CASE REPORT

DPG-plus syndrome: new report of a rare entity

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SUMMARY

Pituitary gland duplication is a particularly rare finding. Different theories have been proposed to explain its pathogenesis, however, this phenomenon is not yet totally understood. Recently, duplication of the pituitary gland (DPG)-plus syndrome has been described, associating DPG with other blastogenic defects. We present the clinical and imaging findings of a newborn girl with DPG, associated with multiple other midline anomalies, including a nasopharyngeal teratoma, palate cleft deformity, bifid nasal bridge, tongue and uvula, hypoplasia of the *basis pontis* and corpus callosum, duplication of the basilar artery and hypothalamic hamartoma. We describe our patient's multidisciplinary team approach and emphasise the importance of reporting upcoming cases, in order to give more insight into the understanding of this complex entity.

BACKGROUND

Duplication of the pituitary gland (DPG) is rare and can occur as an isolated anomaly or be associated with other malformations such as cleft palate, bifid tongue, hypertelorism, agenesis or hypoplasia of the corpus callosum, nasopharyngeal tumours and hypothalamic enlargement.¹⁻³ Recently, DPG-plus syndrome has been described, associating DPG with other blastogenic defects.¹

We present the clinical and imaging findings of a newborn girl with DPG associated with multiple other midline anomalies, including a nasopharyngeal teratoma.

CASE PRESENTATION

A newborn 3030 g (25th centile) Caucasian girl was admitted to our neonatal unit immediately after birth with a nasopharyngeal mass and a palate cleft deformity. She was born to a 38-year-old mother, at 37 weeks, after an uneventful first pregnancy. The family history was unremarkable, with no consanguinity. The ultrasounds at 11, 21 and 33 weeks were reported as normal. Amniocentesis (for maternal age) showed a normal (46,XX) karyotype. The baby was born vaginally (forceps). Apgar scores were 4 and 7 at 1 and 5 min, respectively. The first physical examination revealed hypertelorism, a central cleft palate with a soft cystic mass protruding from the midline oral cavity and bifid nasal bridge, tongue and uvula.

INVESTIGATIONS

CT scans showed a 3 cm diameter nasopharyngeal mass, involving the distal third of the nasal septum, protruding through a large cleft (13.5 mm) in the hard palate (figure 1). The mass was in close association with the cranial base and extended to the

nasopharynx and oral cavity, partially obliterating it. There was also a midline ethmoid bone defect consistent with an absent crista galli and ethmoidal lamina. MRI revealed two small pituitary glands, each with a stalk (figure 2), a duplicated sella, hypoplasia of the *basis pontis* and corpus callosum, duplication of the basilar artery and a thickening of the floor of the third ventricle, suggestive of a sessile hypothalamic hamartoma (figure 3).

Postnatal chromosome profile, abdominal and renal ultrasound, cervical spine radiograph and electroencephalography were normal. The echocardiogram showed mild aortic valve insufficiency. Thyroid function tests and cortisol were also in the normal ranges.

TREATMENT

On day 44 of life, the nasopharyngeal tumour was removed and the bifid tongue was corrected by endoscopic surgery. Macroscopic examination showed a 2.5×2×1.5 cm skin-covered nodular mass with bone fragments. Microscopic examination revealed skin tissue (with epidermis, dermis and hypodermis), muscle tissue, cartilage and bone with bone marrow and hematopoietic tissue. The final histopathological diagnosis was that of a mature teratoma.

OUTCOME AND FOLLOW-UP

At 9 months of age, the patient showed normal weight and height curves in the 25th centile. On physical examination, there was no evidence of tumour recurrence or neuroendocrine deficiencies. The patient's swallowing function was normal, and she was well adapted to solid food. She had mild hypertonic limbs, with otherwise normal motor and developmental milestones appropriate for her age (she could sit and change position unaided, hold objects in her hands, transfer objects from one hand to the other and take them to her mouth, imitate hand-clapping, smile at people, vocalise, distinguish strangers from relatives and support herself in the upright position). The ophthalmological evaluation showed intermittent exotropia with normal visual acuity. The clinical examination was otherwise unremarkable.

DISCUSSION

To the best of our knowledge, only about 40 cases of DPG have been reported in the medical literature.^{1 2} Nevertheless, the real incidence of this malformation may be underestimated, on the one hand, because of a poor survival rate and, on the other, because DPG was also described as an incidental finding in some reports. DPG is not yet totally understood,^{1 2} and different theories have

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Figure 1 Coronal CT image demonstrating a nasopharyngeal teratoma (arrow) with a tooth-like morphology, extending through a large defect in the hard palate.

been proposed to explain it: partial twinning of the anterior part of the body,⁴ teratogen exposure during pregnancy,^{5 6} variant of the median cleft face syndrome⁷ or splitting of the notochord during blastogenesis.⁸

The most commonly associated anomalies described with DPG are: hypertelorism (65%), cleft palate (61%), hypothalamic mass (58%), a broad or duplicated sella (55%), oropharyngeal tumours (55%, usually teratomas), vertebral malformations (55%) and agenesis or hypoplasia of the corpus callosum (39%).³ Other findings less frequently reported include duplication of other facial structures such as lips, tongue and mandible; micrognathia/retrognathia; fistula of the glabella and lower lip; low-set dysplastic ears; cleft basisphenoid bone; duplication of the optic chiasm and basilar artery; aberrant circle of Willis; cerebellar hypoplasia; ventricular enlargement; clival encephalo-coele; hypoplastic pons; third cerebral peduncle; duplicate odontoid process; absent olfactory bulbs/tracts; diaphragmatic hernia; cardiac malformations; urinary anomalies; absent/small thyroid isthmus and choanal atresia.^{1 3 9}

Accordingly, our patient presented with hypertelorism, cleft palate, nasopharyngeal teratoma, bifid tongue and MRI findings suggestive of a hypothalamic hamartoma, duplicated sella, duplication of the basilar artery and hypoplasia of the corpus callosum, in addition to DPG and stalk, and hypoplasia of the *basis pontis*.

Nasopharyngeal teratomas are frequently associated with DPG, however, it is not yet established whether the pituitary duplication and cleft palate are caused by the teratoma or whether the teratoma is a manifestation of the primary pituitary duplication.²

Prenatal diagnosis of nasopharyngeal teratomas is very helpful in the management of these patients, since the malformation can cause airway obstruction and lead to asphyxia soon after birth.¹⁰ Unfortunately, the majority of these tumours, 78% in one study,¹¹ are not detected until birth, even with regular prenatal ultrasound examinations, as was the case in this report. Usually, treatment involves multiple surgical interventions that are patient-specific.^{9 10 12} In our case, the nasopharyngeal tumour was small and did not require an immediate surgical approach. Therefore, excision of the mass could be postponed until the 44th day of life and was combined with correction of the bifid tongue. Preoperative evaluation with CT scans and MRI allowed a better characterisation of the mass¹⁰ and helped to exclude the existence of an intracranial extension.¹³ A multi-disciplinary team (Plastic Surgery, Neurosurgery and Otorhinolaryngology) was involved in the surgical and post-operative management of this patient. The cleft palate will be repaired at a later stage.

The majority of patients with DPG who live past the neonatal period have normal psychomotor development and

Figure 2 Sagittal 3-D FIESTA MR image showing a pituitary gland and stalk (box) on the right and left of the midline. Note that these structures are absent in the midline.

Figure 3 Coronal T2-weighted MR image demonstrating a thickening of the floor of the third ventricle, suggestive of a sessile hypothalamic hamartoma (left), and basilar artery duplication (right).

intelligence.^{3 14 15} At 9 months, our patient presented with mild hypertonic limbs, but, otherwise, motor and developmental milestones appropriate for age.

In most cases, no endocrine abnormalities are recognised, however, DPG has been described in patients presenting with delayed puberty due to hyogonadotrophic hypogonadism.¹⁶

The long-term follow-up of our patient will require a multidisciplinary team (Pediatrician, Pediatric Neurologist, Plastic Surgeon, Otolaryngologist, Ophthalmologist, Cardiologist, Endocrinologist, Physical therapist, Speech therapist), committed to continued clinical surveillance for neuroendocrine anomalies.

We emphasise the importance of reporting upcoming cases of DPG-plus syndrome, since we believe it could contribute to the elucidation of its pathophysiology. Research directed towards the development of the pituitary gland could result in a better understanding of this rare malformation.

Learning points

- ▶ Duplication of the pituitary gland (DPG)-plus syndrome is a rare entity, associating DPG with other blastogenic defects including: cleft palate, bifid tongue, oropharyngeal tumours, hypothalamic enlargement and agenesis or hypoplasia of the corpus callosum.
- ▶ Craniofacial anomalies are frequently the presenting features of DPG-plus syndrome, hence, performing imaging studies in these patients is mandatory to make the diagnosis.
- ▶ The majority of patients with DPG who live past the neonatal period have normal psychomotor development and intelligence.
- ▶ Long-term follow-up of DPG-plus syndrome patients requires a multidisciplinary team committed to continued clinical surveillance for neuroendocrine anomalies.

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REFERENCES

- 1 Manjila S, Miller EA, Vadera S, *et al.* Duplication of the pituitary gland associated with multiple blastogenesis defects: duplication of the pituitary gland (DPG)-plus syndrome. Case report and review of literature. *Surg Neurol Int* 2012;3:23.
- 2 Chariker M, Ford R, Morrison C, *et al.* Pituitary duplication with nasopharyngeal teratoma and cleft palate. *J Craniofac Surg* 2011;22:755–8.
- 3 Slavotinek A, Parisi M, Heike C, *et al.* Craniofacial defects of blastogenesis: duplication of pituitary with cleft palate and oropharyngeal tumors. *Am J Med Genet A* 2005;135:13–20.
- 4 Ahlfeld F. *Die Missbildungen des Menschen. Band I.* Leipzig, Germany: Grunow, 1880.
- 5 Tagliavini F, Pilleri G. Mammillo-hypophyseal duplication (diplo-mammillo-hypophysis). *Acta Neuropathol* 1986;69:38–44.
- 6 Shah S, Pereira JK, Becker CJ, *et al.* Case Report. Duplication of pituitary gland. *J Comput Assist Tomogr* 1997;21:459–61.
- 7 Hori A. A brain with two hypophyses in median cleft face syndrome. *Acta Neuropathol* 1983;59:150–4.
- 8 Morton WM. Duplication of the pituitary and stomatodaeal structures in a 38-week male infant. *Arch Dis Child* 1957;32:135–41.
- 9 Maeda Y, Suenaga H, Sugiyama M, *et al.* Clinical presentation of epignathus teratoma with cleft palate; and duplication of cranial base, tongue, mandible, and pituitary gland. *J Craniofac Surg* 2013;24:1486–91.
- 10 Levine AB, Alvarez M, Wedgwood J, *et al.* Contemporary management of a potentially lethal fetal anomaly: a successful perinatal approach to epignathus. *Obstet Gynecol* 1990;76:962–6.
- 11 Cay A, Bektas D, Imamoglu M, *et al.* Oral teratoma: a case report and literature review. *Pediatr Surg Int* 2004;20:304–8.
- 12 Johnston JM, Vyas NA, Kane AA, *et al.* Giant intracranial teratoma with epignathus in a neonate. Case report and review of the literature. *J Neurosurg* 2007;106:232–6.
- 13 Pavlin JE, O'Gorman A, Williams HB, *et al.* Epignathus: a report of two cases. *Ann Plast Surg* 1984;13:452–6.
- 14 Mutlu H, Paker B, Gunes N, *et al.* Pituitary duplication associated with oral dermoid and corpus callosum hypogenesis. *Neuroradiology* 2004;46:1036–8.
- 15 Vieira TC, Chinem RN, Ribeiro MR, *et al.* Central precocious puberty associated with pituitary duplication and midline defects. *J Pediatr Endocrinol Metab* 2007;20:1141–4.
- 16 Kollias SS, Ball WS, Prenger EC. Review of the embryologic development of the pituitary gland and report of a case of hypophyseal duplication detected by MRI. *Neuroradiology* 1995;37:3–12.

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