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Giant Epignathus Teratoma Discovered at Birth: A Case Report and 7-Year Follow-Up

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Teratomas are tumors composed by tissues derived from the three germ cell layers, and they are relatively uncommon in head and neck. The term epignathus has been applied to teratomas from the oropharynx. This paper reports the case of a giant epignathus teratoma discovered at birth, which was successfully managed and followed up for 7 years. A newborn boy presented a polypoid tumor mass exteriorizing through the mouth over a length of 9 cm, with some surface areas resembling skin and others exhibiting hair. Computed tomography showed that the mass arose deep from the left hemiface. Alpha-fetoprotein (AFP) levels were high (316,000 ng/mL). Surgery was performed and microscopic analysis confirmed the diagnosis of mature teratoma. Because of residual tumor and high AFP levels, the patient was submitted to chemotherapy, resulting in complete regression of the lesion and normalization of AFP levels. Surgical repair of a cleft palate was performed at 5 years of age. At 7 years of age, the patient was in good general health and showed no clinical signs of recurrence. Although epignathus is a rare condition, it should be diagnosed in the fetus as early as possible. Prenatal care provides unquestionable benefits, providing the early diagnosis of anomalies that can jeopardize the life of the fetus and contributing to the indication of cases that require treatment before birth.

Key Words: teratoma, epignathus, newborn, alpha-fetoprotein.

Introduction

The term teratoma is derived from the Greek word "teraton" (meaning monster) and designates tumors arising from pluripotent cells. These tumors are composed by multiple tissues derived from the three germ cell layers (ectoderm, endoderm and mesoderm). Despite variations in the maturation degree, these cells are able to differentiate into and compose identifiable tissues and organs (1–3). Teratomas, which exhibit a marked growth potential, are classified into four general types: (1) dermoid, which contains mesodermal and epidermal elements and is the most common type; (2) teratoid, which contains ectodermal, endodermal and mesodermal elements, but is poorly differentiated; (3) true teratoma, which contains elements of the three germ cell layers that differentiate into recognizable tissues and eventually form rudimentary organs; (4) epignathus, in which the germ cell elements are highly differentiated and form organs or limbs (1,4). However, the term epignathus has been used commonly to define a teratoma that arises from the oropharynx, especially the sphenoid, palatine and ethmoid bones (5).

The incidence of teratomas is 1:4,000 live births. The most common site of teratomas is the sacrococcygeal region, followed by the ovaries, testes, retroperitoneum and mediastinum (5). Only 2 to 9% teratomas occur in the head and neck, and malignant transformation is reported in less than 5% of these cases (6,7). Oral teratomas or epignathi are extremely rare and occur almost exclusively in childhood, usually neonates. In a series of 1,253 different types of teratomas, only six (0.47%) were classified as epignathus (8).

Epignathus occurs at a rate of approximately 1:35,000 to 1:200,000 in live births and has a slight female predominance (3:1) (5). This tumor may be small, interfering only with feeding, or may reach a large size, causing obstruction of the upper airways and consequent death of the newborn. Epignathus may cause multiple malformations and sequelae in the patients, particularly in the case where the tumor mass is between the palatine processes before the sixth week of gestation and grows markedly from the seventh to ninth week. It may prevent fusion of the nasal septum with the bilateral palatine processes, which results in cleft palate formation (4). Thus, treatment of this tumor is complex and requires multiple interventions by a multidisciplinary team (9).

This study reports the case of a giant epignathus teratoma discovered at birth, which was managed successfully and followed up for 7 years.

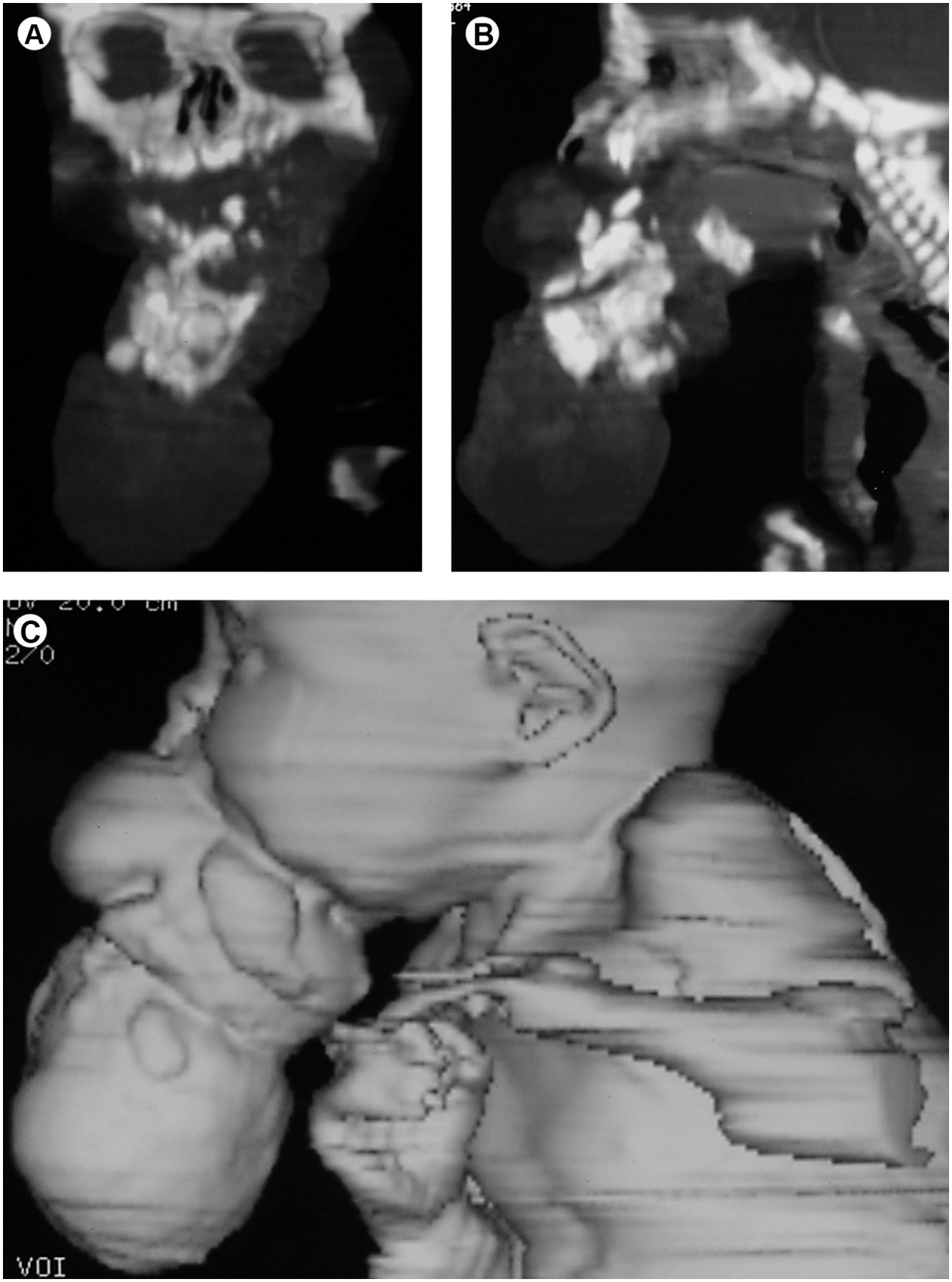

Figure 1. Pre-operative computed tomographic image of the epignathus teratoma. A: CT in coronal plane, showing multiple hyperdense images (with density similar to the mineralized tissue) located in the anterior-lower face. B: CT in sagital plane, showing a deep mass in face, infiltrating the palate and exteriorizing through the mouth. C: Three-dimensional CT image of the extensive tumor mass.

Case Report

The patient was a boy born by vaginal delivery after 40 weeks of gestation, with a birth weight of 2,395 g and prenatal jaundice. The first- and fifth-minute Apgar scores were 8 and 9, respectively. The family medical history revealed that the father had arterial hypertension and diabetes and the mother, primigravida and primipara, reported no health problem, but did not undergo adequate prenatal care, with only three visits at the beginning of gestation. The parents were not consanguineous.

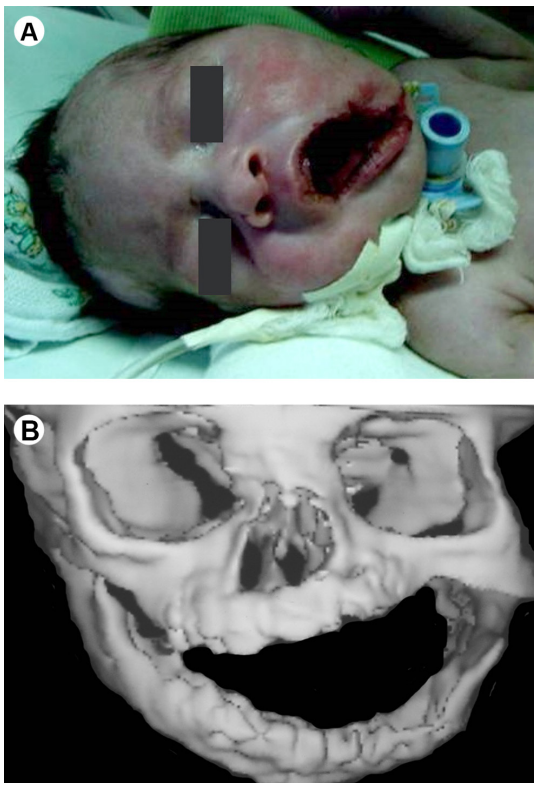

Figure 2. A: Child appearance in the immediate postoperative view. B: Three-dimensional CT of the immediate postoperative.

The infant had a polypoid tumor mass exteriorized through the oral cavity, with some surface areas resembling skin and others exhibiting hair. Clinical examination did not allow locating the site of tumor origin. The mass caused feeding problems, but there was no obstruction of the upper airways. Thus, intubation, tracheostomy nor ventilator support was required. The infant was fed by a nasogastric tube until the day of surgery.

Helical computed tomography of the face and trunk was performed and three-dimensional reconstructions were obtained. The tomography scans showed that the mass arose deep from the left hemiface, infiltrated and compromised the palate, occupied the entire oral cavity and exteriorized through the mouth over 9 cm (Figs. 1A–1C). For diagnostic complementation, beta-human chorionic gonadotropin (B-hCG) and alpha-fetoprotein (AFP) were evaluated. The concentration of the latter was 316,000 ng/mL.

Based on the diagnosis of teratoma, surgery was performed at 14 days of age under general anesthesia (Figs. 2A and 2B). Complete removal of the mass was not possible because of its depth. The surgical specimen measuring 10×7×6 cm and fixed in 10% formalin was sent for histopathological analysis. Microscopic analysis confirmed

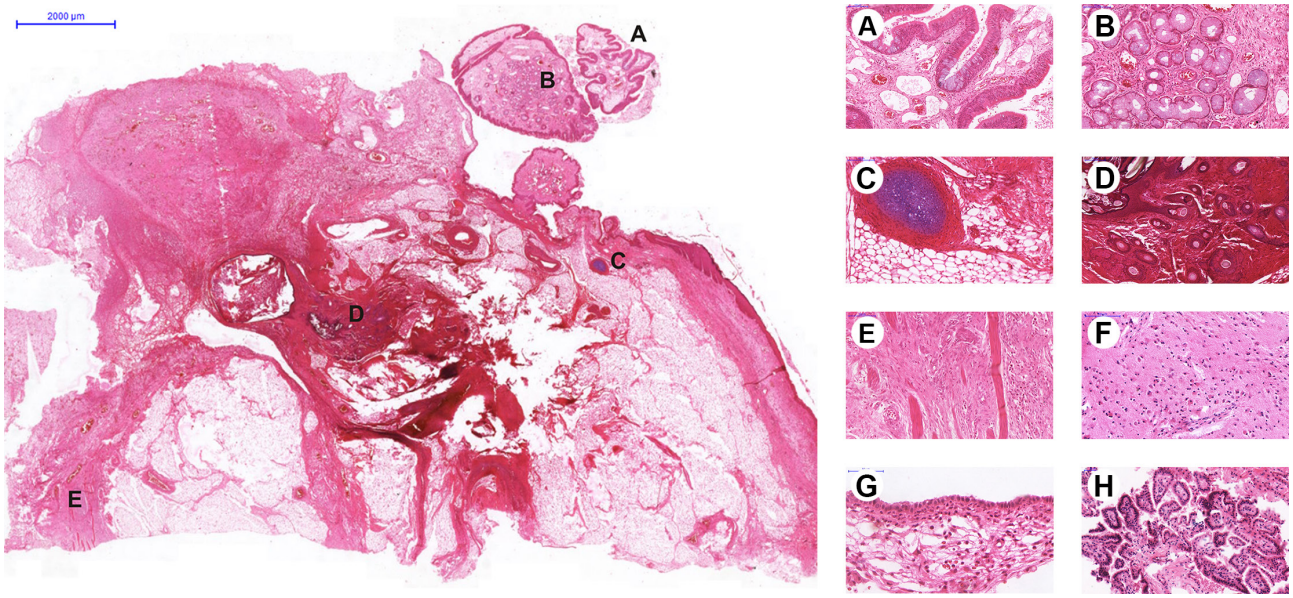

Figure 3. Histologic view of the tumor showing a mature teratoma. A: Ciliated columnar pseudostratified epithelium. B: Glandular elements. C: Cartilage island and adipose tissue. D: Epithelial differentiation with keratinized squamous epithelium and hair follicles. E: Stromal component with smooth muscle. F: Glial tissue. G: Simple cuboidal epithelium. H: Immature neuroepithelium (Panoramic Viewer - scale bars 2000 µm, 100 µm and 50 µm).

the diagnosis of a mature teratoma, with differentiation of tissues of ectodermal, mesodermal and endodermal origin. There was skin with its appendages, adipose tissue, mature nerve tissue, smooth muscle, cartilage and respiratory epithelium as well as other simple cuboidal and stratified epithelium. A small portion of the tumor contained tissues resembling the early stages of differentiation of skeletal muscle cells and neuroepithelium. No cellular atypia was observed in the specimen (Figs. 3A–3H).

On postoperative day 10, the patient was admitted to the intensive care unit because of sepsis and pneumonia. After 2 months of hospitalization, the patient recovered from the infectious process. Because of the residual tumor and high levels of AFP, the patient was submitted to chemotherapy (four cycles of 3 consecutive days consisting of 35 mg/m^2/day cisplatin, 100 mg/m^2/day VePesid and 2,500 mg/m^2/day ifosfamide). The four cycles of chemotherapy were administered for 5 months. After chemotherapy, the residual tumor underwent complete regression and AFP levels were within the normal range (96,000 ng/mL).

The child was followed up and was submitted to surgery for the correction of a cleft palate at 5 years of age. At 7 years of age, the patient was in good general health and showed no clinical signs of tumor recurrence (Fig. 4).

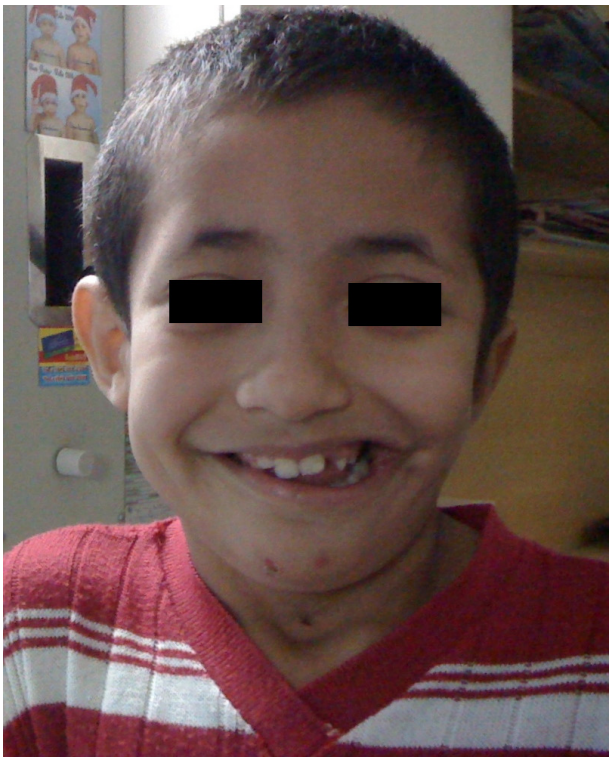

Figure 4. Clinical aspect of the child after 7 years of follow-up in excellent general condition, with minimal facial deformity.

Discussion

Oral teratomas are congenital tumors that develop in the region of the sphenoid, palate or pharynx, called Rathke's pouch. The origin of this tumor has been related to the abnormal migration of primordial germ cells arising from the mediastinum or hypothalamic regions (6), but its etiology remains unknown. For explanation, several theories have been proposed, such as traumatic implantation of skin fragments or mucous membranes in deep planes, lack of fusion of the somatic region during embryogenesis and implantation of pluripotent cells that subsequently grow in a disorganized manner (7). Furthermore, teratomas are associated with different chromosome abnormalities, including trisomy 13, ring X chromosome mosaicism, genetic mutations (HLXB9) and karyotype XXXXY (10–13). An association of epignathus with Aicardi syndrome and Pierre-Robin syndrome has also been reported (6).

A cleft palate, as observed in the present case, is the most common malformation associated with epignathus, which is caused by the formation of a teratoma during early stages of fetal life (between 8 and 12 weeks) before fusion of the palatal shelves. Tsai et al. (5) reported an association of epignathus with other malformations such as bifid tongue, bifid nose, and duplication of the pituitary gland. Teratomas can be classified as mature, immature and with malignant differentiation according to their histological degree of differentiation (7,14). Mature teratomas consist of a variable mixture of skin and its appendages, fat, smooth muscle, cartilage and different types of epithelium. Embryonic tissue may occur as neuroepithelium. If the latter accounts for most of the tumor, the teratoma can be characterized as immature (3). The present case was an extensive epignathus that mainly exhibited a mature histological pattern. However, small amounts of neuroepithelium were observed in focal areas.

Alpha-fetoprotein is a glycoprotein produced by the yolk sac and fetal liver until the 13th week of gestation. The serum concentration of AFP peaks in the 14th week, declines considerably until delivery and returns to normal levels within the first year of life (15). Normal neonatal AFP levels are poorly defined and are directly influenced by birth weight and the duration of gestation (16). In a series of 260 newborns, AFP levels ranged from 15,700 to 146,500 ng/mL (15).

In the present case, the patient had high AFP at diagnosis. This finding, together with the impossibility of completely removing the tumor and presence of foci of immature tissue, led to the decision of chemotherapy (cisplatin, VePesid and ifosfamide), which resulted in the regression of the residual tumor and normalization of AFP levels. Although AFP levels are commonly monitored in cases of teratoma affecting different sites, their relevance

in infantile facial teratomas remains a matter of debate. Nevertheless, AFP has been detected in high proportion of tumors and has been used as a marker of tumor recurrence and progression. Furthermore, normal serum AFP levels are associated with mature teratomas and levels above normal might be related to cases of malignant teratomas (14,17).

Malignant teratomas are rare and most often found in the sacrococcygeal region. The most common type is giant cell carcinoma (6,18). Jordan and Gauderer (19) reported that only 2.5% of teratomas in children are malignant compared to 69% in adults. Immature teratomas in childhood are only considered malignant in the presence of elements of malignant germ cells (usually a yolk sac tumor) and clinical characteristics compatible with malignancy, like metastases (6). No cellular atypia was observed in the present case and AFP levels returned to normal after surgery and chemotherapy. Thus, it was a case of mature teratoma.

Teratomas during intrauterine life may result in the development of polyhydramnios and death of the fetus. Prenatal care permits some measures to save the infant's life and to reduce sequelae. These procedures include ex-utero intrapartum treatment (EXIT) or resection of the tumor at the time of cesarian section and prior to cutting the umbilical cord, called operation on placental support (OOPS) (20,21). In the present case, it was not possible to perform any procedure before the birth of the patient. Since the mother did not undergo prenatal care, the diagnosis of the tumor was only made after birth. Fortunately, despite the great dimensions of the epignathus teratoma, the patient had no breathing difficulties and his feeding problems were solved with the use of a nasogastric probe.

In conclusion, although epignathus is a rare condition, it needs be diagnosed in the fetus as early as possible. Prenatal care provides unquestionable benefits, allowing early diagnosis of anomalies that may jeopardize the fetus' life and contribute to the indication of cases that require treatment before birth. This case is interesting since the patient was not diagnosed before birth and his treatment and follow-up were successful despite the high complexity of this condition. This was possible because the patient was followed up at a tertiary referral center by an experienced multidisciplinary team.

Resumo

Teratomas são tumores constituídos por tecidos derivados das três camadas de células germinativas e são relativamente incomuns em cabeça e pescoço. O termo epignathus tem sido utilizado para designar teratomas que se originam na orofaringe. Este artigo relata o caso de um teratoma epignathus gigante descoberto ao nascimento, o qual foi tratado com sucesso e proservado por 7 anos. Um menino recém-nascido apresentou uma massa tumoral polipoide que se exteriorizava através da boca por uma extensão de 9 cm, com regiões da superfície semelhantes à pele e outras exibindo pelos. Exame de tomografia computadorizada revelou que a massa se originava profundamente na hemiface esquerda. Os níveis de alfa-fetoproteína (AFP) se apresentavam elevados (316.000 ng/mL). Foi realizada cirurgia e a análise microscópica confirmou o diagnóstico de teratoma maduro. Por apresentar lesão residual e altos níveis de AFP, o paciente foi submetido à quimioterapia, resultando em regressão completa da lesão e normalização dos níveis de AFP. Correção cirúrgica de uma fenda palatina foi realizada aos 5 anos de idade. Aos 7 anos de idade, o paciente apresentava um bom estado de saúde geral, sem sinais clínicos de recorrência da lesão. Embora o epignathus seja uma condição rara, seu diagnóstico no feto deve ser realizado o mais precocemente possível. O cuidado pré-natal proporciona benefícios inquestionáveis, permitindo o diagnóstico precoce de anomalias que podem comprometer a vida do feto e contribuindo para a indicação de casos que requerem tratamento antes do nascimento.

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