Neural tube defects

Petra M. Klinge, MD
Associate Professor of Neurosurgery
Warren Alpert Medical School of Brown University
Overview

- Epidemiology, Definition, Classification
- Pathophysiology and associated Disorders: Hydrocephalus and Chiari II Malformation
- Pre- and Postnatal diagnosis
- Surgical Treatment
- Aspects of Fetal Surgery: Results of the MOMS Trial
- Aspects of Translational Research
Spina bifida is one of the most common birth defects,
Worldwide incidence of 1–2 cases per 1000 births, but certain populations have a greater risk.
Highest incidence in Ireland and Wales
More Common if Females

United States, the average incidence is 0.7 per 1000 live births.
Higher on the East Coast than on the West Coast,
Higher in whites (1 case per 1000 live births) than in African Americans (0.1–0.4 case per 1000 live births).
Spina bifida and neural tube defects: Definition and Classification

- Open (aperta):
  - Meningocele: 5%; CSF and meninges
  - Myelomeningocele: 95%; cord and cauda equina tissue extruded

- Closed (occulta):
  50% have cutaneous stigmata ABOVE the gluteal fold
  - Lipomyelomeningocele
  - Filum terminale lipoma
  - “Fatty filum”
  - Dermoid sinus and Dermoid tumors
Overview

- Definition, Classification

- Pathophysiology and associated Disorders: Hydrocephalus and Chiari II Malformation

- Pre- and Postnatal diagnosis

- Surgical Treatment

- Aspects of Fetal Surgery: Results of the MOMS Trial

- Aspects of Translational Research
Pathophysiology:
Defect of neural tube Formation

Weeks 3-4

Three phases:
- Neurulation
- Canalization
- Retrogressive differentiation
Spina bifida: *Hydrocephalus*

- 80-95% incidence of hydrocephalus in myelomeningocele
  - 100% of 35 thoracic lesions
  - 88% of 114 lumbar lesions
  - 68% of 40 sacral lesions
  

- Significant in 20% at birth
Spina bifida: 
Chiari II Malformation

- 99% myelomeningocele patients have radiographic Chiari II; only those with symptoms (1/3 by age 5) require treatment
- Responsible for 15-20% deaths in pediatric myelomeningocele patients (respiratory failure)
- Disruption of the CSF circulation at the level of the Cisterna magna: SYRINGOMYELIA!
Spina bifida and neural tube defects: Risk factors

- Race & Ethnicity.
- Family history of NTD.
- Folate deficiency.
- Some medications (valproic acid).
- Maternal Age.
- Diabetes.
- Obesity.
- Increased body temperature.

GENETICS:

Overview

- Definition, Classification
- Pathophysiology and associated Disorders: Hydrocephalus and Chiari II Malformation
- Pre- and Postnatal diagnosis
- Surgical Treatment
- Aspects of Fetal Surgery: Results of the MOMS Trial
- Aspects of Translational Research
Spina bifida: Pre-natal MRI Imaging
Spina bifida “aperta”: Myelomeningocele defect

- Posterior Vertebral Defect
- Thecal Sac
- Cord Extruded into the Sac (Placode): *plate of embryonic epithelial cells, e.g. the spinal cord!*
Spina bifida „occulta“

Watch for cutaneous stigmata!

Dimple, Skin hemangioma, Subcutaneous lipomas, „Tails“, Skin tracts

MRI Imaging: „Tethered Cord“
Hydrocephalus: MRI Imaging

Imaging: Ventriculomegaly

Pediatric characteristics:

Selective thinning of the occipital lobe!

- Yielding nature of the cranial vault
- Rigid nuclear masses (basal ganglia) in the frontal lobe
Serial HUS in neonatal H.

Intestinal perforation & positive blood cultures: E coli, Pseudomonas and Candida Glabrata
Overview

- Definition, Classification
- Pathophysiology and associated Disorders: Hydrocephalus and Chiari II Malformation
- Pre- and Postnatal diagnosis
- Surgical Treatment
- Aspects of Fetal Surgery: Results of the MOMS Trial
- Aspects of Translational Research
Treatment : MMC

- Closure within 24 hours:

  No evidence exist that immediate or urgent closure of a MMC improves neurologic function BUT reduces risk of infection (after 36 hours wound colonization)

Surgical technique
(Interdisciplinary Neurosurg & Plastic Surg):

- Placode dissected free of arachnoid and allowed to drop into spinal canal
- Dura dissected free of skin and lumbodorsal fascia, and closed,
- Fascia closed
- Skin closed
Sharp microdissection of the placode area
Treatment: Hydrocephalus

- Temporary Spinal fluid „drainage“ (Lumbar puncture or external ventricular drainage, Reservoir)
- Shunt
  - Weight > 2.5 kg
  - No active infection
  - Medically stable
- ETV (Endoscopic third ventriculostomy)
Adjustable valve types

Low pressure range: < 60-70 mmH20 (5 mmHg)

Medium pressure range: 70-120 mmH20 (5 – 8 mmHg)

High pressure range: 120- 200 mmH20 and above (8-15 mmHg)
Endoscopic 3rd ventriculoscopy
Treatment: Chiari II
Overview

- Definition, Classification
- Pathophysiology and associated Disorders: Hydrocephalus and Chiari II Malformation
- Pre- and Postnatal diagnosis
- Surgical Treatment
- Aspects of Fetal Surgery: Results of the MOMS Trial
- Aspects of Translational Research
Rationale for Fetal Surgery

• Despite improved pre-natal diagnostics and health care: Incidence of Spina bifida has stabilized. 3.4/10000 life births US

• Classic treatment is palliative.

• Death rate 10%

• Fetal monitoring _ shows evidence of progression (hydrocephalus, hindbrain herniation, reduced LE movements etc.)

• Translational evidence exsits (animal studies report improved functional outcome and reduced CHIARI FORMATION: Fetal sheep 1993-2003)

• Health care burden from surviviors since implementation of shunt (Joseph H. Piatt Jr, J Neurosurg Pediatrics 6:515-525 2010)
Fetal surgery: Hydrocephalus

- Ventriculo-amniotic shunts or repeat cephalocentesis attempted in 1980s, abandoned because of poor outcomes.
- Incidence of associated nervous system or other anomalies between 70-84%, most not appreciated prenatally.
- Shunt obstruction or migration.
- No clear benefit, as progressive ventriculomegaly not thought to be life-threatening or brain-injuring given capacity of neonatal skull to expand.
Fetal Surgery: Myelomeningocele

1. Pfannenstiel incision to deliver gravid uterus outside abdomen
2. Fetus and placenta located by ultrasound, and 6 cm hysterotomy incision made
3. Amniotic fluid aspirated and reserved
4. Fetus positioned within uterus so that myelomeningocele sac in center of incision (Standard MMC repair)
5. Uterus closed in layers with 1-0 chromic suture
6. Amniotic fluid replaced before last stitch placed
7. Fibrin glue applied to suture line
Overview

- Definition, Classification and Pathophysiology
- Diagnosis and Surgical Treatment
- Aspects of Fetal Surgery
- Results of the MOMS Trial
- Aspects of Translational Research
Management of Myelomeningocele Study (NEJM 2011)

• 5-year, multicenter, randomized controlled trial of 200 patients began in February 2003
• Patients must enroll by their 25th week of pregnancy
• Half assigned to postnatal surgery, and half to prenatal
• Both surgery types done at one of three designated centers (UCSF, CHOP, Vanderbilt)
• Sponsored by the National Institute of Child Health and Human Development
Study design

- Maternal inclusion: US citizen, > 18 years, weight limit, 19-26 weeks of gestation
- Fetal inclusion: T1-S1, Chiari II
- RANDOMIZATION: Pre vs. Postnatal repair
- CESAREAN SECTION at 37 weeks
- Outcome at 12 and 30 months (primary = fetal and neonatal death/criteria for shunt) and (secondary = mental and motor function)
Results at 12 and 30 months F/UP

- N=183 (2003-2010)
- Maternal (30%) complications in pre-natal repair associated with the hysterotomy
- Fetal (13%) complications with prematurity: <30 weeks of gestation!
- BUT: Outcome improved in Pre- vs. Postnatal repair:
  - 68% vs. 98% development of hydrocephalus
  - 40% vs. 82% need of shunt
  - 36% vs. 4% no Chiari II
  - Improved functional level vs. Anatomical level 32% vs. 12%
  - Walking independently at 30 months: 42% vs. 21%
Bigger Question

- Yet, risk of prematurity
- Is a decreased need for shunting enough to justify the risks of prematurity and death?
- No clear benefit in cognition?
- **Policy of current counseling... (Europe vs. US)!!!**
Overview

- Definition, Classification

- Pathophysiology and associated Disorders: Hydrocephalus and Chiari II Malformation

- Pre- and Postnatal diagnosis

- Surgical Treatment

- Aspects of Fetal Surgery: Results of the MOMS Trial

- Aspects of Translational Research: *Diagnose and Target the Metabolic aspects of the Disease!*