Focal dermal hypoplasia: A novel finding in disguise

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ABSTRACT

Focal Dermal Hypoplasia (FDH) or Goltz-Gorlin syndrome is an unusual X-linked dominant syndrome characterised by anomalies of both ectodermal and mesodermal structures.

We present a case report on the management of a 58 year old Caucasian male with Focal Dermal Hypoplasia. This report describes an additional clinical manifestation of an intraosseous mandibular lipoma, which has not been previously described in cases of FDH. Intraosseous lipomas in the head and neck region are reported in only seventeen cases in isolation of any associated syndrome.

Diagnosis was hindered due to similitude with Nevroid Basal Cell Carcinoma Syndrome (Gorlin-Goltz Syndrome) which despite similar nomenclature, is an exclusively separate condition

This novel finding encourages clinicians to consider unusual differential diagnoses in such cases and highlights the importance of avoiding eponyms to prevent confusion with similar conditions

1. Background

Focal dermal hypoplasia (FDH), or Goltz-Gorlin syndrome (MIM no.305600) is a rare X-linked dominant disorder syndrome characterised by anomalies of both ectodermal and mesodermal structures. Although the first official reports by Goltz, Peterson, Gorlin, and Ravits appear in 1962, it is thought that the earliest description of this condition as '*atrophoderma linearis maculosa et papillomatosis congenitalis*' could date back as early as 1921.^{1–3} There are 200–300 reported cases of FDH, although this is likely to be underestimated as many cases with milder features can go unrecognised.^{4,5}

FDH is associated with a mutation of the PORCN (porcupine homologue) gene located on Xp11.23 chromosome, which has variable expression.^{6,11} PORCN codes for a transmembrane endoplasmic reticulum protein, which allows signalling and secretion of Wnt proteins involved in embryonic tissue development.¹¹ The majority of mutations are single nucleotide substitutions or small deletions/insertions that can be identified through sequence analysis.⁹ De novo mutations occur in 95% of females and 100% of male patients with FDH, when there is no family history.^{5,8}

2. Clinical features

Clinical features vary depending upon the severity of FDH. Skin defects occur in 95% of FDH patients, with congenital dermal hypoplasia allowing impingement of adipose tissue on the epidermis, resulting in nodules overlying thin atrophic skin.⁵ It is debated whether

this feature is a primary dermis defect resulting in secondary fat herniation, or whether there is a primary developmental abnormality resulting in dermal hypoplasia and development of adipose hamartomas.^{7,10}

An overview of the craniofacial manifestations of FDH is outlined in Table 1.

3. Goltz-Gorlin syndrome versus Gorlin-Goltz syndrome

Nevroid Basal Cell Carcinoma Syndrome (Gorlin-Goltz Syndrome) is an autosomal dominant inherited disorder characterised by the presence of multiple Odontogenic Keratocyst, in addition to variable osseous, ophthalmic, neurological and cutaneous abnormalities.²⁵ Despite similarities in nomenclature to Goltz-Gorlin Syndrome (FDH), the two conditions are exclusively separate entities, despite both having significant craniofacial manifestations. Confusion between the two conditions is evident in the literature, where Manzi et al report a case of FDH whilst inaccurately describing Gorlin-Goltz Syndrome.¹³ For this reason, Gorlin suggests that avoidance of eponyms will help avoid misdiagnosis and confusion between the two conditions.³

4. Case report

This report discusses the case of a fifty-eight year old Caucasian male referred to Luton and Dunstable Oral and Maxillofacial Surgery department following an incidental finding of an asymptomatic radiolucency in the left mandible by his general dental practitioner. His

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Table 1
The facial and oral manifestations of FDH.^{9,10,14,17,18,19,20,21,22,24}

FACIAL	ORAL
facial asymmetry with mild hemihypertrophy	hypoplasia/atrophy of alveolar ridges
microstomia	high arched palate
underdevelopment of mandible	striations of palate (similar to skin lesions)
prognathism	absent/small uvula
jaw cysts	median cleft of tongue
prominent and pointed chin	hemihypoplasia of tongue
cleft lip and/or palate	long pointed deviated tongue
narrowed nasal tip and bridge	absence of labial sulcus
external ear deformities (thin, protruding and low set)	high mandibular and maxillary frenum
notching of nasal alae	additional frenum
microcrania	papillomas
sparse, brittle hair	hyperkeratosis of buccal mucosa
areas of alopecia on scalp	gingival hypertrophy
clouding of cornea	irregular spacing/crowding and tooth rotations
	malocclusion
	hypodontia of primary and permanent dentition
	microdontia
	supernumerary teeth
	teeth of variable size and shape (notched incisors)
	dysplastic teeth (enamel defects and subsequent caries)
	submerged teeth
	delayed tooth eruption

Fig. 1. Facial view demonstrating strabismus of the left eye, facial asymmetry, pointed chin and mandibular prognathism.

medical history included Focal Dermal Hypoplasia (diagnosed through sequence analysis revealing hemizygous mutation of the *PORCN* gene¹¹) with cryptochidism, hypogonadism and osteoporosis. His specific clinical manifestations of FDH included facial, dermatological and ophthalmic abnormalities associated with his condition (Figs. 1 and 2).

Extraoral examination revealed a firm bony swelling, predominantly of the left body of the mandible, with no overlying erythema or associated lymphadenopathy. Intraoral features included buccal and lingual bony expansion of the left body of mandible. Other dental abnormalities included microdontia and hypodontia restored with removable prostheses. Soft tissue examination revealed multiple

Fig. 2. Hyperpigmentation of the legs along the Lines of Blaschko.

Fig. 3. Preoperative Orthopantomogram showing multilocular radiolucency of the left body of the mandible.

intraoral papillomas.

An orthopantomogram (Fig. 3) radiograph revealed a large radiolucent lesion of the left mandible extending from the lower left canine region to lower left second molar with obvious septation and marked asymmetry of the mandible. A CT scan of the mandible suggested the lesion being consistent with the appearance of an Odontogenic Keratocyst (Fig. 4a–c).

The patient was consented for excision of the papillomas and enucleation of the lesion in the left mandible under general anaesthesia. Upon surgical exploration, it became obvious that this was not a cystic lesion as previously anticipated, but had the macroscopic clinical appearance of an intraosseous lipoma. A mucoperiosteal flap was raised to facilitate two bony access fenestrations, made anterior and posterior to the mental nerve. The friable material was excised with removal of some septal bone to facilitate access to the whole cavity.

Histopathological examination of the mandibular lesion revealed mature adipose tissue (Fig. 5) with no cellular atypia, in keeping with an intraosseous lipoma. Microscopic analysis of the papillomas confirmed squamous cell papilloma with no evidence of dysplasia or malignancy.

Postoperative healing (Fig. 6) was uneventful with a mild transient disturbance to the function of the left mental nerve. The patient remains under yearly review with no further complications reported.

5. Discussion

Intraosseous lipomas are benign tumours of the bone consisting of mature adipose tissue with no cellular atypia. They account for less than 0.1% of benign tumours of the bone.^{19–21} They present largely in the long bones and predominantly in the fourth and fifth decades of life,¹⁶ although a literature search reveals seventeen documented cases of intraosseous lipoma in the head and neck region in isolation of any associated syndrome, such as FDH.

The aetiology is unknown but they are generally accepted to be benign tumours of the medullary adipose tissue.²⁵ It is hypothesised

Fig. 4. Preoperative CT facial bones whiereports the lesion as a suspected Odontogenic Keratocyst a) Coronal view showing multilocular radiolucency of left mandible b) Sagittal view showing displacement of the inferior dental canal c) Axial view showing expansion of the left body of mandible.

they are formed due to trauma (possible tooth extraction), infection or infarction of the inferior dental artery. Lipomas can undergo secondary changes as a result of impaired blood supply and traumatic injury leading to infarction, haemorrhage and calcification. In this case,

trauma may not be the only factor in its formation. A defect causing abnormality and dysfunction of the mesodermal cells¹² (as seen in FDH) can result in differing degrees of calcification of the bone matrix, whereby hypo- or aplasia of bony matrix allows development of naevoid ectopic fat, especially in areas of decreased bone density^{12,4,23}. It is interesting to note that adipose hamartomas are an established cutaneous clinical feature in FDH, and would suggest that further cytogenic studies are required in this field to establish whether lipomatous neoplasms of the skeleton may also be associated with chromosomal abnormalities, such as those seen in FDH.²⁰

Intraosseous lipomas are benign tumours and are usually asymptomatic for many years and can present on routine radiographs as an incidental finding or as a result of pain, swelling or paraesthesia. In the head and neck, surgical intervention is dictated by the degree of facial disfigurement, or symptoms such as compression of the inferior dental nerve when they enlarge or risk of pathological fracture.

Radiologically they appear as radiolucent lesions with a well corticated outline. The central lesion may appear with some radio-opacities due to fatty necrosis and calcification.²⁵

CT or MRI can be useful in diagnoses by detection of fat within the lesion, but this is dependent on the stage of an intraosseous lipoma and calcification, so may not be detected.

The clinical and radiological features of an intraosseous lipoma are similar to those of other odontogenic tumours (cemento-osseous lesions, calcifying epithelial odontogenic tumours, solitary bone cysts, intraosseous haemangiomas and odontogenic myxomas), including the Odontogenic Keratocyst. The similarities in nomenclature of Goltz-Gorlin and Gorlin-Goltz can mislead clinicians into misdiagnosing the lesion as an Odontogenic Keratocyst which is reported in Gorlin-Goltz Syndrome. For this reason and to reduce future diagnostic confusion, it is suggested that the preferred names Focal Dermal Hypoplasia (Goltz Gorlin) and Nevroid Basal Cell Carcinoma Syndrome (Gorlin-Goltz) are used in a clinical setting.

Intraosseous lipomas, being such rare tumours, are seldom considered in the differential diagnosis of radiolucent lesions within the facial skeleton. They can often be misdiagnosed as aggressive lesions and diagnosis is confirmed histopathologically. The histopathological features of intraosseous lipomas can be subdivided using Milgram's classification. Stage 1 lesions consist of sheets of adipocytes without distinctive abnormal cytologic features (normal fat). In stage 2, the lesions are composed partly of viable adipocytes and partly of fat necrosis and calcification. In stage 3, the lesions exhibit extensive fat necrosis, calcification, cyst formation, and reactive peripheral or intralesional ossification, with occasional aggregates of viable fat cells.¹⁵

Whilst there is no evidence of malignant transformation in intraosseous lipomas, histopathological analysis should be used to correlate clinical findings and exclude malignancies including liposarcoma. Treatment is usually limited to simple conservative surgical excision. They usually do not recur after surgical removal, although removal can be complicated due to adherence to local adjacent tissues.

Multidisciplinary patient management in conjunction with a geneticist can aid the Oral and Maxillofacial team to identify and appropriately manage patients with unusual genetic syndromes.

6. Conclusion

This is the first reported case of an intraosseous lipoma in FDH, a phenomenon rarely seen in the head and neck. Whilst it is suggested that lipomatous lesions of the skeleton may be an addition to the commonly accepted adipose hamartomas that arise within the dermis, further corroboration with genetic studies is clearly needed. An important learning point is to avoid eponyms in conditions with similar nomenclature to reduce the incidence of misdiagnosis.

Fig. 5. Histopathology of lesion showing mature adipose tissue consistent with a lipoma.

Fig. 6. Postoperative orthopantomogram (15 months) demonstrating bony healing of left mandible.

Conflict of interest

None.

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