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Pituitary Duplication With Nasopharyngeal Teratoma and Cleft Palate

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Abstract

Pituitary gland duplication is a rare malformation of unknown cause that is often associated with a nasopharyngeal teratoma, among other secondary malformations. This clinical report describes a case of pituitary gland duplication with a nasopharyngeal teratoma, cleft palate, and hypothalamic hamartoma, as well as the surgical management of this patient. This case also raises the question of whether the nasopharyngeal teratoma is the cause of the pituitary duplication above and the cleft palate below or whether it is a result of the primary duplication of the notochordal process. Various theories are presented in an attempt to answer this question, but the exact cause of these malformations remains equivocal. Future research in this topic may elucidate the answer to this question.

Pituitary gland duplication is a rare malformation, with approximately 40 reported cases documented in the medical literature.¹⁻¹⁹ Aside from a poor survival rate, pituitary gland duplication usually contains several secondary malformations such as cleft palate, agenesis of the corpus callosum, abnormalities of the circle of Willis, hypothalamic hamartoma, and an abnormality of the dentate nucleus.¹⁶ On the other hand, duplication of the pituitary gland can also be an isolated finding.¹³

Among the cases of pituitary duplication containing secondary malformations, an association has also been made with the presence of nasopharyngeal teratoma. This article raises the question of whether the teratoma is the cause of the pituitary duplication above and the cleft palate below or whether it is a manifestation of the primary duplication of the notochordal process. We report a case of congenital nasopharyngeal teratoma in association with pituitary duplication, as well as the surgical management of the associated cleft palate.

CLINICAL REPORT

A 3710-g white female infant was referred to the craniofacial surgery service on day 3 of life because of feeding difficulties secondary to a large nasopharyngeal mass and cleft palate deformity. She was born to a 29-year-old woman, G1P1A0, at 38 weeks after a complication-free pregnancy and delivery. APGAR scores were 8/9 at delivery. The family history was significant for epilepsy in two paternal uncles and Down's syndrome in one paternal uncle. A physical examination of the patient revealed a normal external facial examination. The intraoral examination revealed a soft, nodular mass covered with fine hair protruding down through the middle third of the vomer (Fig. 1). This mass measured approximately $3 \times 2 \times 2 \text{ cm}^3$ and was confluent with the vomer, which was hypoplastic posteriorly. There was a bilateral postincisive cleft palate, and the anterior vomer was not contiguous with the premaxillary segment.

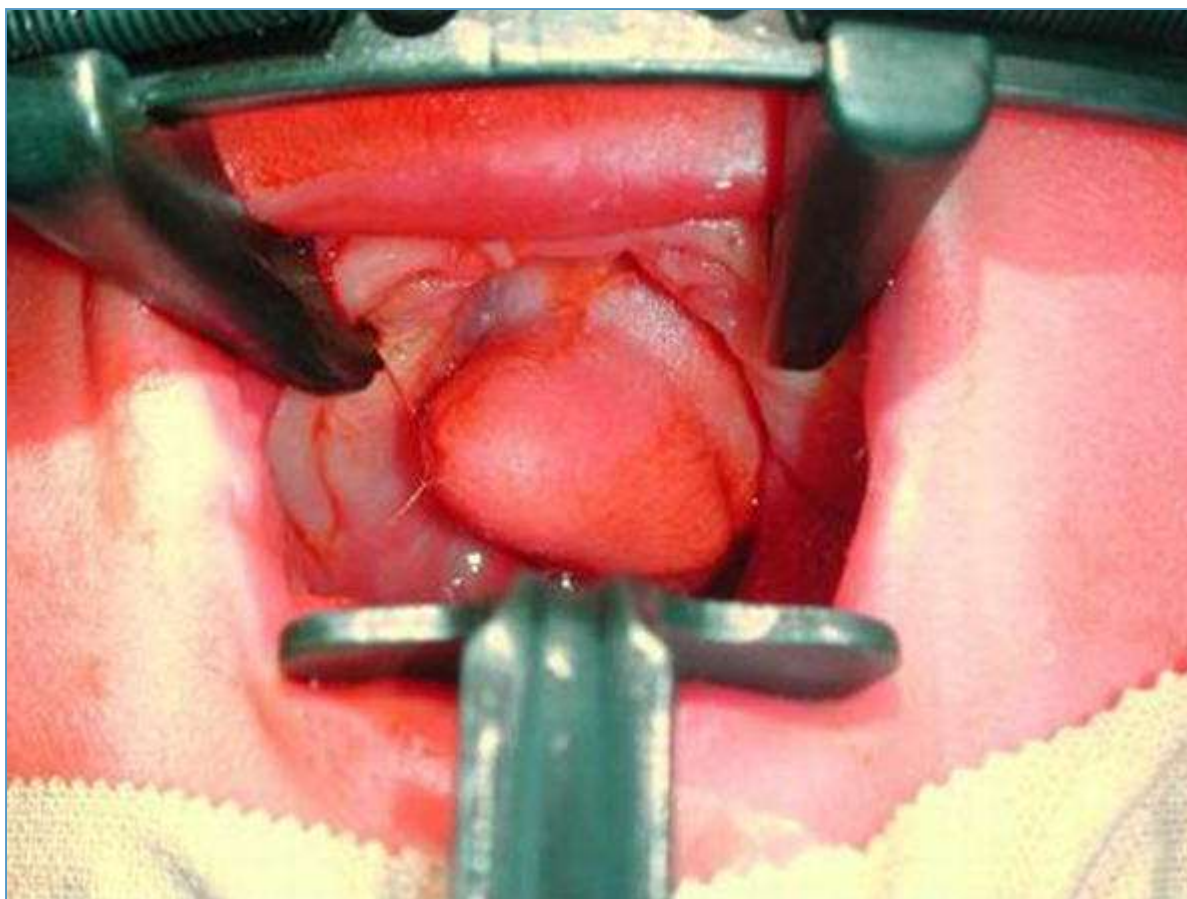


FIGURE 1. Intraoral examination of the patient showing a nasopharyngeal teratoma extending through a cleft in the middle third of the vomer, as well as a bilateral postincisive cleft palate.

Computed tomographic scans demonstrated the nasopharyngeal mass (which involved the vomer as well as the nasal septum) extending through a large defect in the hard palate. It was determined to contain both lipomatous and ossific components (Fig. 2). The nasopharynx was partially obliterated by the mass, which was closely associated with the cranial base. There was also a defect in the midline sphenoid bone consistent with a persistent craniopharyngeal canal. A magnetic resonance (MR) image was obtained to further evaluate the intraoral mass (Fig. 3) and any other associated cranial anomalies. Abnormal bifurcation of the clivus was demonstrated on imaging, and it was closely associated with the patent craniopharyngeal canal (Fig. 4). Intracranially, 3 main findings were observed: a duplicated pituitary gland and stalk (Fig. 5), tubomammary fusion, and a midline hypothalamic mass along the floor of the third ventricle. The corpus callosum and dentate nuclei were normally formed. Note that the prenatal ultrasound did not demonstrate the mass or the cleft palate. One could conjecture that the mass filled the palatal area obliterating the cleft on the ultrasound study.

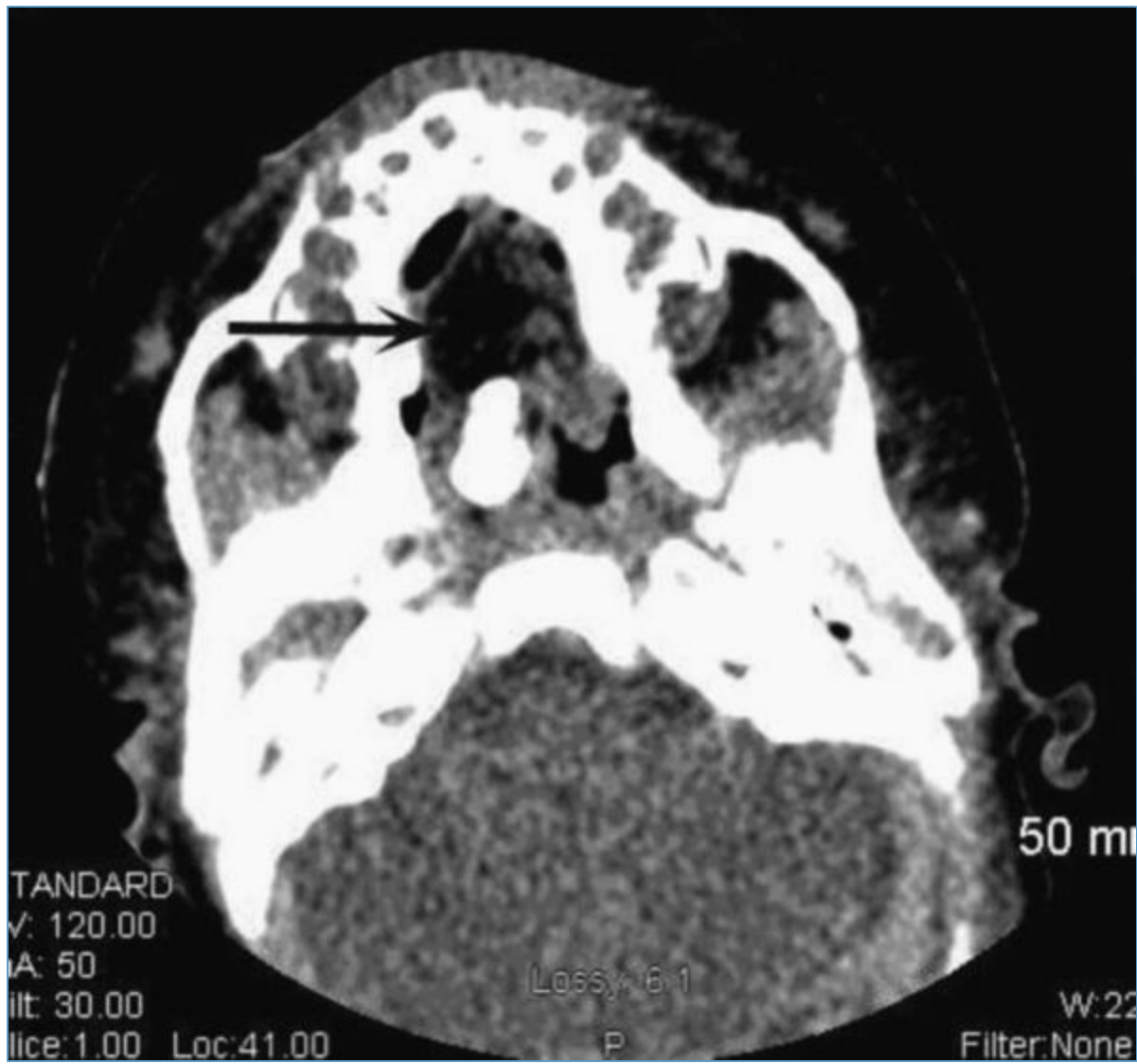


FIGURE 2. Transverse computed tomographic scan demonstrating the nasopharyngeal teratoma (arrow) extending through a large defect in the hard palate and containing both lipomatous and ossific components.



FIGURE 3. Sagittal MR image showing another view of the nasopharyngeal teratoma (arrow).



FIGURE 4. Sagittal MR image demonstrating a nasopharyngeal teratoma (large arrow) and a patent craniopharyngeal canal (small arrow). The box demonstrates a hamartoma at the base of the third ventricle or fusion of the tubomammary bodies.



FIGURE 5. Coronal MR image showing duplicated pituitary gland and stalk (arrows).

The patient underwent surgical excision of the nasopharyngeal mass on day 4 of life. The tumor was dissected off the dura and was the superior extent of the excision. Coverage of the dura, as well as closure of the defect, was accomplished with mucosal flaps from the remaining septum. Gross pathology noted a $3.2 \times 1.5 \times 1.4\text{-cm}^3$ skin covered fingerlike mass with internal white hairs up to 3 cm in length. Microscopic examination revealed adipose tissue, hair follicles, salivary glands, and a tooth bud. The tissue diagnosis was a benign teratoma.

The patient was noted to be healing well from the excision at 1 month. However, because of poor feeding and gastroesophageal reflux, the patient underwent a Nissen fundoplication with placement of a feeding gastrostomy. The palatal defect was closed at the age of 9 months using a V-Y pushback technique (ie, Veau-Wardill-Kilner). The patient's thyroid function tests, chromosome profile, electroencephalograph, echocardiogram, and ophthalmologic evaluation were normal. The clinical examination

at 1 year revealed a normal growth curve with no evidence of any neuroendocrine deficiencies. The patient was seen at the age of 5 years. The feeding tube has been removed. Her swallowing function and endocrine function remains normal. There was no evidence of recurrence of the teratoma clinically and by MR imaging.

DISCUSSION

The embryological origin of the pituitary gland is often misquoted as arising from 2 separate structures, an upward extension of oral ectoderm, and a downward evagination of diencephalon neuroectoderm.¹⁰ The true origin of the pituitary, as first described by Gilbert²⁰ in 1934, is from a single structure: the adhesion of the surface and neuroectoderm in a small area on the ventral surface of the developing head. The primordium of this gland is first distinguished at the gestational age of 22 days.¹³

Duplication of the pituitary gland was first described in 1880 by Ahlfeld²¹ in a patient with partial duplication of the brain. At that time, the hypophyseal duplication was attributed to a partial twinning of the anterior part of the body.²¹ However, now, many different theories exist to explain this phenomenon, which is not yet completely understood.

One of the more recent theories to describe the cause of pituitary duplication was initially postulated by W.M. Morton in 1956. He hypothesized that this malformation resulted from a duplication of the prechordal plate and the anterior end of the notochordal process at the 15th to 16th day of pregnancy.¹ This event presumably leads to the formation of 2 areas of persistent contact between neural and surface ectoderm resulting in 2 pituitary glands. The cleft created by the splitting of the prechordal plate and the notochordal process is filled by invaginating mesenchyme. In the developing face, this medial collection of mesenchyme (organized into a mass) hinders the fusion of normally formed lateral structures resulting in a midline cleft. The location of the midline mass governs the location of the clefts.¹⁰ If, as seen in the case of our patient, the mass interferes with the development of the lateral palatine processes, the result is a hard and soft palate cleft. Our case seems to be very similar to other documented cases of pituitary duplication with a nasopharyngeal teratoma.¹⁰

The most commonly associated anomaly described with a duplication of the pituitary is the presence of a midline hypothalamic mass along the floor of the third ventricle. This finding was observed in our patient, who exhibited a hypothalamic hamartoma. The above-mentioned theory first proposed by Morton also supports an explanation of this phenomenon. The notochord plays an important role in influencing ependymal differentiation, and experimental splitting of the notochord has demonstrated thinning of the ependymal layer. Therefore, duplication of the notochord leads to 2 areas of low mitotic activity in the diencephalon and, subsequently, the formation of 2 median eminences. The mass observed in these patients exists between these 2 eminences and consists of abnormal cells, which normally migrate laterally to

form the hypothalamic nuclei.¹⁰

Another one of the more recent theories of pituitary duplication, described by Shah et al,¹¹ explains the duplication in the presence of the median cleft face syndrome. The formation of a median cleft in early embryology by a midline inclusion dermoid leads to the splitting of the pituitary anlage and the formation of 2 pituitary glands. Therefore, in contrast to the first theory, the mass is the cause of the split rather than an effect of it. The presence of pituitary duplication in the existence of a midline mass, cleft, palate and sphenoid, according to Shah et al, may represent a spectrum of the median cleft face syndrome. This includes cranium bifidum occultum frontale, V-shaped hairline, and clefting of the nose, upper lip, and premaxilla. There was no evidence of any of these findings in our patient.

Although no mechanism or exposure has been consistently described in association with pituitary duplication, reports have cited uterine bleeding early in pregnancy,¹ maternal surgery early in gestation,⁴ vaginal herpes,⁵ digoxin,⁵ meclizine,⁷ smoking,¹¹ cortisone,¹¹ and naproxen¹¹ as possible contributors. None of these events or exposures occurred in our patient.

Teratomas, defined as true neoplasms arising from all 3 germ layers, occur in roughly 1 in 4000 live births. Of these, most occur in the sacrococcygeal area. Head and neck teratomas comprise approximately 1% to 10% of congenital cases. Conditions with a pure oral presentation, as in our case, occur very rarely.²² Prenatal ultrasound has been shown useful in diagnosis, largely in cases where oral obstruction has occurred resulting in polyhydramnios.²³ However, a large portion of these tumors, 78% in one study,²² are not detected until birth even with regular prenatal ultrasound examinations.

Because teratomas of the oral cavity tend to protrude out of the mouth as they enlarge and because infants are obligate nasal breathers, infants with pure oral teratomas tend to have better respiratory outcomes than children with other head and neck presentations.²⁴ At presentation, ultrasound examination of the mass is useful to document solid and cystic components. Computed tomographic scans are important for clinical suspicion of extensive cranial involvement or communication with intracranial structures, whereas MR imaging gives a clear picture of the neuroanatomy. True diagnosis of the mass is often only possible with histopathologic examination.²²

Treatment of oral teratomas is focused on complete excision of the tumor, with early excision advised especially if the airway is compromised.^{25,26} Although malignant degeneration in oral teratomas is not well documented, a 90% degeneration rate has been documented in other areas of the head and neck.²⁷ Adjuvant chemotherapy has not been shown to be beneficial even in tumors with immature features.²⁸ Surgical management of the clefts should proceed at the normal time course.

anomalies, continued clinical surveillance for neuroendocrine disorders is also important. Reviewing the literature reveals about 30 cases of pituitary duplication with less than half of these cases involving a nasopharyngeal teratoma.¹⁻¹⁹ Whether this case represents a spectrum of notochord duplication or is the manifestation of a teratogen on the morphogenesis of embryologic structures is open for debate. Future research further defining the stage-by-stage processes at the microscopic and cell signaling level involved in the development of the embryologic cranial base may eventually define the true cause-and-effect relationship in this constellation of malformations.

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Key Words: Pituitary gland duplication; hypophyseal duplication; nasopharyngeal teratoma

