APPRAOCH TO A DYSMORPHIC INDIVIDUAL

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Incidence:

About 15% of all newborn babies will have at least one minor malformation (i.e. one that does not interfere with normal functioning), and these usually go unnoticed. However, their presence should prompt the clinician to look for a major malformation, as children with one or more minor malformations are more likely to have a major malformation.

- If there are no minor malformations, the probability of a major malformation is 1.4%.
- If there is one minor malformation, the probability of a major malformation is 3%.
- If there are two minor malformations, the probability of a major malformation is 11%.
- If there are three or more malformations, the risk of a major malformation is 90%.

About 3% of all children born will have a significant congenital malformation, i.e. one that will interfere with normal functioning. These congenital malformations are responsible for a large proportion of neonatal and infant deaths, and account for about 30% of all admissions to paediatric hospitals. It is therefore important to recognize both major and minor malformations as they may lead to the early detection and early intervention, as well as the identification of high-risk individuals in the family.

Suspicion

A genetic aetiology should be suspected if the child has

- Congenital anomalies e.g. major anomaly or > 2 minor anomalies.
- Growth deficit e.g. short stature, failure to thrive
- Developmental delay, mental deficit or developmental regression
- Failure to develop secondary sexual characteristic
- Ambiguous genitalia
- Or simply “doesn’t look right”

The complete analysis of a dysmorphic child is summarized in the table shown. While this complete analysis is usually done in a geneticist’s clinic, certain features of the patient’s history and physical examination can be easily mastered by the general practitioner/paediatrician.
Approach to a dysmorphic child (Adapted from Aase)

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ANALYSIS

1. HISTORY

- Pedigree and Family history:
  a. Consanguinity increases the risk for an autosomal recessive disorder
  b. Male patient with similarly affected male siblings or maternal male relatives suggests an X-linked disorder
  c. Vertical transmission suggests an autosomal dominant disorder, especially male to male transmission
  d. History of miscarriages, stillbirths, or early neonatal deaths suggests the possibility of a parental balanced chromosome rearrangement

- Pregnancy and birth history
  a. History of uterine malformations, small pelvic dimensions or oligohydranmios suggest possible aberrant forces causing malformation
  b. Abnormal lie of foetus, delayed onset and/or decreased fetal movement suggests abnormal foetal tone
  c. Placental morphology may give clue to diagnosis e.g. large placenta in Beckwith Wiedemann Syndrome.
  d. Birth measurements may provide clue to onset of insult i.e. symmetrical intrauterine growth retardation suggests early onset whereas asymmetrical intrauterine growth retardation suggests late onset
  e. Environmental hazards for the fetus
   1. infectious agents--viruses(rubella, CMV, herpes, varicella), bacteria(treponema, pallidum), parasites(toxoplasma)
   2. physical agents--radiation(high level only), heat (derived internally as in fever or externally as in saunas)
   3. drugs and chemicals-- environmental (methyl mercury), nonprescription (ethanol, cocaine), prescription (anticoagulants, antineoplastics, anticonvulsants, isotretinoin)
   4. maternal factors--diabetes mellitus, PKU

- Growth and development
  1. Examine growth patterns
  2. Determine developmental status

- Previous investigational studies
  1. Prenatal investigations
  2. Biochemical results
  3. Xrays
  4. Specific metabolic testing
2. PHYSICAL EXAMINATION

**General principles:**
- To determine if physical feature is a major anomaly, minor anomaly or a normal variant.
- Take measurements of finding to determine if the physical feature is abnormal. Standard tables and graphs of age norms for many such physical dimensions are available.
- Compare with other family members.

**Findings that suggest a possible underlying genetic aetiology include**

**General**
- Short stature or tall stature
- Failure to thrive or obesity
- Unusual head circumference: microcephaly or macrocephaly
- Unusual head shape: e.g. brachycephaly, scaphocephaly, trigonocephaly
- Altered body proportion: e.g. short spine, short limbs, long limbs

**Facial features**
- Synophrys (fused eyebrows)
- Hypotelorism or hypertelorism
- Palpebral fissures that are upslanting or downslanting.
- Short palpebral fissures (The length of the palpebral fissure is usually equal to the distance between the two eyes)
- Short or long nose. (The nose is usually 2/3 to ¾ the length of the distance between the nasal bridge and the upper lip)
- Ears that are low-set or posteriorly rotated.
- Ears that are simple or abnormally shaped
- Lips that are thin/full, tented, down turned or cleft
- Philtrum that is long or smooth.
- Palate that is high arched or cleft.
- Uvula that is bifid or absent
- Prognathia or micrognathia

**Hands and feet**
- Brachydactyly (short fingers)
- Arachnodactyly (long fingers),
- Clinodactyly (incurved fingers, usually the fifth),
- Syndactyly (fusion of digits)
- Polydactyly (extra digits),
- Dysplastic nails
- Abnormal creases

Skin and hair
- Abnormal skin pigmentation e.g. haemangioma, cafe-au-lait spots, streaks or whorls.
- Abnormal amounts of hair e.g. alopecia, hirsutism or hypertrichosis
- Abnormal hair line e.g. low hairline (posteriorly or anteriorly) or receding hair line
- Altered hair colour e.g. white forelock

Musculoskeletal
- Short neck
- Abnormal chest shape or size e.g. pectus carinatum, pectus excavatum, short sternum
- Abnormalities of the nipples e.g. widely spaced, supernumerary, inverted nipples
- Abnormalities of the spine e.g. anencephaly, encephalocele, myelomeningocele or stigmata of spina bifida occulta (hair, lipoma, deep dimple)
- Unusual joint shape e.g. flaring
- Abnormal joint mobility e.g. hypermobility or reduced range of motion

Abdomen
- Abdominal wall defects e.g. omphalocele, gastroschisis
- Hepatosplenomegaly
- Nephromegaly
- Ambiguous genitalia

SYNTHESIS

The number of malformation syndromes described is increasing with each day. Hence, there is little value in memorising the features of each disorder. Instead, it may be better to refer to a physician who is more familiar with these conditions, has access to certain laboratory studies, able to interpret these results and provide genetic counseling.

The principles include
1. Determining the underlying pathogenic mechanism i.e. deformation, disruption, dysplasia or malformation
2. Determining if it is a single system or multi-system defect
3. For multiple anomalies,
 Diagnosis depends on recognising the pattern of anomalies, and is not made on
the basis of a single defect. Individual defects are usually nonspecific and rare
defects may be found in several conditions.

4. Comparison with known cases
   • Literature search e.g. PubMed
   • Database search e.g. OMIM, POSSUM, OMD
   • Personal experience

CONFIRMATION

1. Lab tests
   • Indications for chromosome analysis
     o multiple congenital anomalies
     o ambiguous genitalia
     o developmental delay with major and/or minor anomalies of non-CNS
       structures
     o any person with two single gene disorders
     o history of multiple miscarriages
   • Indications for metabolic screening:
     o Metabolic disorders known to cause dysmorphism include lysosomal
       disorders, peroxisomal disorders and disorders of cholesterol metabolism
   • X rays to look for bony changes
   • Autopsy

2. Clinical course
3. Birth of other similarly affected relatives

INTERVENTION

1. Treatment:
   • Symptoms
   • Underlying cause
2. Counselling
   • Diagnosis, natural history, prognosis and management
   • Recurrence risk
   • Reproductive options
3. Follow-up
   • Identification and counseling of at risk family members
   • Surveillance for complications
   • Correction of diagnosis
Useful References: