Duplication of Pituitary Gland-plus Syndrome presenting with a Transcranial Dermal Cyst

Purpose of this case report

- To promulgate the clinical presentation and Multi-disciplinary team management of a very rare and complex craniofacial malformation-DPG-plus syndrome
- To review the endocrine complications associated with this syndrome

Case report

- A term new-born female was found to have a cleft palate and an unusual lump on the dorsum of tongue by her mother on day 1 of life

Antenatal History: Intrauterine fetal growth retardation during 3rd trimester of pregnancy

Birth Weight: 2.98 kilograms (9th percentile)

Ethnicity: Caucasian

Family: non-consanguineous marriage, no h/o any significant illness except that her father was born with Gastrochisis

Day 9 of life: re-admitted acutely with difficulty in feeding and obstructive breathing

Stertal, tracheal tug and cyanosis in supine position

Examination by Cleft palate surgeon

Cleft palate appearance was highly unusual (wide u-shaped cleft approximately 17 mm defect and a bifid uvula)

She also had soft dysmorphic features like hypertelorism, low set ears, micrognathia

A small dimple and sinus on nasal bridge with hair protruding out of it

Cardiovascular, respiratory, abdominal, spine, neurological and limb examinations were normal

Initial Management:

- Referral to the Cleft palate team
- Nursed in 30 degrees upright position at home and slept on an aeroesoo nappess

Radiological Findings

- At five months of age:
  - Underwent craniofacial and brain Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) scan, which revealed
    - A duplicated pituitary gland
    - Both anterior and posterior elements of pituitary gland were duplicated with separate infundibular
    - Thickening of floor of third ventricle (hypothalamic hamartoma) in continuity with the anterior aspect of the midbrain, with mamillary bodies not being separately identified (tubomamillary fusion)
    - Duplication of basilar artery, broad flat Sella and cleft in odontoid peg
    - A large right nasopharyngeal teratoma
    - A trans cranial nasal dermoid cyst and cyst extending from external nose, through the nasal bones and through the frontal region to juxta to right orbit.
  - CT scan of skull base confirmed the midline cranial osseseous defect.

- She was suspected to have DPG-plus syndrome

Craniofacial MRI scan at five months of age

Referrals and Results

1) Paediatric neuro-ontology Multi-Disciplinary Team (MDT) meeting and assessment by craniofacial team (maxillofacial, plastic and neurosurgery): possibility of Double Pituitary Gland-plus (DPG-plus) syndrome as the likely diagnosis.

- The following results were obtained:
  a) Baseline pituitary function tests including TSH, Free T4, t early morning Cortisol and IGF-1, which were within normal limits
  b) Germ cell tumor markers total HCG < 5 uI (normal), AFP 112 kU (within normal limits for a chronological age of 6 months)
  c) Involvement of Genesteel and CGH array testing: CGH showed a DNA copy number variant 16q23.2 0.2MB, not known to be related to DPG-pl us syndrome
  d) Cleft Lip and Palate service: monitored feeding and provided support to the family.

Surgical Management

1) Resection of nasopharyngeal mass at 8 months of age, in view of progressive airway obstructive symptoms and cyanosis in supine posture

- Histopathology revealed the nasopharyngeal mass to be a mature benign teratoma and the tongue polyp, a hamartoma
  - 2 months post-op: breathing and feeding significantly improved

2) Cleft palate repair at 15 months of age - modified Von Langenbeck repair method

- 1 month Post-operatively - noted to have good repair except for a fistula within the mid-posterior third of the hard palate - plans made for an elective closure in future

3) Trans-cranial dermoid cyst and nasal pit resection was performed at 27 months of age, in view of

- Progressive transcranial extension of the nasal dermoid from its superficial dermal opening to the falx intracranially, and an increase in the lesion’s overall size

- Histologically, dermoid cyst was lined by keratinised squamous epithelium and contained adnexal structures with no evidence of malignancy

- Post-operative MRI scan confirmed that complete resection was achieved

Growth and Development

At 3 years of age:

- This child has normal growth, development and neurological examination and significant improvement in speech (with speech and language therapy) and
  - Her weight is tracking between the 50th-75th centile, length is 98 th-99.6th centiles

Endocrinology

- Baseline endocrine tests including LH, FSH, Estradiol, morning cortisol, thyroid function tests, IGF-1 and serum osmolality performed at 7 months, 16 months and again at 27 months of age are within normal limits

Follow-up Plan

- She remains under continued MDT surveillance and is planned to have annual surveillance Craniofacial MRI scans, due to risk of recurrence of teratoma and association of precocious puberty with hypothalamic hamartoma

Duplicated pituitary gland-plus syndrome

- Duplication of pituitary gland in association with other midline craniofacial anomalies - also described as “DPG-plus syndrome” – is an extremely rare developmental anomaly with only 52 cases reported worldwide so far

- Proposed pathogenetic mechanism (Morton’s theory): splitting of rostral notch chord and prechordal plate during blastogenesis

References

7. PENNA, Gustavo Cancela et al. Duplication of the hypophysis associated with precocious puberty: presentation of two cases and review of pituitary metastimates of DPG plus syndrome.

Case significance

- This case report adds significantly to the growing body of literature on the clinical presentation and complex management of children with DPG-plus syndrome
- This patient is also the first reported case of DPG syndrome with a nasal dermoid and intradural extension of the dermoid


Endocrine manifestations of DPG-plus syndrome

- Central Precocious Puberty (CPP) is the most common reported endocrine manifestation in association with DPG-plus syndrome
- Delayed puberty and secondary hypogonadism are other pituitary hormone abnormalities that have been reported in a few cases
- Of the 40 cases reported till 2011, 11 female children survived beyond infancy and 7 of these female children developed CPP
- The exact mechanism for development of CPP in these patients is still unknown
- Interruption of lateral cell migration and possible duplication of hypothalamic nuclei with resultant tubomamillary fusion has been hypothesized as a possible mechanism
- Treatment with Gonadotropin releasing hormone analogs has been reported to be successful and causes arrest of further pubertal progression

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