Dysmorphic Features: Isolated Dysmorphologies

Background
1. Dysmorphic features
   - Abnormal body variations that can be measured or characterized (congenital anomalies or birth defects’)
     - Singular anomalies often diagnostically insignificant, but multiples can aid the dx of a larger synd

Epidemiology of dysmorphology
- Incidence of major malformations is approximately 2-3% of live births
- Congenital malformations account for approximately 20% of infant deaths
- This summary is limited to dysmorphic features that may be found on physical exam

Pathophysiology
1. Etiology is diverse but may include genetic, infectious, chemical or metabolic causes
   - Physical causes may include decreased amniotic fluid, compression, torsion
2. Different organ systems are susceptible to teratogenesis during different stages of development
   - Most major malformations occur in the embryonic period (3 to 8 weeks)
   - Functional defects and minor malformations may occur throughout the fetal period (9-38 weeks)
     - CNS, sensory organs, teeth, and external genitalia remain susceptible

Diagnosis
1. Abnormalities of the head and face
   - Size - etiology of macro / microcephaly is diverse and poorly understood
     - Macrocephaly - Occipitofrontal circumference above 98th percentile for age. Often associated with megalencephaly
     - Microcephaly - Occipitofrontal circumference 2 SD below mean for age
2. Abnormalities of the skull and facial bones
   - Craniosynostosis - Premature fusion of one or more cranial sutures
     - Appears on physical examination as abnormal head shape
       - Dolichocephaly: premature sagittal suture closure; long skull with a prominent forehead and occiput; approximately 1.9 per 10,000 births
       - Brachycephaly: premature coronal suture closure; short skull with a high, wide forehead; approximately 0.8 per 10,000 births
       - Trigonocephaly: premature metopic suture closure; triangle-shaped skull; approximately 0.67 per 10,000 births
     - Craniosynostosis is an indication for referral to a neurosurgeon to prevent neurologic complications
   - Micrognathia - a reduction in size in part or all of the mandible
     - Relatively common (approximately 1 in 100 newborns)
- Often part of a multiple congenital anomaly syndrome; can also be familial, teratogenic, or mechanical (e.g. in oligohydramnios sequence)
  - Malar hypoplasia - characteristic of Treacher-Collins syndrome
3. Abnormalities of the ear
  - Size: Microtia is characteristic of trisomy 21
  - Protrusion: may be secondary to compression / injury, hypotonia, collagen defects, turner syndrome
  - Auricular tags ("ear tags"): anomalous nodules or protrusions, usually anterior to the ear
    - Common (approximately 1% of newborns), usually isolated (approximately 95% of cases)
    - If no other obvious defect present, and family history negative, not significant
  - Auricular pits: depressions, dimples, or fossae antr or slightly superior to the ear
    - Common (approximately 1% of newborns), not significant
  - Abnormalities of the ear (including abnormal position, rotation, or shape) assoc w/ renal anomalies
4. Abnormalities of the eye
  - Coloboma (absent tissue in the eye - iris)
    - Isolated (primary ocular defect), including familial
    - Syndromic, most commonly CHARGE syndrome (coloboma, heart defects, atresia of the nasal choanae, retardation of growth / development, genitourinary anomalies, ear abnormalities)
      - W/o a positive family history for isolated coloboma, echocardiography and renal ultrasound are indicated
  - Cataracts (incidence 2 / 10,000 births)
    - Isolated (most common, 50-60% of cases)
      - Hereditary (most commonly autosomal dominant), sporadic / idiopathic
      - Galactosemia / galactokinase deficiency (sole clinical manifestation)
    - With other defects
      - With ocular defects
      - Ocular disorders (e.g. anirida, microphthalmia)
      - With other non-ocular congenital anomalies
      - Chromosomal disorders (trisomies 13, 18, 21; XO syndrome)
      - Intrauterine infections (esp. TORCHES)
      - Metabolic disorders (e.g. Zellweger, galactosemia, Smith-Lemli-Opitz)
      - Chromosomal analysis and genetic testing are indicated
  - Red reflex
    - Test should be performed in a darkened room, from a distance of 18 inches
      - Potential causes for an abnormal red reflex
        - Cataracts
        - Foreign bodies
Isolated Dysmorphologies

5. Abnormalities of the mouth and palate
   o Cleft lip and/or palate
     ▪ Assoc w/ many syndromes; sometimes isolated
     ▪ In combination w/ other malformations, chromosomal analysis indicated
   o Micrognathia
     ▪ Oculo-auriculo-vertebral spectrum disorders (with other craniofacial findings)
     ▪ Treacher Collins syndrome (with malar hypoplasia)
     ▪ Robin sequence (with cleft palate)
     ▪ Teratogens (including radiation and drugs)
   o Facial asymmetry
     ▪ Asymmetric facies at rest
       • Absence / hypoplasia of facial bones, soft tissue
       • Oculo-auriculo-vertebral spectrum disorders (see above, with micrognathia)
     ▪ Asymmetric crying facies
       • Absence / hypoplasia of depressor anguli oris muscle; may be associated with other malformations

6. Abnormalities of the nose
   o Arhinia (partial or complete absence of nose), bifid nose, polyrrhinia, and nostril coloboma: all sporadic and very rare
   o Choanal atresia
     ▪ Presumptively diagnosed by the inability to pass a rubber catheter more than 32 mm into the nose
     ▪ Associated anomalies, including CHARGE syndrome and Treacher Collins syndrome, occur in 50% of cases
   o Proboscis (blind-ended, tubelike structure)
     ▪ Holoprosencephalic proboscis is the m/c form, w/ a poor prognosis
     ▪ Other forms (lateral nasal, supernumerary, and disruptive probosci) are rare

7. Abnormalities of the neck
   o Webbing
     ▪ Characteristic of Turner syndrome and Noonan syndrome
Neck masses

- Congenital, developmental, neoplastic, or inflammatory
  - In children, inflammatory > congenital / developmental > neoplastic
  - 80% of neck masses in children are benign

Anterior triangle masses

- Thyroglossal duct cyst (m/c, behind adenopathy)
  - Midline, painless, moves with swallowing, elevates with tongue protrusion

- Dermoid cyst (teratoma)
  - Midline, most commonly submental, does not move w/ swallowing or elevate with tongue protrusion; distinguish from thyroglossal duct cyst
  - May become secondarily infected and painful

- Thyroid mass (thyrotoxicosis, thymoma)

- Sialadenitis
  - Exquisitely tender; may be secondary to dehydration, poor hygiene, obstruction

- Branchial cyst
  - Common, anterior to SCM; may become secondarily infected; can cause abscess

Posterior triangle masses

- Lipoma
- Vascular / lymphatic malformation

Masses in either triangle

- Lymphadenitis (most common)
- Infantile hemangioma
- M/c congenital malformations
  - Appear at or after birth; rapid proliferation from 6 to 18 months followed by slow involution over 6 to 8 years

- Rhabdomyosarcoma
  - Common; painless, expanding mass, may cause obstruction
  - Neuroblastoma
  - Lymphoma
  - Abscess

- Masses in the sternocleidomastoid
  - Fibromatosis coli
  - Diffuse muscular swelling; presents as torticollis

8. Abnormalities of the limbs

- Polydactyly
  - Use the following terminology:
    - Preaxial: involving the radial side of the limb
      - Duplication of a normal biphalangeal thumb (type I)
      - Opposable thumb w/ three phalanges (type II)
      - Duplication of the index finger, w/ or w/o a thumb (type III)
- Postaxial: polydactyly on the ulnar or fibular side of the limb
- Central: duplication of the second, third or fourth digit
  - Often occur simultaneously w/ syndactyly
- Syndactyly: failed separation of the digits
  - May be cutaneous (involving soft tissue) or osseous (involving the bones)
  - Often occur w/ polydactyly, brachydactyly, or camptodactyly
- Limb deficiencies
  - Use the following terminology:
    - Total (amelia) or partial (meromelia) absence of limb
    - Terminal (all segments beyond a point involved) or intercalary (proximal segment involved w/ at least part of distal segment present)
    - Transverse (extending across the width of the limb) or longitudinal (extending along the length of the limb)
    - Upper or lower limb; right or left side
    - Bones involved; portion of bone deficient (proximal, middle, distal)
  - Etiology may include:
    - Genetic causes (30% of cases)
    - Vascular disruptions (35% of cases)
    - Teratogens, including maternal diabetes, thalidomide, warfarin, cocaine (4% of cases)
    - Unknown cause (32% of cases)
- Constriction rings: distinctive soft tissue depressions encircling a limb (esp. the digits but also the limbs, neck, trunk, or head)
  - May involve a single limb, more commonly involves multiple limbs; associated w/ other deformations, including amputations, skin defects, syndactyly, and club-foot
  - Incidence approximately 1 per 10,000 live births; low recurrence risk

9. Genitourinary abnormalities
- Male
  - Cryptorchidism: failure of one or both testes to descend
    - Common, esp. w/ lower birth weights
    - 3-4% of male infants w/ BW >2500 grams, 21-23% of male infants with BW <2500 grams; incidence falls to 0.8% at 3 months
    - Normal in the preterm male; examination should be repeated at intervals postnatally
    - Dx at birth or later, based on palpation of the scrotum
    - To exclude retractile testis, examine in various positions or in a warm bath
    - Isolated, or may be related to various male pseudohermaphroditic syndromes
    - Treatment should involve first hormonal stimulation, followed if necessary by surgical release of the testes (orchidopexy) to improve fertility and reduce cancer risk
- Inguinal hernia: hernation of the abdominal contents into the inguinal canal
  - Direct (medial to the inferior epigastric artery) or indirect (lateral to the artery)
  - Common (incidence of 20 to 30 per 1000 male live births)
    - Occurs occasionally in females (3 to 4 per 1000 female live births)
    - Esp. preterm infants
    - Recurrence risk for siblings is high (approximately 30%)
  - Usu. isolated; may be associated with Marfan, Ehler-Danlos or cutis-laxa syndromes
  - Risk of incarceration of hernial contents higher in infants than children or adults
  - Repair involves replacement of abdominal contents into the abdomen and ligation of the hernial sac
- Male pseudohermaphroditism: abnormalities of external genitalia that preclude determination of genetic sex from physical examination alone
  - Of greatest concern to the family physician and the parent is deciding the sex of rearing
- Hypospadias: displacement of the urethral meatus from the tip to the ventral surface of the penis
  - Common (approximately 4 in 1000 male births)
  - Dx may be made at birth based on visual inspection, or later in life based on deviation of the urinary stream
  - Usu. isolated; may be part of a syndrome; urogenital anomalies especially assoc. w/ more severe (i.e., proximal) forms of hypospadias
  - Should be distinguished from congenital adrenal hyperplasia (enlarged clitoris) by the presence of testes
- Female
  - Vaginal atresia: absence of the lower third of the vagina, w/ normal external vagina, cervix, and uterus
    - Occurs in approximately 1 in 40,000 female births
    - Most cases of "absent vagina" are Müllerian aplasia (below); only about 10% are isolated vaginal atresia
    - Presents as amenorrhea, often endometriosis secondary to retrograde menstruation through the uterine tubes
    - Usu. occurs as an isolated anomaly, but may also occur as a component of a major malformation syndrome
    - Tx requires surgical creation of a neovagina
  - Müllerian aplasia: absence of vagina, uterus, uterine tubes, and cervix
    - Occurs in approximately 1 in 4000 to 5000 female births
    - Rarely diagnosed before puberty; more commonly pts present with amenorrhea (but otherwise normal sex characteristics)
• Associated urinary tract anomalies (e.g. ectopic kidney, renal agenesis, etc.) and skeletal abnormalities common

- Clitoromegaly: isolated hypertrophy of the clitorus (w/o other signs of masculinization)
  • Dx at birth; may be isolated, related to an endocrine disorder, or related to a multisystem disorder
  • May complicate determination of sex; palpation of testes to distinguish from a normal penis
  • Tx involves correction of the etiologic factor and possibly surgical correction

- Ambiguous genitalia: external genitalia that display both male and female characteristics
  • Causes include:
    o Chromosomal aneuploidies
    o Deficiencies in adrenal steroid synthesis (e.g. congenital adrenal hypoplasia)
    o Multiple anomaly syndromes
  • Requires consultation with specialists in genetics, urology, endocrinology, and family counseling
  • Sex of rearing is of primary importance

- Hermaphroditism: presence of both ovarian and testicular tissues
  • Patient may be 46,XX (approximately 60% of cases), 46,XY (approximately 7% of cases), or mosaic (approximately 33% of cases)
  • Must exclude male and female pseudohermaphroditism
  • Of greatest concern to the family physician and parent is deciding the sex of rearing

10. Miscellaneous abnormalities
  o Anal / rectal atresia
    • Relatively common (approximately 1 in 2500 births)
    • Detected at birth or soon after, based on visual inspection or failure to pass meconium
    • Associated with genitourinary malformations (e.g. rectourethral fistula, renal malformations), various other malformations (gut atresias, vertebral anomalies, etc.)
  o Spina bifida
    • Myelomeningocele or meningocele
      • Readily diagnosed prenatally or at birth based on the presence of the lesion on an infant's back
    • Spina bifida occulta
      • Less readily visible; diagnostic signs include neurological impairment below the lesion, and cutaneous markers on the surface of the lesion, including a tuft of hair ("faun's beard"), hemangioma, or lipoma
    • Spina bifida is also associated with cardiac, anal, renal, abdominal wall, facial, and ophthalmic defects
    • Suspicion of spina bifida should be investigated via CT or MR
References

10. Stevenson &c. 288.

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