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 megalencpaly
        - 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 olygohydramnios sequence)
    - Malar hyploplasia - 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 postive 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, micropthalmia)
            - 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

        - Opacities
        - Iris abnormalities
        - Retinal abnormalities (including tumors, e.g. retinoblastoma
    - Dark spots, asymmetry, markedly diminished reflex, or a white reflex are all indications for referral to an ophthalmologist
    - Pos family hx for retinoblastoma; congenital, infantile, or juvenile cataracts; or retinal abnors should be referred to an ophthalmologist for a complete eye examination, regardless of the findings of the red reflex test
  - Inner canthal fold, Brushfield spots (white / gray spots on iris): characteristic of Trisomy 21
5. Abnormalities of the mouth and palate
  - Cleft lip and/or palate
    - Assoc w/ many syndromes; sometimes isolated
    - In combination w/ other malformations, chromosomal analysis indicated
  - 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)
  - 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
  - Arhinia (partial or complete absence of nose), bifid nose, polyrrhinia, and nostril coloboma: all sporadic and very rare
  - 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
  - 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
  - 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 torticollisis

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 sydromes
            - 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 hypospadia
            - Should be distinguished from congenital adrenal hyperplasia (enlarged clitorus) 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:
            - Chromosomal aneuploidies
            - Deficiencies in adrenal steroid synthesis (e.g. congenital adrenal hypoplasia)
            - 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
    - 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.)
    - 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

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