Early Human Development xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Best practice guidelines

Hirschsprung disease and anorectal malformation

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ARTICLE INFO

Available online xxxx

Keywords:
Congenital abnormalities
Neonatal intestinal obstruction
Hirschsprung disease
Anorectal malformation

ABSTRACT

Hirschsprung disease and Anorectal Malformations are congenital disorders presenting in neonates with distal intestinal obstruction. Hirschsprung disease is associated with a functional distal bowel obstruction resulting from the abnormal development of the enteric nervous system and ensuing aganglionosis of the distal gut. Anorectal Malformations comprise a spectrum of anatomical anomalies causing a mechanical bowel obstruction. Both conditions are frequently associated with congenital abnormalities/syndromes, which require careful assessment and evaluation. Surgical intervention is usually required for both conditions with careful preparation and meticulous technique. Long-term follow-up allows early identification and treatment of potentially debilitating symptoms, which include faecal incontinence.

Contents

1. Introduction

Hirschsprung disease and Anorectal Malformations are congenital disorders that require early recognition, meticulous neonatal management and careful follow-up. To avoid lifelong, troublesome functional

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http://dx.doi.org/10.1016/j.earlhumdev.2014.09.016
0378-3782/

sequelae a well-coordinated multidisciplinary approach is needed from an early stage. Although Hirschsprung disease is known to be primarily a physiological defect and Anorectal Malformations are primarily an anatomical anomaly, aetiology remains incompletely understood in each. Ongoing research has the potential to not only improve clinical management but also advance the understanding of normal development.

Since both conditions are most commonly only identified postnatally, accurate decision-making and parental counselling in the early neonatal period are particularly important. The aim of this article is to illustrate common presenting features, highlight associated abnormalities and describe the initial management for each condition.

2. Hirschsprung disease

2.1. Definition and pathophysiology

Hirschsprung disease (HD) is a congenital disorder caused by aganglionosis in an affected segment of the bowel. Ganglion cells act as relay points within the enteric nervous system, coordinating relaxation. In their absence, the aganglionic zone becomes spastic and symptoms are caused by the ensuing functional distal intestinal obstruction [1].

The length of the affected segment varies. The most distal point is always down in the rectum, at the dentate line. This conveniently means that rectal biopsy can confirm or refute the diagnosis without the need for more invasive biopsies. The proximal extent can vary but lies most often within the rectum or sigmoid ("Classic-segment disease") [2]. In around 10% of infants a longer segment is affected, most often the whole colon (Total Colonic Aganglionosis) or at the most severe end of the spectrum, the entire small bowel. This is an important cause of intestinal failure.

The area between the aganglionic zone and normal bowel is termed the Transition zone. Here, ganglion cells are present but the nerves of the enteric nervous system are abnormal and motility is impaired. Above the Transition zone, the bowel is dilated but histologically normal (Ganglionic zone). The aim of surgical treatment is to remove the Aganglionic zone and Transition zone, and restore intestinal continuity by anastomosing the ganglionic bowel to the rectum.

2.2. Aetiology

HD is the commonest congenital gut motility disorder with an incidence of 1 in 5000 live births. There is a male preponderance in classical segment HD but conversely, females are more likely to have long segment disease. HD is an isolated phenomenon in approximately 70% of cases, with 20% of HD being found in conjunction with another congenital anomaly, characterised by abnormalities of the GI tract, cardiac defects, polydactyly or craniofacial malformations such as cleft lip/palate. The residual 10% comprise syndromic HD, which include the Mowat–Wilson, Smith–Lemli–Opitz and Congenital Central Hypoventilation syndromes and Multiple Endocrine Neoplasia type 2b (MEN 2b). By far the most frequent association is with Down syndrome, which is seen in 90% of syndromic HD. Patients with Down syndrome are estimated to have a 100-fold increase in risk of HD compared with control. HD is a neurocristopathy, and is therefore also associated with other disorders of neural crest cell migration and differentiation, such as Shah-Waardenburg syndrome, characterised by sensorineural hearing loss, iris and hair hypopigmentation and typical facies.

2.3. Genetics

Inheritance patterns in HD are complex and a polygenetic mode of inheritance exists, with a low sex-dependant penetrance and variable expressivity [3]. This is manifested clinically by discrepancies between individuals with known mutations but not expressing the HD phenotype, and the variable length of the affected bowel segment. Several specific gene mutations have been associated with HD, including genes in the RET and Endothelin signalling pathways and SOX10. Isolated HD follows a non-mendelian pattern, with the principle genetic defects identified in the RET and Endothelin pathways. Defects in the RET pathway are the most common and important as they infer the possibility of MEN2b and therefore medullary thyroid carcinoma. Recent studies have shown associations between RET and chromosome 21 gene dosage, perhaps providing a clue to the increased risk of HD seen in Down syndrome. Initial studies looking at differing levels of components of the endothelin signally pathways between male and female mice may also provide a basis for the gender differences. Syndromic HD manifests a variety of inheritance patterns depending on the syndrome in question, the majority of which demonstrate straightforward mendelian inheritance. Shah-Waardenburg provides the majority of evidence thus far, via SOX10 mutation analysis and the WS4 mouse model.

Genetic counselling for a sex-modified multifactorial congenital malformation such as HD is a challenge. The overall risk for a sibling of an affected child is 4% (relative risk = 200), but this varies enormously dependant on the gender of the proband and the length of the affected bowel. The highest recurrence risk is for a male sibling of a female proband with long segment disease (33%), with lowest being for a female sibling of a male proband with classical HD (1%); this is known as Carter's Paradox [3].

2.4. Presentation

HD is usually diagnosed postnatally, although there may be generic features of intestinal obstruction on antenatal imaging such as polyhydramnios, increased abdominal girth and distended bowel loops. It is more likely that HD would be suspected antenatally either because of a family history, or because of indirect antenatal features, such as those suggestive of Down syndrome.

Neonates commonly present at around 48 h of life with distension, bilious vomiting and failure to pass meconium. AXR typically demonstrates gaseous distension affecting a number of loops (see Fig. 1a).

A careful antenatal, family history and postnatal assessment should be taken to help differentiate between the following causes of distal intestinal obstruction in a neonate:

- Hirschsprung disease
- Meconium ileus/cystic fibrosis
- Meconium plug
- Small Left Colon Syndrome (seen in infants of diabetic mothers)
- Ileal atresia
- Colonic atresia
- "Missed" anorectal malformation
- Malrotation with volvulus
- Sepsis.

Infants can present later in the neonatal period, or even as older children. A history of constipation from the first month of life, delayed passage of meconium beyond 24 h, a positive family history of HD or associated syndromes or failure to thrive with abdominal distension should alert clinicians to the possibility of HD. Hirschsprung associated enterocolitis (HAEC) is a particularly important complication. HAEC is a condition of intestinal inflammation, characterised clinically by fever, abdominal distension, diarrhoea and sepsis [4]. This serious and potentially fatal complication may be the presenting feature and is often mistaken for gastroenteritis.

2.5. Initial management

Once initial stabilisation has been performed, enteral feeding should be suspended and a nasogastric tube should be passed. Intravenous fluids should be given at maintenance rates with replacement as needed. Broad spectrum intravenous antibiotics are often used at least

Please cite this article as: Wetherill C, Sutcliffe J, Hirschsprung disease and anorectal malformation, Early Hum Dev (2014), http://dx.doi.org/10.1016/j.earlhumdev.2014.09.016