CLINICAL NOTE

Facial Infiltrating Lipomatosis

Physical, Radiological, and Histopathological Findings

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Facial infiltrating lipomatosis (FIL) is a rare congenital disorder associated with infiltration of mature lipocytes into adjacent soft tissue. Common findings include hemifacial enlargement, skeletal overgrowth, ipsilateral macroglossia, cutaneous capillary blush, mucosal neuromas, and dental changes. While benign, recurrence is common after surgical treatment. We report a case of this rare disorder and discuss the physical, radiological, and histopathological findings.

REPORT OF A CASE

A 3½-year-old girl was found to have progressive left hemifacial enlargement since birth. Physical findings included asymmetric enlargement of the left ear, cheek, tongue, teeth, mandible, neck, and parotid and submandibular glands. In addition, hyperplastic papillae of the anterior third of tongue and premature loss of primary teeth with premature eruption of secondary teeth were noted. Otherwise, there were no neurological, audiological, or developmental abnormalities. Her prenatal course and birth were unremarkable except for polyhydramnios, and family history was negative for any known genetic disorders.

Initially, she was thought to have hemifacial hyperplasia. Because of the increased incidence of visceral malignancy associated with this condition,[1] serial α-fetoprotein analysis and abdominal ultrasonography were performed and findings were normal. At age 18 months, she was diagnosed as having obstructive sleep apnea on polysomnogram and underwent adenotonsillectomy with improvement of symptoms postoperatively. At age 21 months, magnetic resonance imaging was performed, which confirmed the physical findings. Soon after, she developed speech abnormality due to her hemitongue enlargement. Two months after her third birthday, she underwent carbon dioxide laser–assisted partial glossectomy and removal of her left buccal mucosal mass. Histopathological analysis revealed multiple mucosal neuromas, a finding encountered in FIL, multiple endocrine neoplasia type 2B (MEN2B), Cowden syndrome, and Bannanyan-Riley-Ruvalcaba syndrome but not in hemifacial hyperplasia. Results of subsequent molecular testing for MEN2B, Cowden syndrome, and Bannayan-Riley-Ruvalcaba syndrome were all negative. Therefore, review of clinical, radiological, and histopathological data confirmed the diagnosis of FIL.

Since the diagnosis, at age 5 years, the patient was noted to have difficulty chewing due to recurrent enlargement of her left buccal mucosal neuromas and an unpleasant appearance due to enlargement of her lower lip. She underwent successful carbon dioxide laser excision of her left buccal mucosal neuromas and inferior cheiloplasty without complications. We continue to follow her regularly.

COMMENT

Facial infiltrating lipomatosis was first described in 1983 by Slavin et al.[2] How-

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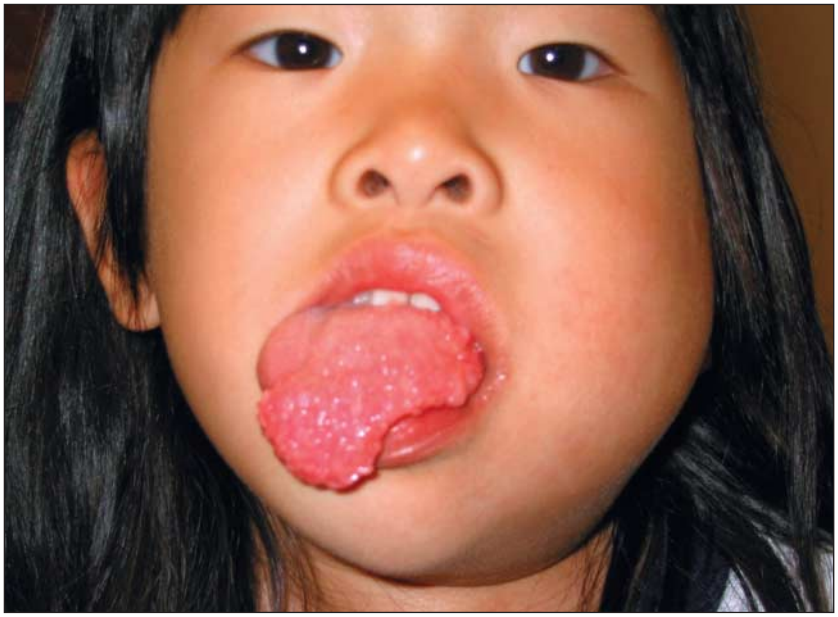

Figure 1. A 3½-year-old girl with progressive left hemifacial enlargement. Note enlarged left side of the tongue and mucosal neuromas.

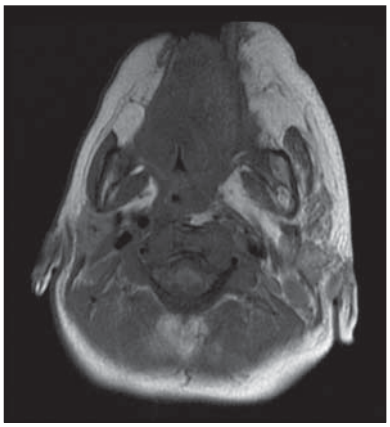

Figure 2. Axial T1-weighted fast spin-echo magnetic resonance imaging. Note asymmetric enlargement of left hemitongue and fatty infiltration of left cheek (bright).

ever, a review by Kang et al[3] indicated that FIL may have been previously misdiagnosed as hemifacial hyperplasia owing to some overlapping phenotypes. However, a careful evaluation of physical, radiological, histopathological, and molecular findings can distinguish FIL from other disorders. Facial infiltrating lipomatosis can be characterized by (1) unilateral hemifacial enlargement, (2) presence at birth, (3) hypertrophy of underlying bone, (4) lipomatous infiltration of muscle and soft tissue with mature adipocytes, (5) mucosal neuromas, (6) absence of malignant characteristics, and (7) tendency for recurrence after resection.

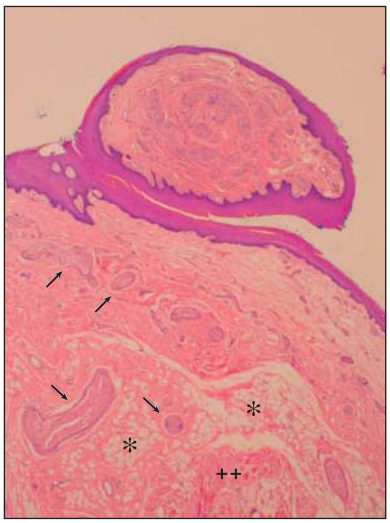

Figure 3. A hematoxylin-eosin stain (original magnification ×100) of a biopsy specimen taken from the superficial aspect of the tongue shows a neuroma causing a pseudopapillomatous appearance. Additional abnormal nerves (arrows) are present below the surface, surrounded by fibrosis. *There is diffuse infiltration by mature adipocytes. ++Sparse skeletal muscle can be seen in the bottom right.

PHYSICAL FINDINGS

In FIL, a diffuse swelling of one side of the face and neck is noted usually from birth (**Figure 1**). This condition seems to affect both sexes and either side of the face. Commonly, ipsilateral macroglossia and macrodontia is also found in addition to enlargement of underlying bone,[4] which can lead to a bite deformity.[5] As in hemifacial hyperplasia, premature loss of primary teeth with premature eruption of secondary teeth can also be seen.[6] Some patients with FIL have faint cutaneous capillary stains of the face that can become more pronounced after surgical resection and increased density of facial hair on the affected side.[7] In our patient, hypertrophy of ipsilateral tongue papillae and buccal mucosa were found, characteristics which, to our knowledge, have not been previously described.

RADIOLOGICAL FINDINGS

Many of the aforementioned physical findings can be appreciated radiographically. Magnetic resonance imaging is probably the most helpful study because it shows diffuse fatty infiltration and increased thickness of subcutaneous fat on the affected side (**Figure 2**). Specifically, a bright signal on both T1- and T2-weighted spin-echo sequences with fatty extension into adjacent soft tissue is found.[8] Computed tomography can also be helpful because it typically shows a nonencapsulated diffusely infiltrating low- attenuation mass that usually measures between –65 H (Hounsfield unit) and –125 H in addition to bony changes.[9]

HISTOPATHOLOGICAL FINDINGS

Histopathological analysis is important in obtaining the correct diagnosis. There is infiltration of normal tissue by mature adipocytes, which help distinguish FIL from lipoblastomatosis and liposarcoma that have undifferentiated or immature adipocytes.[10,11] Areas of normal tissue involved include submucosa, dermis, skeletal muscle, and parotid, submandibular, and minor salivary glands. An increased number of small vessels and mucosal neuromas is also seen (**Figure 3**).

MOLECULAR FINDINGS

While FIL is thought to be caused by a somatic mutation involving local increase in tissue growth factors,[7] molecular studies can be useful to rule out other disorders. Testing for *RET* mutation (MEN2B) and *PTEN* mutation (Cowden syndrome and Bannayan-

Riley-Ruvalcaba syndrome) is recommended. Interestingly, in 2 separate case reports, an association with cytomegalovirus was described.[12,13]

DIFFERENTIAL DIAGNOSIS

Several disorders may mimic FIL, most notably hemifacial hyperplasia. Hemifacial and hemitongue enlargement are common in hemifacial hyperplasia. However, the presence of mucosal neuromas and the infiltration of soft tissue by mature adipocytes are not typically associated with hemifacial hyperplasia. Diffuse neck swelling is seen in lymphangioma, while more localized soft-tissue enlargements can be found in lipoblastomatosis or liposarcoma. On histopathological analysis, FIL lacks the typical lymphatic channels found in lymphangioma and the undifferentiated or immature adipocytes found in lipoblastomatosis and liposarcoma.

Mucosal neuromas are present in MEN2B, Cowden syndrome, and Bannayan-Riley-Ruvalcaba syndrome[14]; however, molecular testing for the *RET* or *PTEN* mutation can differentiate them from FIL. Similar cutaneous findings are seen in infiltrating angiolipoma or facial angioma; however, these two lack the skeletal findings and mucosal neuromas of FIL. Lipomatosis can also be found in Proteus syndrome and encephalocraniocutaneous lipomatosis.[15] Unlike Proteus syndrome, FIL usually presents at birth and does not involve areas outside of the head and neck. Encephalocraniocutaneous lipomatosis, unlike FIL, manifests in the central nervous system.

TREATMENT

While no definitive treatment exists for FIL, various forms of surgical treatment have been attempted with limited success owing to high recurrence rates and surgical risk to important anatomic structures. Earlier literature favored aggressive surgical treatment,[2,3] but recent articles have recommended a more conservative approach.[7] We also recommend a conservative surgical approach with treatment only for symptomatic cases such as sleep apnea, speech dysfunction, and gross cosmetic deformity. We also emphasize the importance of a multidisciplinary approach involving medical, surgical, genetic, dental, speech, developmental, and counseling specialties.

CONCLUSIONS

Facial infiltrating lipomatosis is a rare disorder that causes hemifacial enlargement. As a result, it can be confused with other disorders, in particular, hemifacial hyperplasia. A combination of specific findings on physical, radiological, and histopathological examinations and molecular testing can aid in diagnosis. Facial infiltrating lipomatosis is characterized by (1) unilateral hemifacial enlargement, (2) presence at birth, (3) hypertrophy of underlying bone, (4) lipomatous infiltration of muscle and soft tissue with mature adipocytes, (5) mucosal neuromas, (6) absence of malignant characteristics, and (7) tendency for recurrence after resection. Of these, histopathological findings of mature adipocyte infiltration of soft tissue and the presence of mucosal neuromas are the most specific features. Therefore, when FIL is suspected, biopsy is recommended. Because of frequent recurrence, we recommend conservative surgical management for functional or cosmetic problems.

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