Congenital Granular Cell Tumour - Case Report and Review of Literature

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Abstract

Rationale: Congenital orofacial swellings in neonates are mainly limited to vascular malformations and neuroectodermal benign tumours. Congenital granular cell tumour (CGCT) is a rare condition affecting neonates with a prevalence rate of 6 in 1 million. Our report provides a brief review of diagnosis and management. **Patient Concern:** A 4-day-old female neonate was brought in with the chief complaint of a single, lobulated mass protruding from the right side of the oral cavity. The inability to achieve lip seal and suckling resulting in feeding problems was the primary concern. **Diagnosis and Treatment:** Surgical excision of the lesion was carried out under general anaesthesia. Resected mass was confirmed to be a CGCT upon histopathological evaluation. **Outcome:** One-year follow-up showed satisfactory healing with no evidence of recurrence. **Take-away Lesson:** Ultrasonography and other imaging modalities help in differentiating it from vascular malformations. Simple surgical excision suffices to treat the condition.

Keywords: Congenital granular cell tumour, congenital tumours, S-100

Introduction

Congenital granular cell tumour (CGCT) is a rare benign tumour with a characteristic appearance of a proliferative pedicled, soft-tissue outgrowth associated with the pre-maxilla, alveolus and palatal region. It is synonymously known as gingival granular cell tumour (GCT), congenital epulis, congenital myoblastoma[1] or Neumann's tumour as it was first described by German Pathologist, Dr. Franz Ernst Christian Neumann in 1871.[2] Being an uncommon tumour of infancy, CGCTs are generally solitary and pedicled masses, measuring in size from a few millimetres to as large as 7.5 cm.[1] Multiple CGCTs have been reported only in 17% of cases.[1]

The aetiology is unknown and was correlated to the hormonal imbalance of the mother leading to a female-to-male ratio of 8:1 and maxilla-to-mandible ratio of 3:1. Clinically, CGCT is reported to regress spontaneously in a few days to weeks, leaving a sessile mass.

In our case scenario and literature review, various diagnostic modalities and literature were performed. Initial clinical and radiographic assessment [computed tomography (CT) and ultrasonography (USG)] was done to rule out haemangioma, teratoma or a bony neoplasm. Once ruled out, the lesion was managed with surgical excision under general anaesthesia.[3]

Case Report

A healthy 4-day-old female neonate with no antenatally diagnosed anomaly was clinically detected with a mass protruding from the right side of the mouth at birth with no systemic complication. Problems with establishing a lip seal and breastfeeding/suckling resulted in an episode of hypoglycaemia. Upon clinical examination, the soft-tissue mass was pale red, lobulated, with irregular boundaries, pedunculated, measuring approximately 5 cm × 3 cm in size, extending extra-orally from the right commissure of

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the oral cavity with a wide attachment at the right anterior palate [Figure 1]. Tongue movements were unrestricted. There were no other apparent orofacial abnormalities or maternal history.

USG revealed a solid mass arising from the right alveolar ridge with significant parenchymal arterial and venous vascularity along with a stalk [Figure 2]. No gross hypoechogenicity was noted. Colour flow Doppler imaging was suggestive of an intensively vascular lesion with multiple branching of arteriovenous channels.

CT scan of the patient under sedation revealed a hypodense soft tissue lesion in the anterior region of the maxilla with no vascular abnormalities [Figure 2]. With a differential diagnosis of CGCT, the patient was taken up for surgical excision under general anaesthesia. The stalk/pedicle of the lesion was secured with 2-0 silk suture and excision was carried out in toto using electrocautery [Figure 3a-d].

The post-operative recovery was uneventful with good healing of the surgical site [Figure 4]. The excised lobulated specimen measuring 3.5 cm × 2.5 cm × 1.5 cm on histopathology revealed focal acanthosis with stratified squamous epithelium. Subepithelial tumour cells were large polygonal cells with abundant granular eosinophilic cytoplasm and a prominent vascular stroma. The patient was kept under regular follow-up for 12 months with no signs of recurrence observed [Figure 5].

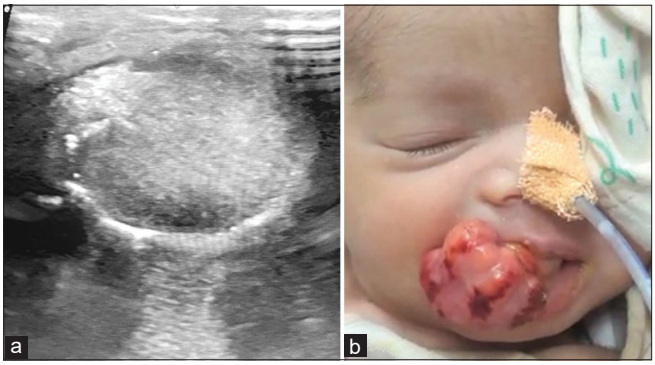

Figure 1: (a) Pre op USG of the lesion, (b) Clinical appearance of the lesion

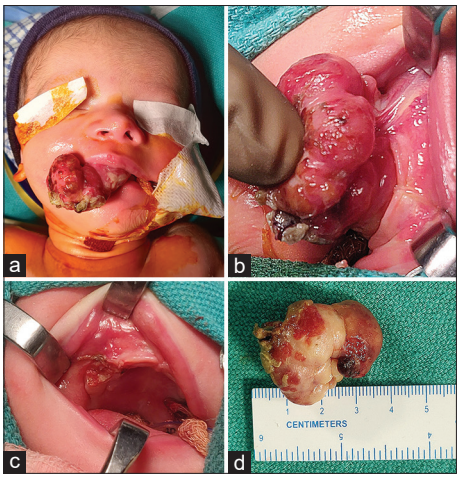

Figure 3: Intra-operative picture (a and b) Lesion, (c) post-excision (d) excised lesion

Discussion

In 285 reported cases, CGCT being a benign tumour associated with the jaw was reported along with a 10% occurrence of intraosseous cases of arm[4,5] and other extra-alveolar sites. Aetiology being unknown like in our case, the hypothesis correlating with hormonal imbalance was correlated by injecting oestrogen in the uterine cervix of newborn mice.[6] However, neither oestrogen nor progesterone hormonal receptors were detected in the CGCT. CGCT is usually diagnosed at birth. Use of 3D USG and magnetic resonance imaging (MRI) (low homogeneous T2 intensity compared to cerebral parenchyma) can prenatally diagnose CGCT mostly by the third trimester of pregnancy (as early as 26 weeks of pregnancy).[7] Enlarged CGCT can cause mechanical obstruction of the oral cavity secondary to swallowing resulting in polyhydramnios prenatally with two such cases being reported. Early diagnosis can help in the psychological preparation of the family for surgical intervention. As Doppler USG remains the gold standard diagnostic tool compared to MRI for diagnosis and confirming pre-natal and post-natal CGCT, it was one of the diagnostic modalities in our case.

CGCT-associated functional complications such as hypoplasia of incisors, midface hypoplasia, feeding difficulties and breathing are to be managed immediately.[6] In our case,

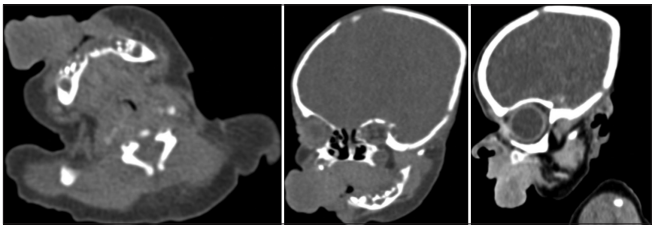

Figure 2: Pre-operative non-contrast computed tomography of the head and face

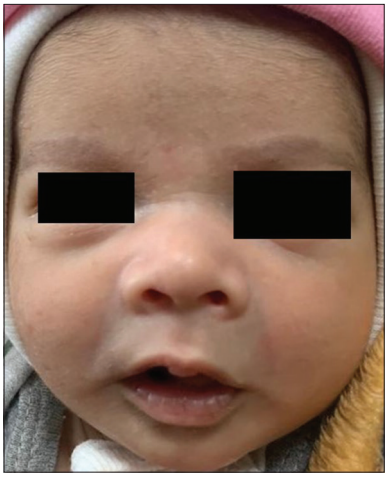

Figure 4: Post-operative picture after 6-month follow-up

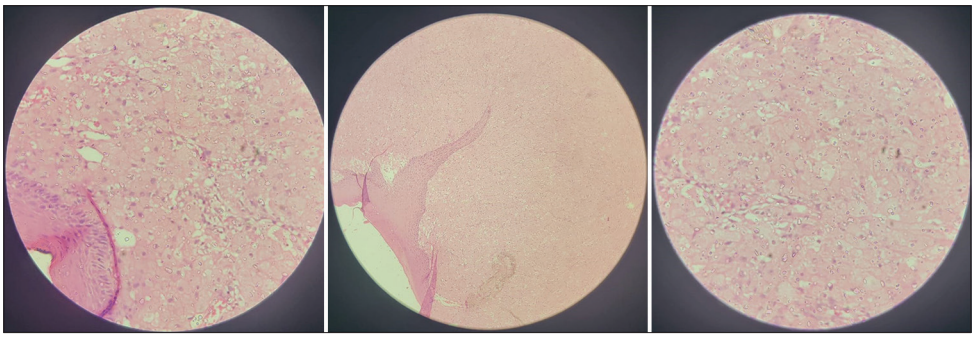

Figure 5: Photomicrograph of the histopathological appearance of the lesion

feeding was hampered and was the primary concern. Depending upon the size of the lesion, treatment modalities were reported in the literature varying from conservative management to surgical excision. Reports of spontaneous regression and the absence of recurrence with incomplete resection further support this theory. Smaller lesions can be treated conservatively to avoid unnecessary surgery. Since there have been no cases of recurrence even after incomplete excision of the tumour,[5] we planned for surgical excision of the lesion under general anaesthesia, and the prognosis in CGCT is favourable.

The histological classification of lesions in the neck-and-head region established by the WHO in 2005[8] classified CGCT as a benign tumour consisting of eosinophilic cells containing granules in the cytoplasm and mainly presenting in the alveolar region.

It characteristically demonstrated a flattened or attenuated surface epithelium lacking rete ridges with an underlying proliferation of large cells possessing an eosinophilic cytoplasm and round-to-oval nuclei.

The resultant immunohistochemical profile of CGCT cells is positive for vimentin, neurokinin-1 receptor (NK-1) (NK1 receptor)/C3, neuron-specific enolase S-100, NGFR/p75, inhibin-alpha and PGP 9.5. This does not confirm any particular cell type for the histogenetic origin of CGCT but may rather reflect a local metabolic or reactive change, providing supporting evidence that the lesion is non-neoplastic.

In addition, the granular cells were non-reactive for CGCE S-100, laminin, CD34, CD68, nerve growth factor receptor (NGFR)/p75, inhibin-alpha, chromogranin, desmin, keratin, smooth muscle actin, CD31 and glucose transporters (GLUT)-1,[9] which further contributes to the distinction between a CGCT and the adult GCT [Table 1].

Ki-67 protein and proliferating cell nuclear antigen (PCNA) labelling indices were also estimated for further differentiating GCT from CGCT. In our case, the Ki-67 was 13.2% and PCNA was 36.8% suggestive of non-neoplastic origin [Table 2]. For normal gingiva, it is less than 5%, while for plaque-induced gingivitis, it is about 10%.

Some CGCTs may demonstrate non-classical features, such as fibrosis and spindle cell proliferation, fibrosing pyogenic granuloma, infantile myofibromatosis, rhabdomyoma, rhabdomyomatous choristoma or juvenile xanthogranuloma,[10] which were absent in our case.

Pre-natal differential diagnosis includes rhabdomyosarcoma, GCT, oral teratoma-epignathus, lymphatic malformations, dermoid cyst, haemangioma, lymphatic malformations and melanotic pigmentation neuroectodermal tumours.[10]

Table 1: Adult granular cell tumour versus congenital granular cell tumour[8,9]

Adult (GCT)	Congenital epulis (CGCT)
Occurs in adults between 20 and 60 years of age	Occurs in newborn
Involves multiple organs	Only in gum pads
A malignant variant is reported	Does not recur and has no malignant potential
HP: Pseudo-epitheliomatous hyperplasia present	Absent
HP shows more conspicuous nerve bundles	Less conspicuous nerve bundles
HP shows less vascularity	More vascularity in a plexiform arrangement
GCT origin from Schwann cells was widely accepted due to the presence of Leu-7, peripheral nerve myelin P0/P2 proteins, and 75 kDa NGFR-IR/trk gene	Hypothetically, the origin of CGCT was correlated with histocyte, myogenic, and mesenchymal cell origins (PGP9.5 protein), but no consensus has been reached
Immunohistochemistry study expresses S-100 protein markers	Negative for S-100 protein
Recurrence 8%	No recurrence

GCT: Granular cell tumour, CGCT: Congenital granular cell tumour, HP: Histopathology

Table 2: Differential diagnosis based on histopathology[10]

Differential diagnosis	Correlating feature	Differentiating features
Soft-tissue odontoma	Sheets of granular cells	Loose myxoid stroma with enamel, dentine and pulpal elements
Neuroectodermal tumour of infancy: If lacking its typical melanin pigment	Similar nesting pattern and age at presentation	Peripheral large cells (which stain for S-100, HMB-45 and cytokeratin) and small neuroblastic cells (which stain for synaptophysin, GFAP and S-100)

These masses can be distinguished based on their location and sonographic appearance. Oftentimes, teratomas have calcifications. Haemangiomas can have a solid or cystic appearance and develop outwardly from subcutaneous tissues. Its histological similarities to the GCT/myoblastoma (GCT), which develops in adults at several intraoral sites, including the tongue, have made it more difficult to make an appropriate diagnosis.

Conclusion

With the aetiology being unknown and clinical features resembling GCT, a thorough clinical and radiological workup needs to be done before management. Surgical excision with regular follow-up remains the gold standard treatment modality like in our case.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's parent(s) has given her consent for her images and other clinical information to be reported in the journal. The patient's parents understand that her name and initial will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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