrophy alongside the oral cavity, the oropharynx, the floor of the mouth and the tongue, obstructive sleep apnea, and hypoxia were observed by polysomnogram monitoring in some cases.

Among all the 58 cases in previous literatures, 38 patients (64%) got at least 1 plastic surgery, whereas the recurrence rate was 79% (Table 1). Only a very few cases had a good cosmetic result after a single surgery, whereas others required multiple operations. On an average, 1.95 operations had been performed for each recurrent case. Fortunately, there was no case of distal metastasis reported before.

### Treatments of CILF

The treatment modalities available were liposuction and excision. Although the tumor is benign, the rate of recurrence is very high after surgical excisions. Multiple surgeries are needed for cosmetic reasons. Debulking surgeries were usually performed through a rhytidectomy incision, during which doctors needed to try to preserve the facial nerve. Sometimes, osseous reduction operations of the zygoma, maxilla, and mandibule were performed if necessary.

In 2013, Tracy et al<sup>35</sup> reported a new therapeutic protocol involving surgical resection and targeted chemotherapy. Doctors analyzed the surgical specimen and found the expression of c-kit (CD117) and platelet derived growth factor receptor. Imatinib and celecoxib were prescribed as personalized targeted chemotherapy, which demonstrated improved facial symmetry without evidence of disease progression. Combining surgical and medical intervention may allow for a synergistic approach to controlling this rare disease, which could be the future treatment paradigm.

Because the *PIK3CA* gene mutation is the promising pathogenic theory, PI3K inhibitors, which are currently used in clinical trials for patients with cancer, may play a therapeutic role in patients with CILF.<sup>10</sup> Even if the disorder could not be cured, PI3K inhibitor might prevent progression or recurrence of CILF.

However, as an extremely rare disease, there were not so many reports about CILF. Therefore, a proper surgical treatment was always operated according to the surgeon's experiences. Moreover, the adjuvant treatment was still in research. Besides, facial appearance is very important to everybody. Thus, it is significant to give a psychological guidance along with the process of multiple surgical treatments. Comprehensive treatment is crucial for such a disease, and more cases are needed to conclude a better therapy.

## CONCLUSIONS

Congenital infiltrating lipomatosis of the face is a very rare disease. In this article, we reported 1 new case in our hospital, and reviewed the related literatures including 58 cases all over the world. Although CILF has a benign behavior, the gradual continuing progress and high recurrence rate asked us to learn more about it. Because facial appearance is very important, the efficacy of surgical treatment, adjuvant therapy, and psychological intervention are significant to both patients and doctors. Thus, a proper collection and analysis of the reports of such a disease are very important to help us learn more do more for those patients.

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