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Prenatal diagnosis and multidisciplinary management: a case report of congenital granular cell epulis and literature review

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Abstract

Congenital granular cell epulis (CGCE) is a rare benign soft tissue lesion that usually originates from the neonatal gingiva and can lead to difficulty in breathing and feeding upon birth. This current case report describes a female newborn with a gingival mass that was identified by prenatal fetal ultrasonography. At birth, the oral mass was observed to protrude from the mouth, which adversely affected feeding. The lips could not be closed. The breathing was unaffected. Through a multidisciplinary team approach involving several healthcare professionals, the mass was successfully removed under general anaesthesia during an uncomplicated surgical procedure. Postoperative histopathological examination confirmed that the mass was a CGCE of the newborn. The infant recovered well after the operation.

Keywords

Newborn, congenital granular cell epulis, prenatal diagnosis, multidisciplinary management, case report

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Introduction

Congenital epulis is a rare benign tumour with an incidence of 0.0006%.[1] It is also known as congenital granular cell epulis (CGCE) and was first reported by Neumann in 1871.[2] The lesions are often similar in colour to oral mucosa, pedicled or unpedicled, range in size from a few millimetres to >10 cm, and they are more common in female newborns (male:female ratio, 1:8∼10).[3] CGCE usually occurs on the gingival mucosa of the maxillary or mandibular anterior alveolar ridge (maxilla:mandible ratio, 3:1).[4] It is not usually associated with deformities of dentition and other systems.[5] CGCE mostly presents as single lesions, but approximately 10% are multiple lesions.[6] Large or multiple tumours can lead to airway obstruction and feeding difficulties. At present, there have been rare reports of recurrence or malignant transformation of CGCE.[7] Histologically, the tumours are characterized by large and round polygonal cells, rich eosinophilic granular cytoplasm and round or oval mild basophilic nuclei.[3] Several hypotheses about the origin of congenital gingival tumours have been proposed, including muscle cells, nerve cells, fibroblasts, tissue cells and mesenchymal cells, but no consensus has been reached.[3] This lesion is similar to adult granulosa cell tumour (GCT), but they are solid tumours originating from different tissues, and there are differences in epidemiology and immunohistochemistry.[8]

Congenital granular cell epulis is usually diagnosed at birth and prenatal diagnosis is not common, but there are also reports of intrauterine prenatal diagnosis by three-dimensional ultrasound and magnetic resonance imaging (MRI), mostly limited to the third trimester of pregnancy (as early as 26 weeks of pregnancy).[9] The intrauterine diagnosis of large CGCE can provide guidance in choosing the mode of delivery, as large lesions may affect normal vaginal delivery and require caesarean section.[10] In addition, identifying tumours during the fetal period allows families to prepare psychologically for neonatal surgery. Although several cases of mass regression have been reported,[5] the generally accepted preferred treatment is still surgical resection under general or local anaesthesia. Children with respiratory and digestive tract obstruction should be operated on as soon as possible after birth.[11] The multidisciplinary cooperative management of oral and maxillofacial surgeons, neonatal paediatricians, radiologists, anaesthesiologists, otorhinolaryngologists, obstetricians and gynaecologists can optimize the diagnosis, treatment and prognosis of children.[9] Knowledge of this pathology helps in better diagnosis and treatment, which lead to a better quality of life for the affected children and help to return confidence and emotional stability to parents.[12]

Case report

A 29-year-old female (G3P2 + 1) conceived naturally. On 29 November 2020, fetal ultrasound at 30 gestational weeks of pregnancy in Sichuan Provincial Maternity and Child Health Care Hospital, Chengdu, Sichuan Province, China revealed a gingival mass. No abnormalities were found in other systems. Amniocentesis karyotype and chromosome microarray analysis showed no abnormality. At 30 + 4 gestational weeks, a fetal head MRI examination showed a mass between the upper and lower lips of the fetus. It was approximately 1.6 × 1.5 cm in size, part of the edge was smooth and the specific properties were unknown (Figure 1a).

At 14:46 on 3 February 2021, a caesarean section was performed in Jinniu District Maternity and Child Health Hospital, Chengdu, Sichuan Province, China because there was 'no desire for vaginal trial labour

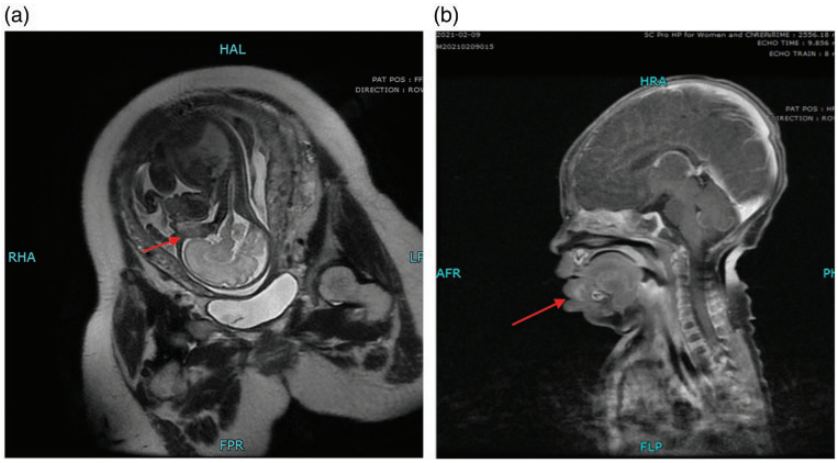

Figure 1. (a) Fetal magnetic resonance imaging showing a T2-weighted image of the fetal profile, in which an ovoid T2-hyposignal mass originating from the mandibular alveolar mucosa can be clearly seen (arrow). (b) Magnetic resonance imaging after birth. On the right side of the lower gingiva, there was a kind of round local convex mass with a smooth edge and uneven signal.

in patients with a scarred uterus'. The birth weight was 3650 g and the Apgar score was 10-10-10 in 1-5-10 min. After the child was born, the obstetrician found that a $2 \times 2 \times 2$ cm pink lump could be seen in the lower gums, protruding from the mouth. The lips could not be closed. The tumour did not break and bleed (Figure 2a). The rest of the newborn's systems were normal upon examination. There was no shortness of breath or cyanosis, no moaning, no reduced crying and movement, no fever, no screaming, no irritation or convulsion, and no other system manifestations. The newborn with the 'gingival lump' was transferred to the Neonatal Intensive Care Unit, Sichuan Provincial Maternity and Child Health Care Hospital and milk was fed with a gastric tube within 1 h after birth.

Four days after birth, the blood examination showed that the tumour markers were elevated (alpha-fetoprotein: 56080.00 IU/ml; cancer antigen 199: 42.45 U/ml) and the other blood tests were normal. Two days after birth, lateral digital radiography examination of the head showed that there was no obvious abnormal high density shadow in the soft tissue in the oral cavity and in the soft tissue protruding from the oral cavity. Colour ultrasound examination showed that the lower gingiva was slightly to the right and showed a heterogeneous low echo of approximately $1.9 \times 1.4 \times 1.6$ cm. The boundary was clear, the shape was regular, the flake echo was slightly higher and no obvious blood flow signal was found. Five days after birth, an MRI scan showed that there was a round local protruding mass on the right side of the lower gingiva, with a smooth edge, approximately $1.6 \times 1.8 \times 1.3$ cm in size (anterior and posterior diameter $\times$ left and right diameter $\times$ upper and lower diameter), with uneven signal intensity, T1WI and T2WI signals, nodular watery signal shadow in the central area of the lesion, and progressive contrast enhancement in the solid part of the lesion (Figure 1b). No definite abnormal changes were found in the shape and signal of the adjacent structure, and no exact abnormal enhancement

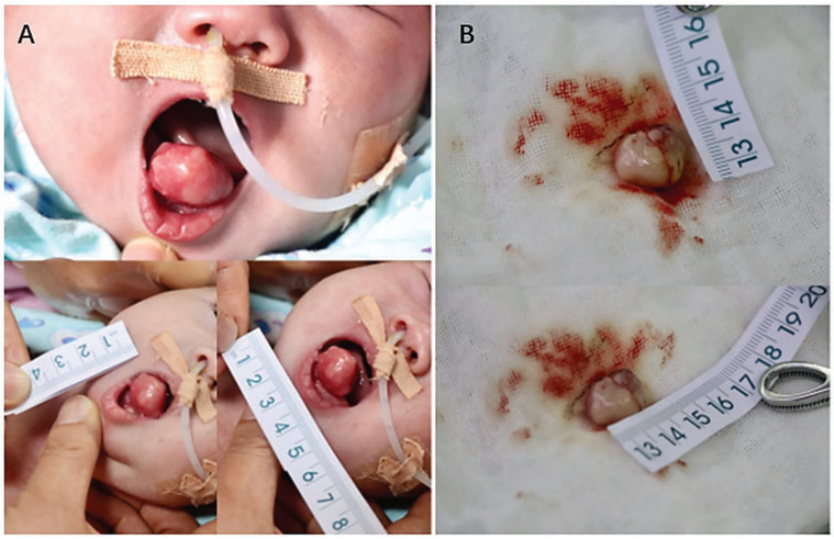

Figure 2. (a) Preoperative aspect of the tumour mass localized at the anterior part of the mandible. (b) Resected specimen at 19 days after birth following a lower gingival mass resection biopsy under general anaesthesia.

was seen in the enhancement. The lower gingiva was slightly to the right of the cystic-solid nodule, which was closely related to the right lower gingiva, and the remaining structure was clearly delineated. Considering benign lesions, a teratoma might have been possible.

On 22 February 2021, 19 days after birth, a lower gingival mass resection biopsy was performed under general anaesthesia. After the effect of general anaesthesia was induced, the infant was intubated through nasotracheal intubation and laid in the central position of the supine position. The gingival pedicled mass in the mandibular anterior tooth area was found, the size was approximately $2.5 \times 2.5 \times 2.0$ cm, the surface mucosa was intact, there was no redness and swelling and the movability was moderate. The mucous membrane of the normal tissue was incised outside the lesion, then the bone surface was incised whilst carefully protecting the deciduous tooth germ, so that the lesion could be completely removed. The mass was cut open and the section was solid, showing white fibrous tissue (Figure 2b). During the operation, the frozen section results showed congenital epulis (Figure 3a). After the operation, the infant was transferred to the ward with an endotracheal intubation balloon positive pressure ventilator and ventilated with normal frequency ventilation. The ventilator was removed smoothly the next day after the operation and milk was gradually fed combined with parenteral nutrition support. Five days after the operation, the stomach tube was removed and the patient was transferred to full oral feeding. The infant ate well and her body weight increased to the standard expected.

The results of paraffin sections of frozen tissues on 25 February 2021 suggested that the 'gingival mass' was a granular cell tumour, whilst the results of further immunohistochemical examination were awaited (Figure 3b). The immunohistochemical results of 3 March 2021 showed that the tumour cells were pan-cytokeratin (P-CK)

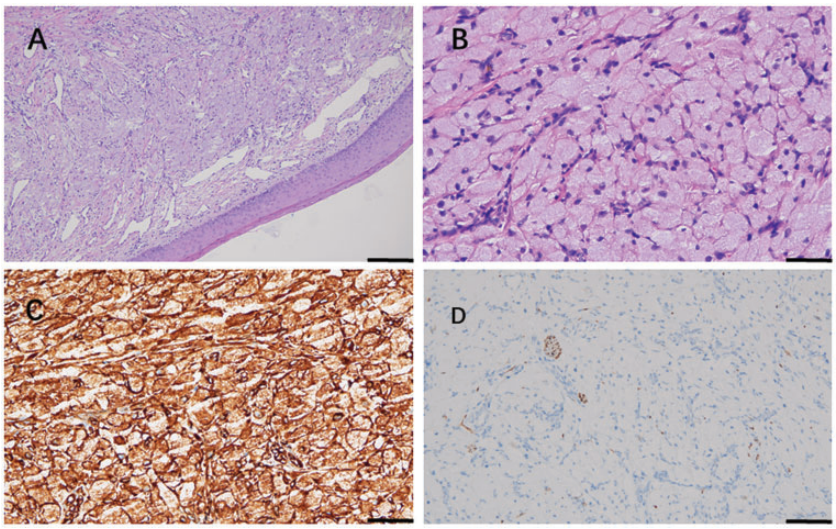

Figure 3. Representative photomicrographs of the resected tumour mass localized at the anterior part of the mandible: (a) low power view of the lesion shows a mass with overlying, thin squamous epithelium (haematoxylin and eosin [H&E], scale bar 200 μm); (b) the mass was characterized by proliferation of polygonal cells with eosinophilic, granular cytoplasm and eccentric, benign-appearing nuclei (H&E, scale bar 50 μm); (c) lesion cells were positive for vimentin immunostaining (scale bar 50 μm); (d) unlike granular cell tumour in adults, lesion cells of congenital granular cell epulis were negative for S-100 immunostaining; the S-100-positive cells in the image represent interstitial cells (scale bar 100 μm). The colour version of this figure is available at: http://imr.sagepub.com.

(–), Smur100 (S-100) (–), neuron-specific enolase (NSE) (–), calretinin (–), CD68 (–), vimentin (+) and specially stained periodic Acid-Schiff (PAS) (–). Combined with the morphology, immunophenotype and special staining, it supported the diagnosis of CGCE in this newborn.

The publication of this clinical information required the written informed consent of the infant's parents. The reporting of this study conforms to CARE guidelines.[13]

Discussion

Congenital granular cell epulis is a unique and rare benign lesion that occurs in the alveolar ridge mucosa of the jaw of the newborn.[1] Neumann first described this tumour in 1871 and since then several different names have been used, including congenital epulis, neonatal congenital gingival tumour, congenital granular cell tumour, congenital granular cell lesion and neonatal gingival granular cell tumour.[14–16] In 2005, the histological classification of head and neck lesions by the World Health Organization identified CGCE as a benign tumour composed of eosinophils containing granules in the cytoplasm, mainly in the gingival region.[17] According to this definition, many countries refer to a mass that appears in the gingival mucosa at birth and has the histological characteristics of granulosa cell tumour as CGCE. CGCEs are usually found in the maxillary gingiva, and the incidence ratio of maxillary gingiva and mandibular gingiva is approximately 3:1, while tongue and laryngotracheal involvement is rarely reported.[18–20] The incidence of this benign tumour in women is significantly higher than that in men (8∼10:1).[1,21]At present, the pathological mechanism of CGCE

remains unclear. Based on the sex preference of the incidence of CGCE and its intrauterine origin, some researchers speculate that the development of CGCE is closely related to maternal hormones, but it has not been confirmed by research.[3] The infant described in this current case report was a female newborn with a mass in the lower gingival mucosa, which was a relatively rare site.

Prenatal diagnosis of CGCE is uncommon. It has been reported that most of the cases of prenatal diagnosis were limited to the third trimester of pregnancy (no earlier than 26 weeks of pregnancy).[22–25] Imaging examinations usually indicate pedicled masses originating from alveolar mucosa (mainly maxilla). Larger ones can lead to oral mechanical obstruction, leading to prenatal polyhydramnios and postpartum feeding or breathing problems. The differential diagnosis of prenatal oral masses should include teratoma, haemangioma, lymphatic malformation, cephalocele, dermoid cyst and other benign and malignant soft tissue masses.[22] Doppler ultrasound imaging can narrow the scope of differential diagnosis by showing the blood supply vessels entering the mass through the pedicle,[23] but the prenatal and postpartum ultrasound examination in this current case did not show a blood flow signal entering the mass. Three-dimensional ultrasound can better evaluate fetal facial anatomical abnormalities than two-dimensional ultrasound; and it can provide better information about the appearance of the tumour and its relationship with the respiratory tract, making prenatal counselling more convenient.[24]MRI helps to narrow the scope of differential diagnosis and evaluate airway obstruction, thus helping to determine the type of delivery (caesarean section versus vaginal delivery). As previously reported,[25,26] the mass shows low and uniform T2 signal intensity compared with the brain parenchyma on prenatal CGCE, which was consistent with the MRI findings of the fetal head in this current case. After birth, the tumour tissue had a slight T1 high signal edge with a muscle signal on T1-weighted image. After gadolinium enhancement, there may be contrast enhancement around the tumour, but this is not found in all cases.[25,26] In this current case, postpartum MRI showed T1WI, T2WI and other signals, a nodular watery signal shadow was seen in the central area of the lesion, and the solid part of the lesion showed progressive enhancement on a contrast-enhanced scan, so it was possible that it was a teratoma. The imaging findings of CGCE are heterogeneous and the diagnosis indicated by the imaging features of the mass is often inconclusive, so the diagnosis mainly depends on histopathological examination.

Histologically, CGCE is characterized by large and round polygonal cells, rich eosinophilic cytoplasm and round or oval mild basophilic nuclei.[3] Several hypotheses about the origin of congenital gingival tumours have been proposed, including muscle cells, nerve cells, fibroblasts, tissue cells and mesenchymal cells, but no consensus has been reached.[3] The main differential diagnosis of CGCE is GCT as they have significant histological similarities, so it is difficult to distinguish them by the appearance of cells under a light microscope.[8,21] However, studies have shown that the epidemiological characteristics of the two lesions are different: GCT is common in adults, while CGCE occurs only in newborns.[21] They also show different immunohistochemical characteristics: GCTs are believed to originate from Schwann cells in the neuroectoderm, while CGCEs are speculated to arise from stroma or neuroectoderm.[21] Immunohistochemical staining of S-100 is often helpful to distinguish between the two (positive for GCT, negative for CGCE).[3,8,21] The immunohistochemical results for the current case

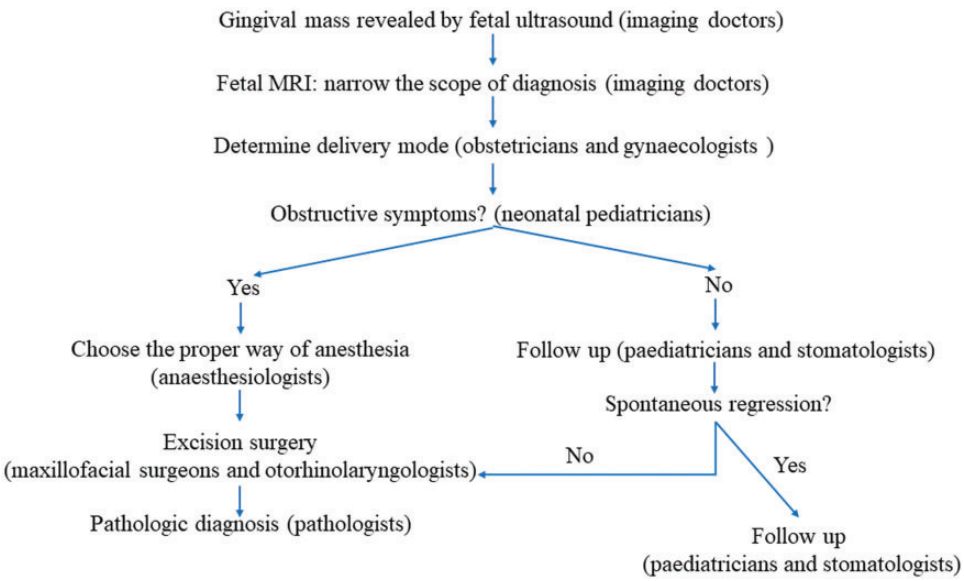

Figure 4. Multidisciplinary management flow chart of congenital granular cell epulis. MRI, magnetic resonance imaging.

showed P-CK (–), S-100 (–), NSE (–), calretinin (–), CD68 (–), vimentin (+) and specially stained PAS (–), which supported the diagnosis of CGCE in newborns.

Although prenatal diagnosis often fails to determine the specific nature of oral masses, the identification of fetal tumours remains clinically important because it can help clinicians to develop an intervention plan in advance with multidisciplinary cooperation. It also allows families to be psychologically prepared for neonatal surgery. Although several cases of CGCE self-regression have been reported,[5] the incidence rate is very low (eight in more than 200 cases, follow-up duration ranged from 10 months to 5 years). It is recognized that surgical resection is the first choice of treatment. For children with obstructive symptoms, it should be carried out as soon as possible. General anaesthesia is recommended for lumpectomy, but local anaesthesia is also a clinical choice when the mass is small or when the mass affects intubation. If a lesion is detected during pregnancy, it is also possible to remove it during delivery, which eliminates additional procedures such as anaesthesia and intubation, and provides a free airway and unobstructed oral cavity immediately after birth,[27] but it has not been widely used in the clinic. At present, there are rare reports of malignant transformation and recurrence of CGCE after resection, so there is a tendency for narrow resection and no need for radical resection to minimize the risk of destruction of the inferior alveolar bone and developmental tooth buds.[28] For those patients that do not suffer from obstructive symptoms, ongoing follow-up can be undertaken with elective surgery planned according to the nature of the CGCE (no malignancy, self-regression and no recurrence). The choice of when to subsequently excise the lesion should be decided by a multidisciplinary team of healthcare

professionals that includes the anaesthetists that can assess the safety of anaesthesia in newborns and infants.

In summary, CGCE begins in the fetal period and can affect the route of fetal delivery. Children with respiratory and feeding obstruction need active surgical treatment shortly after birth. Prenatal–postpartum integrated diagnosis and treatment programmes require the cooperation of a multidisciplinary team of healthcare professionals that includes imaging doctors, obstetricians, gynaecologists, neonatal paediatricians, oral and maxillofacial surgeons, otorhinolaryngologists, anaesthesiologists and pathologists to ensure the safety of children (Figure 4). As shown by the diagnosis and treatment of this current case, improving awareness of the disease in various hospital departments and increasing multidisciplinary communication and cooperation will certainly optimize the clinical diagnosis, treatment and prognosis of such cases.

In conclusion, a rare case of CGCE was herein reported. Prenatal imaging examination showed a tumour of the anterior gingival margin of the fetus, which was resected under general anaesthesia 19 days after birth. The nature of the tumour was confirmed by immunohistochemistry. Under multidisciplinary management, the child had a good prognosis after surgery. Although this lesion has been reported for more than 100 years, because of its rarity, further information on the cellular origin, pathogenesis and prenatal diagnosis is required.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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