Une cause-pas si fréquente-de mégavessie

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CHU ROUEN NORMANDIE

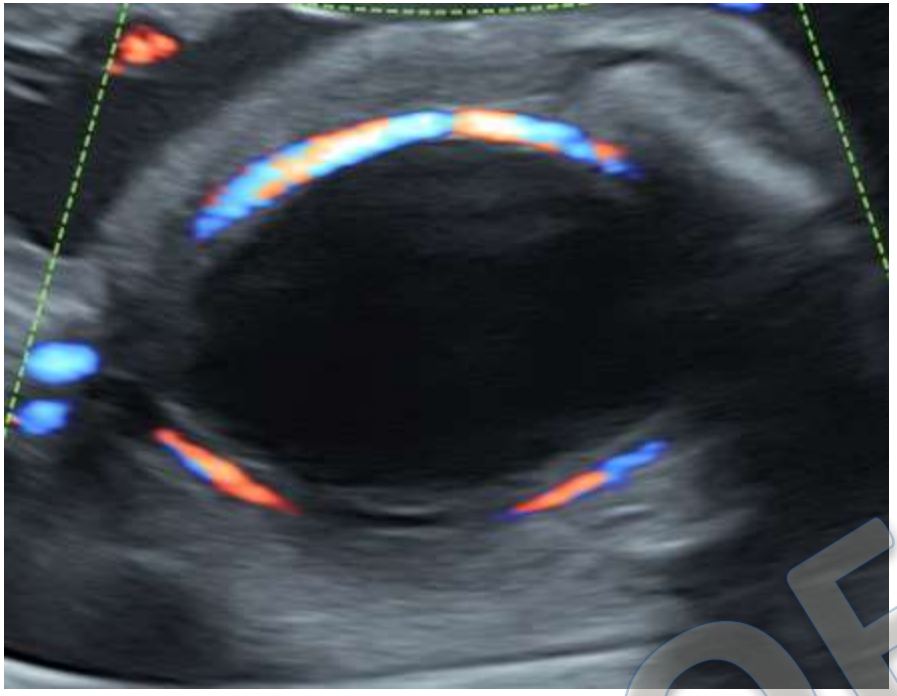
Clinical data

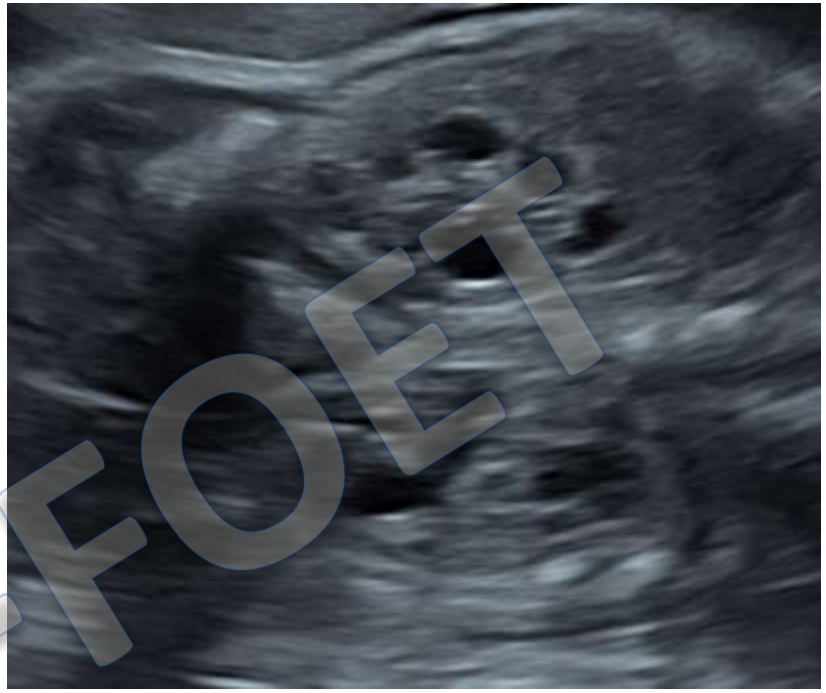
- First pregnancy of a 34-year-old G1P1 patient, who has had amenorrhea for the 7 past years.
- First ultrasound at 20 WG displayed
  - Omphalocele
  - Enlarged bladder
  - Hyperechogenic bowel
  - **Female fetus**
- Patient was referred to our hospital at 23 WG

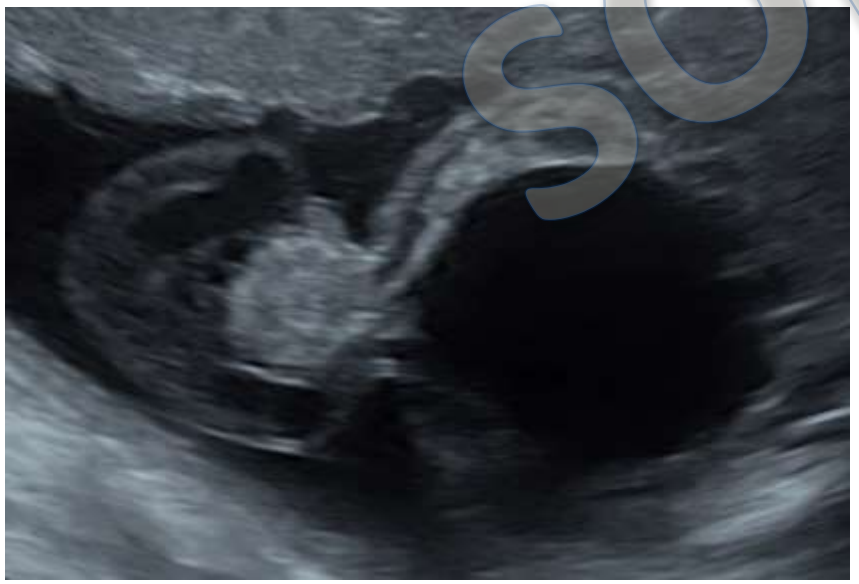
Clinical data

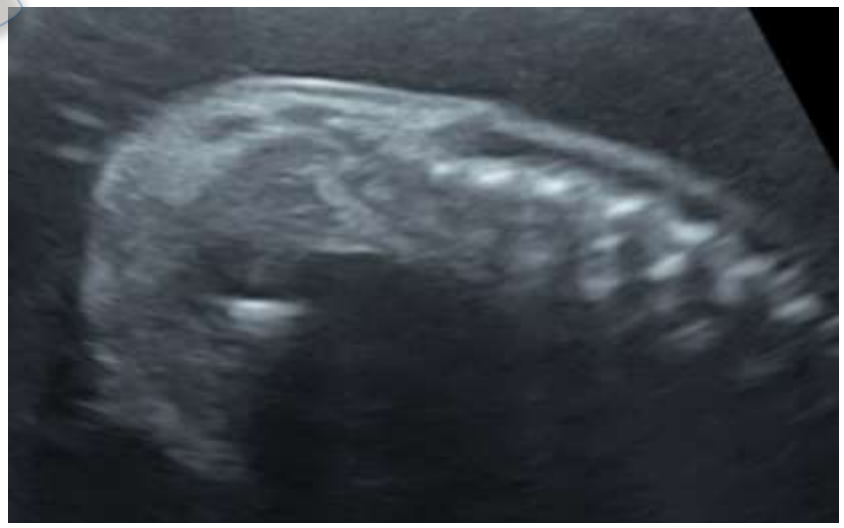
- Ultrasound at 23 WG
  - Signs were confirmed
  - Megabladder > 6 cm
  - Moderate hydronephrosis was present
  - Amniotic fluid normally abundant

- MRI at 28 WG



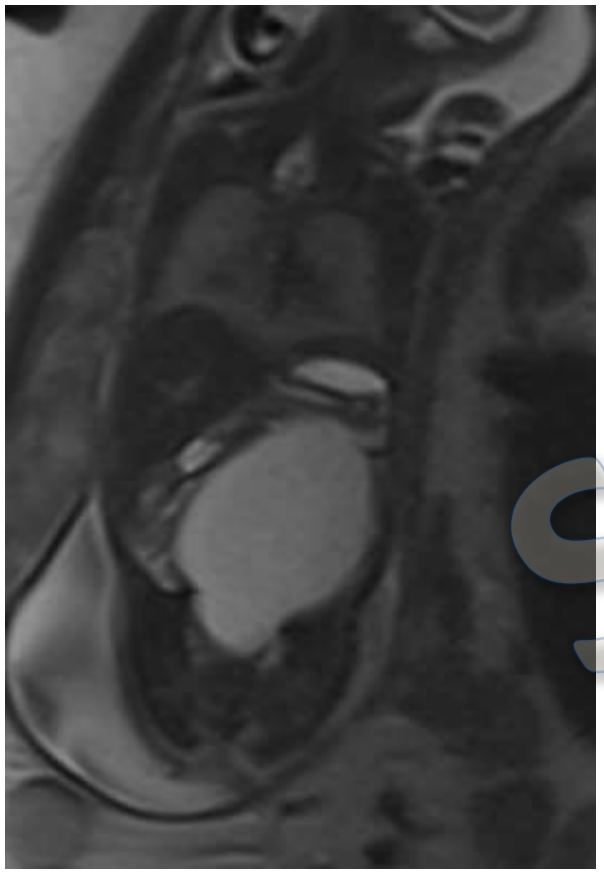


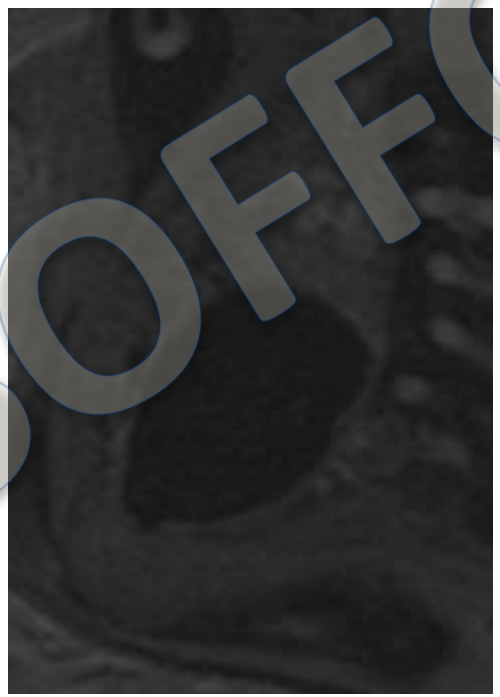


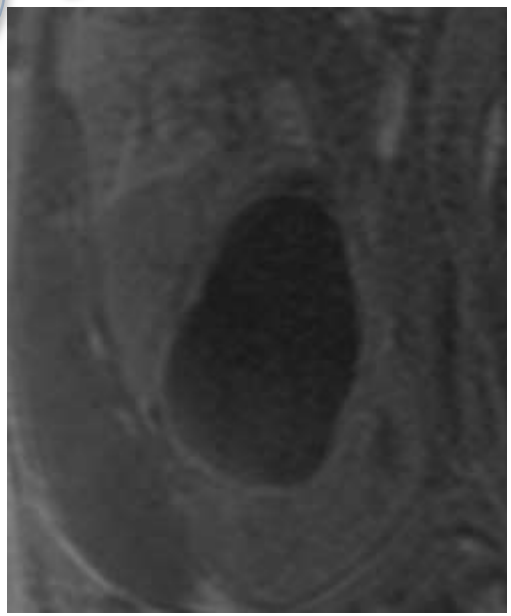


Dr Brasseur

MRI findings at 28 WG: confirms megacystis with thin wall; no colon was seen







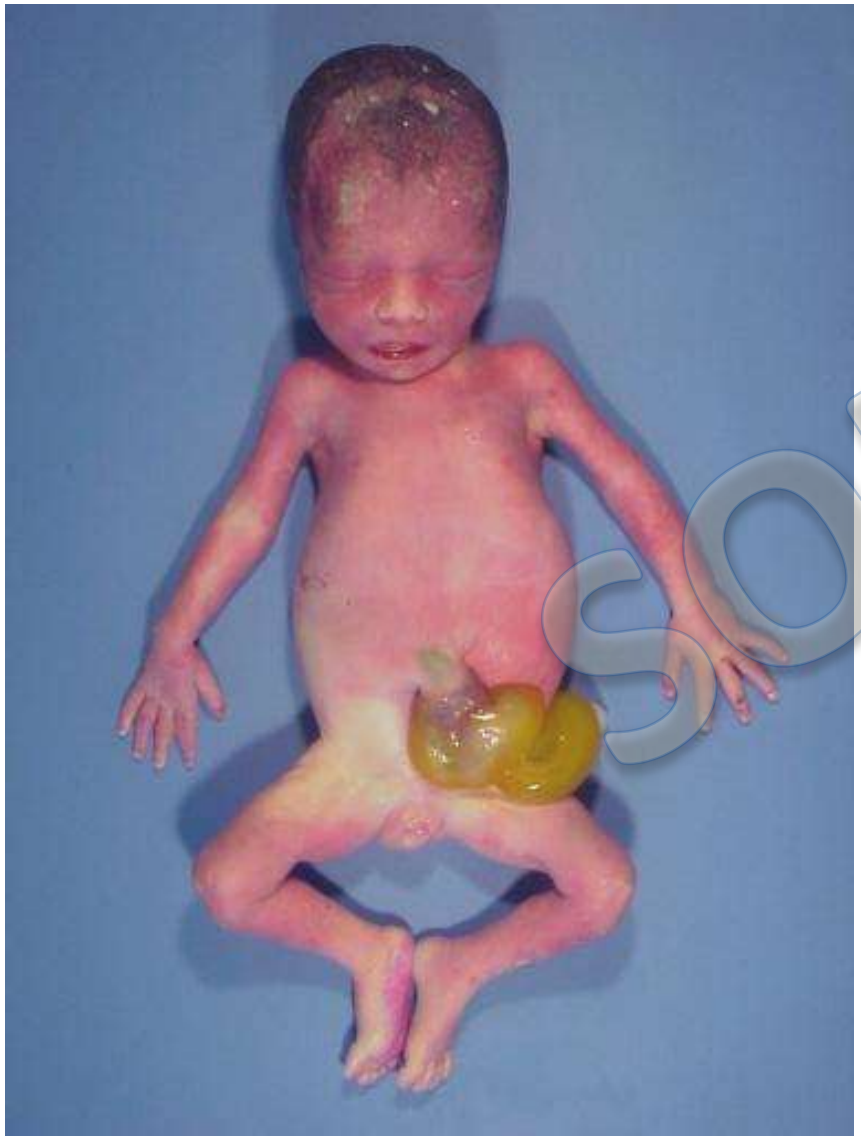
T2

T1

Work up

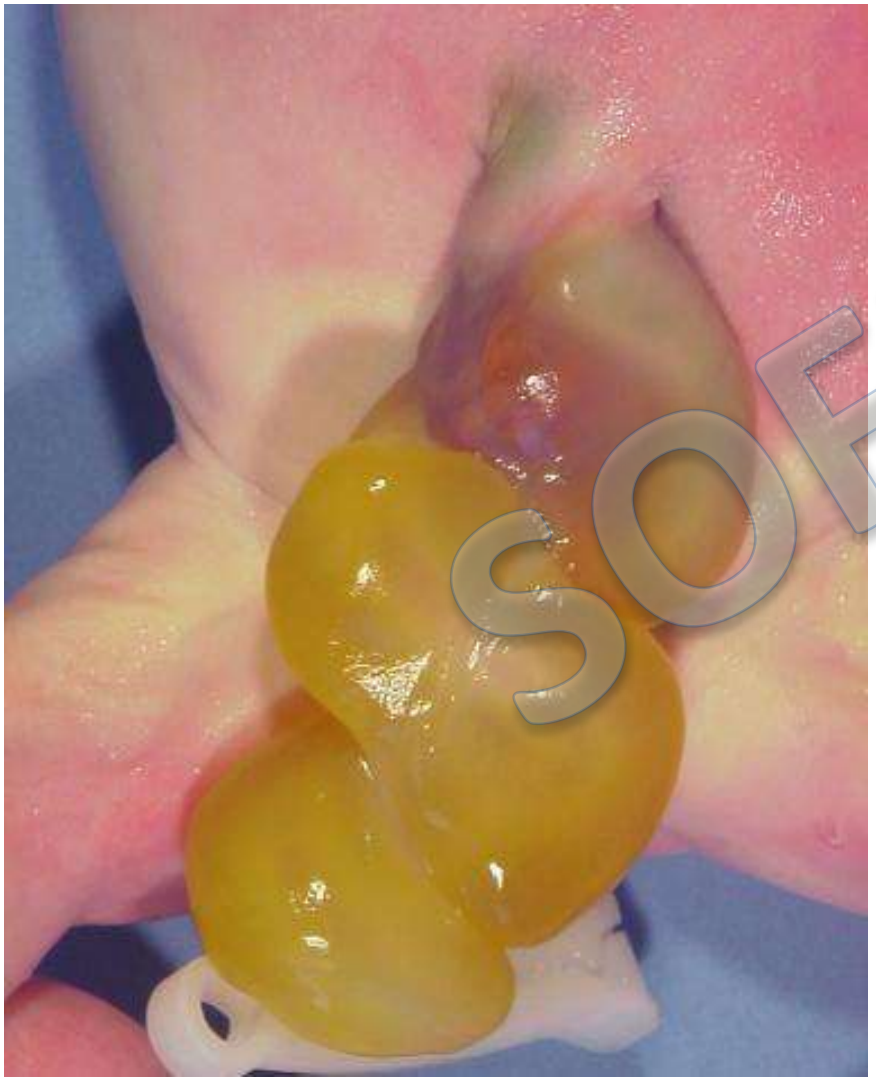
- Karyotype and CGH array were normal
- Female fetus
- Megacystis, thin wall, no signs of obstruction
- Colon not seen
- No other abnormalities
- Uncertain prognosis
- After counselling, parents decided to terminate the pregnancy
- TOP was performed at 29+4 WG

Post mortem findings



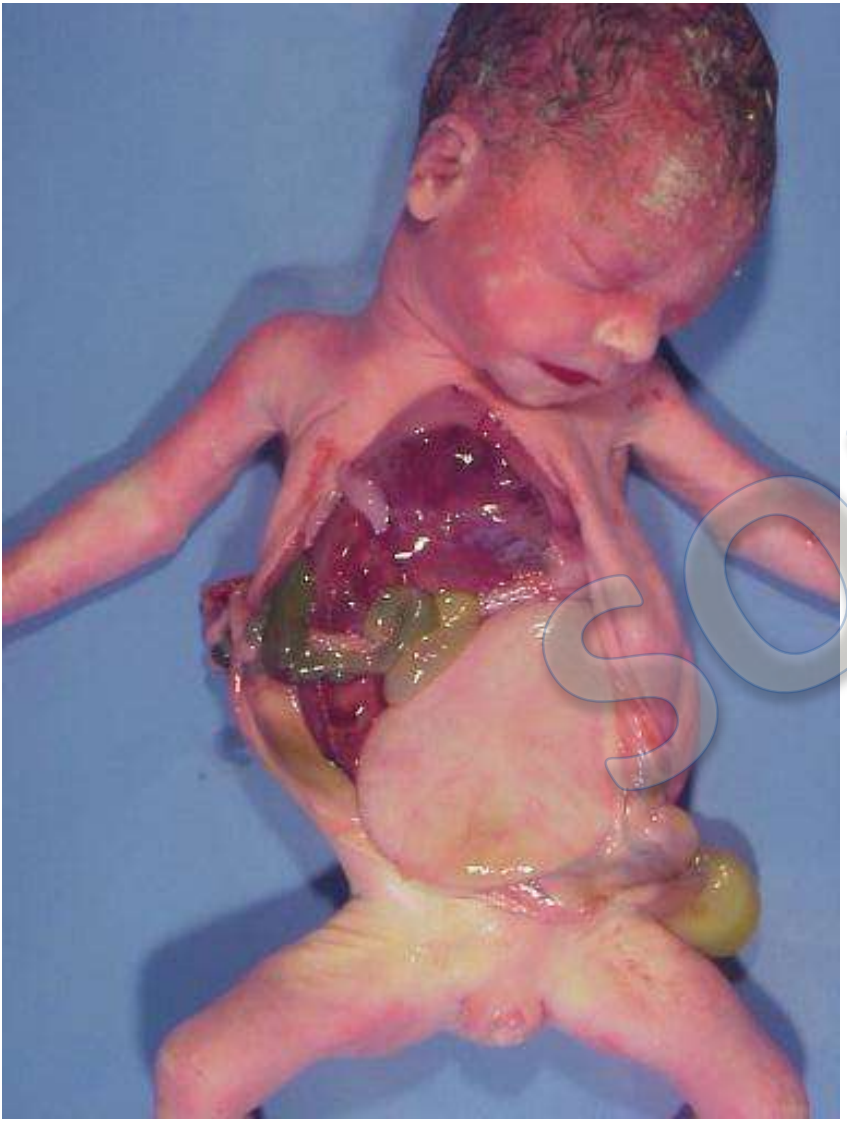
- Female fetus
- Weight and biometry : no IUGR
- Abdominal enlargement
- Genitalia and anus are normal

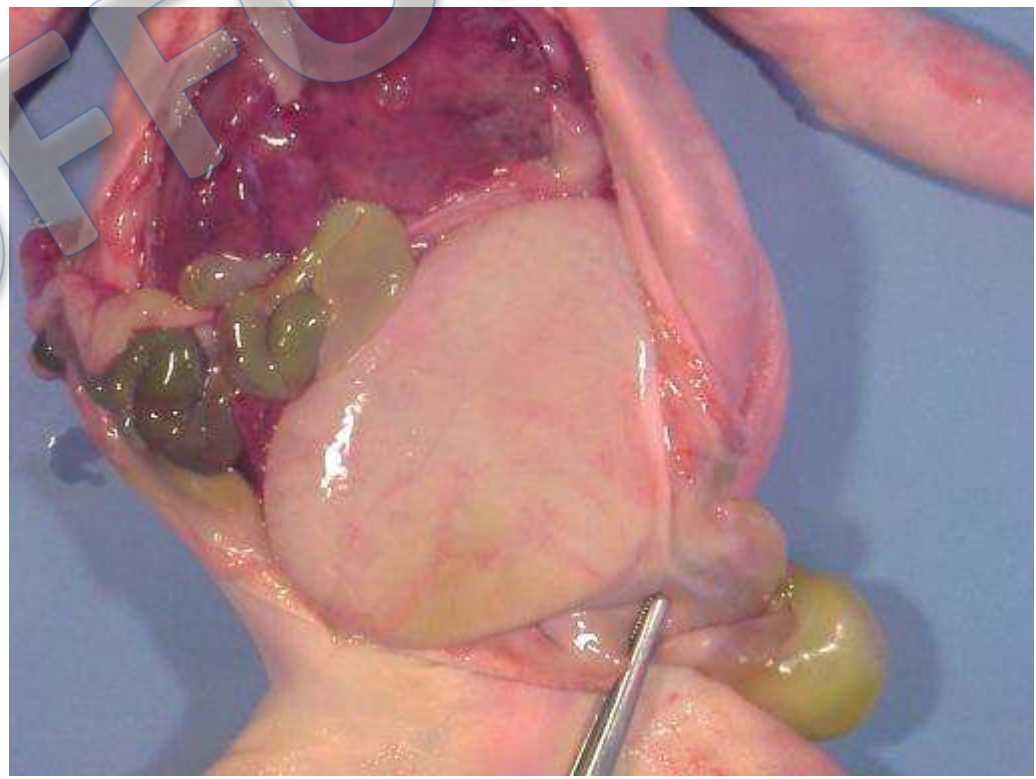
Post mortem findings

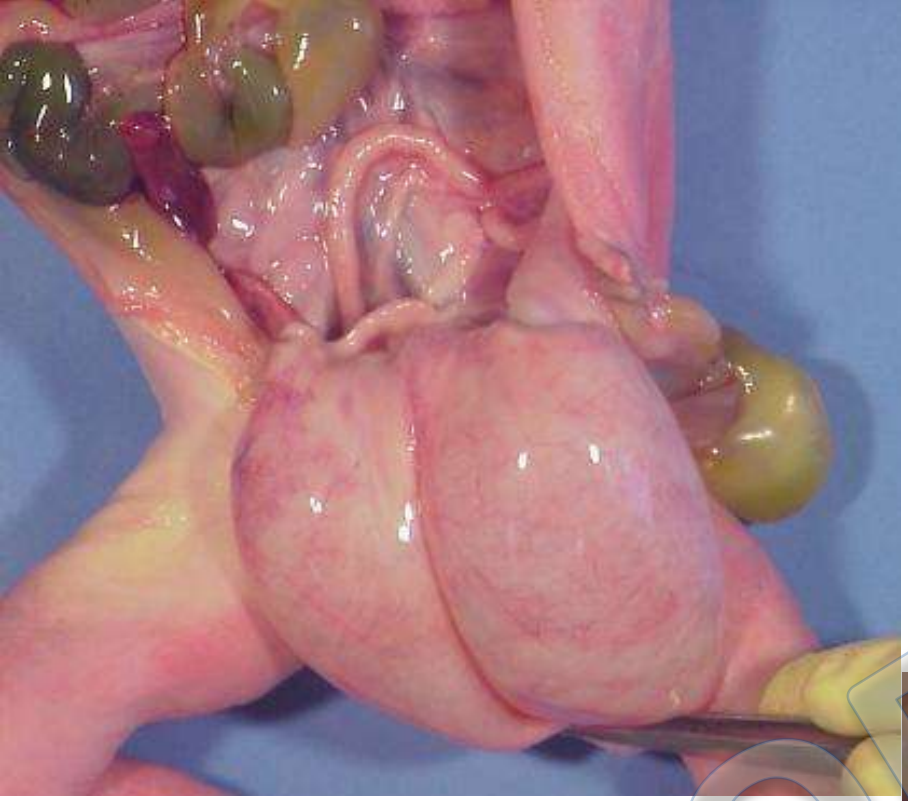


- **Omphalocele contains caecum, appendix, part of right colon and distal part of ileum**

Post mortem findings

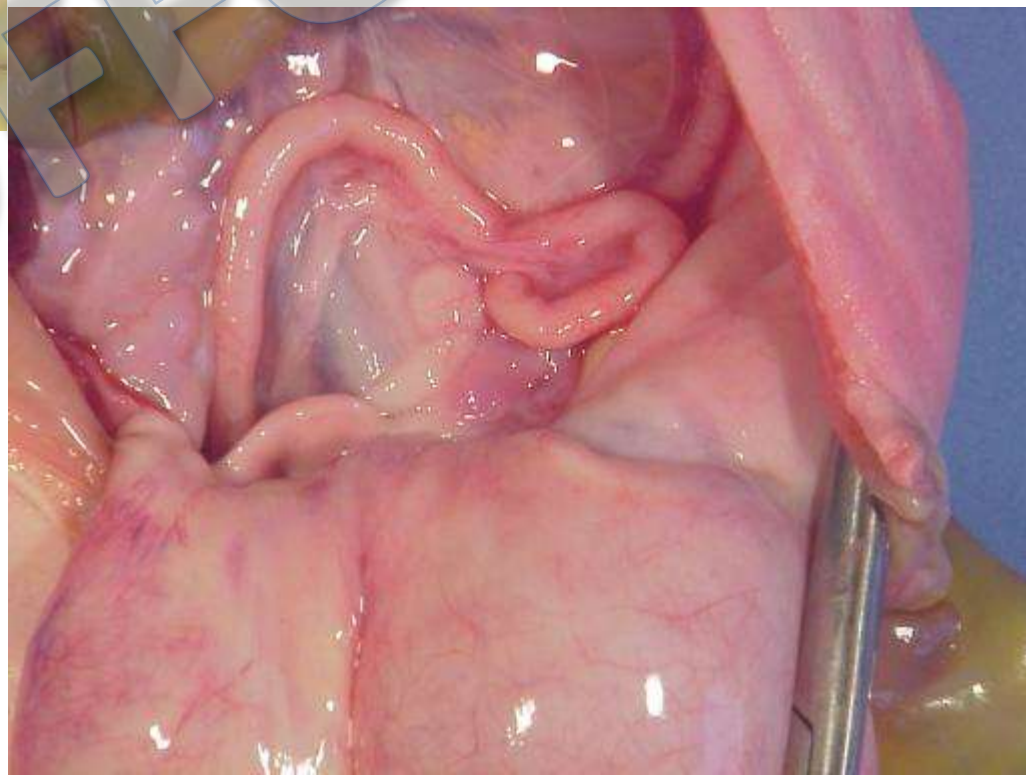


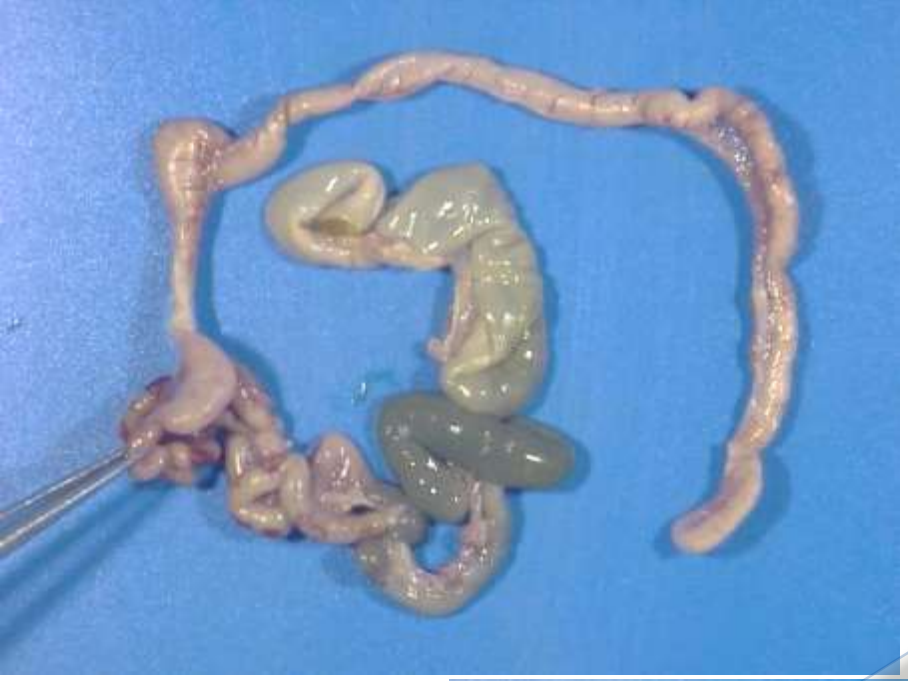




Megacystis 7.5 x 6.4 cm
Thin wall

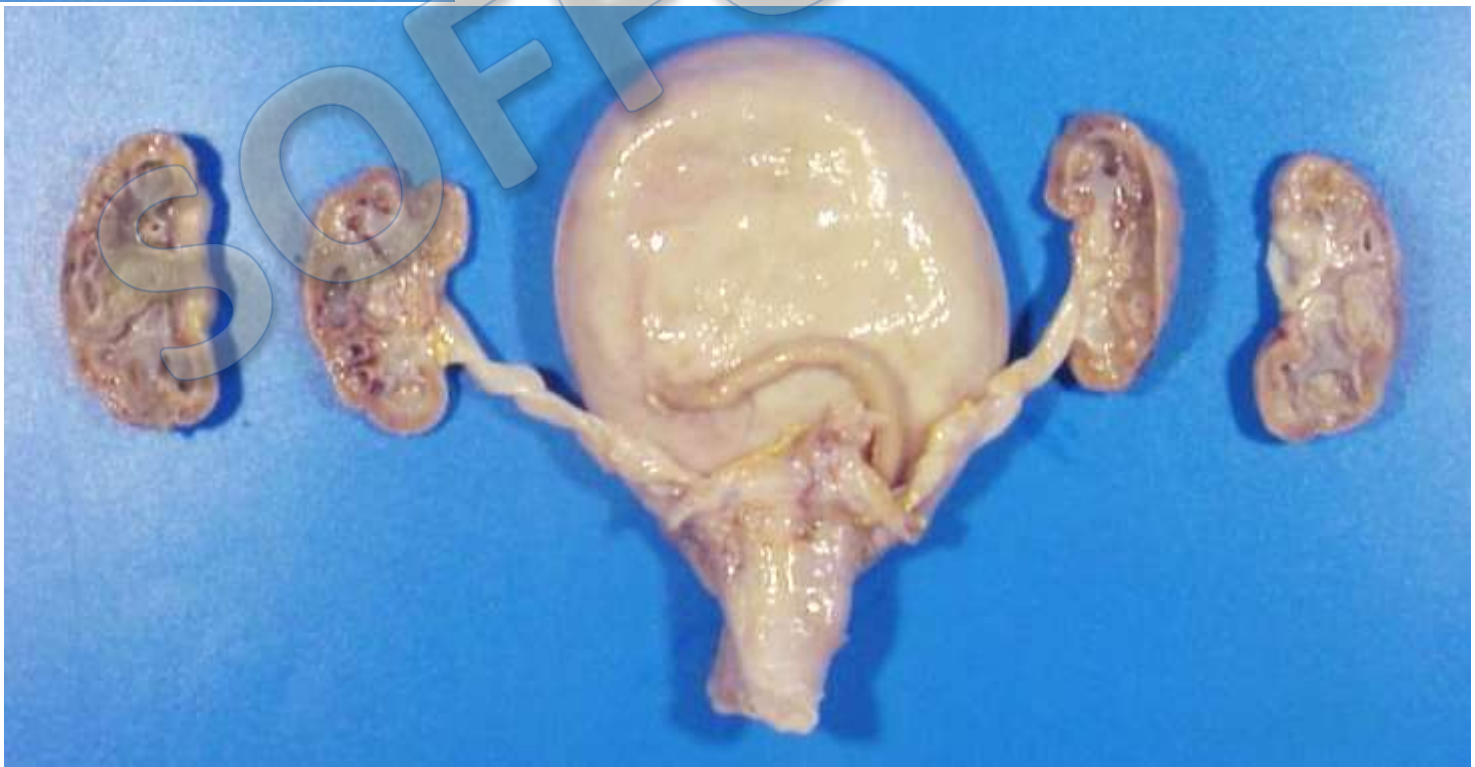
Colon is present short and tubular
3 to 4 mm diameter
Contains no meconium
Intestinal malrotation



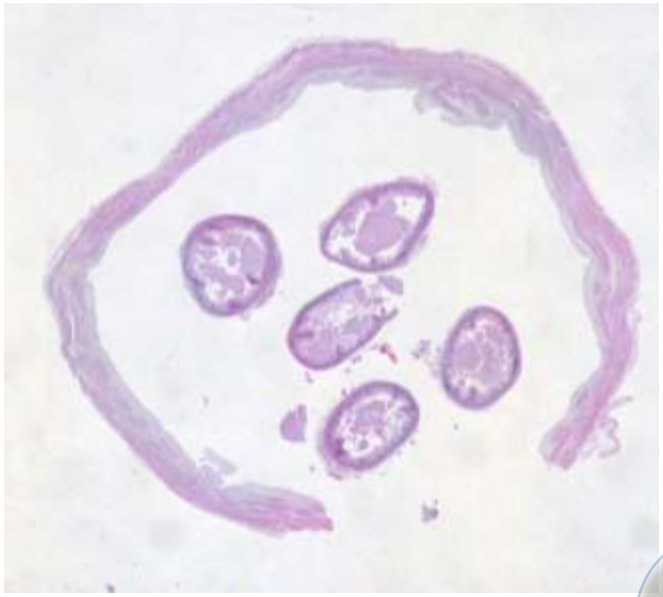


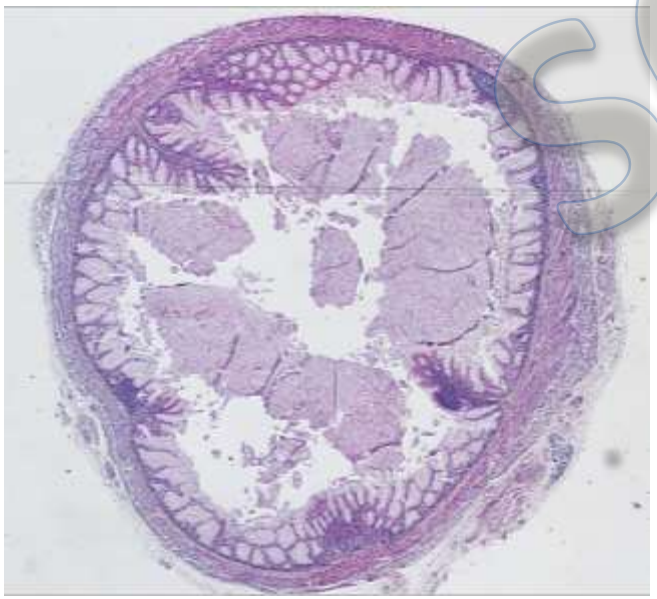
Microcolon, distal micro-ileum, dilated jejunum

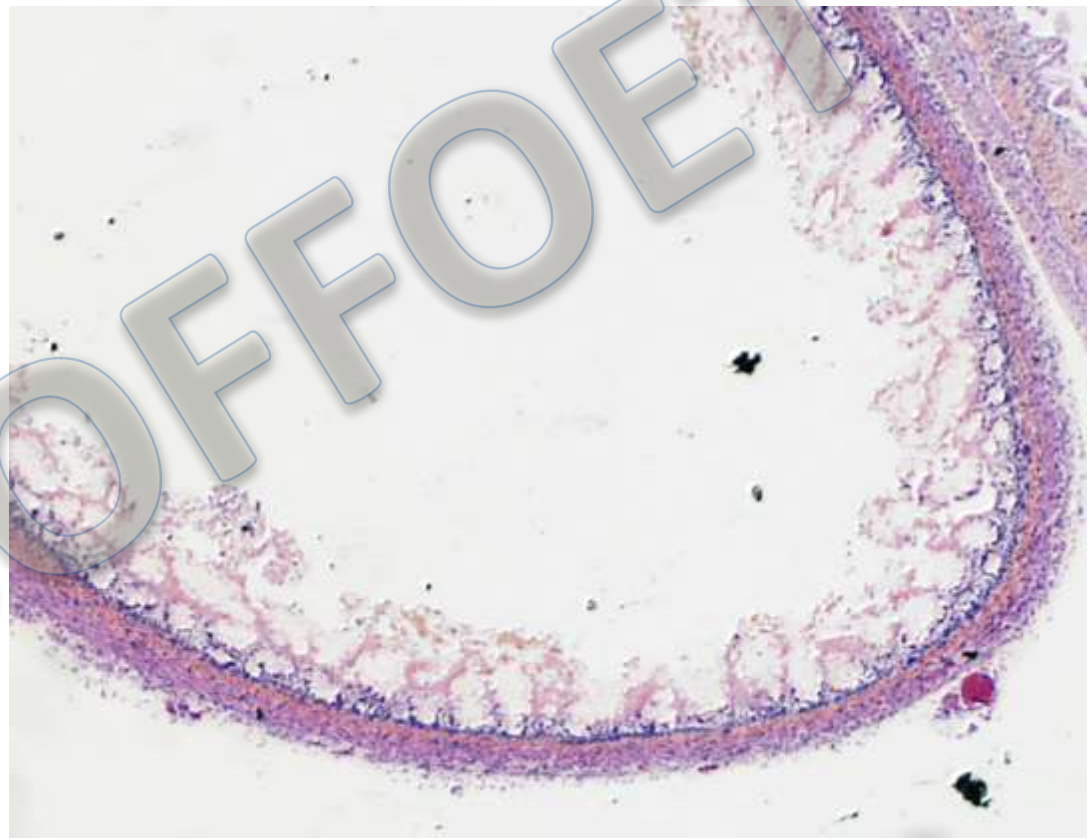
Bilateral hydronephrosis

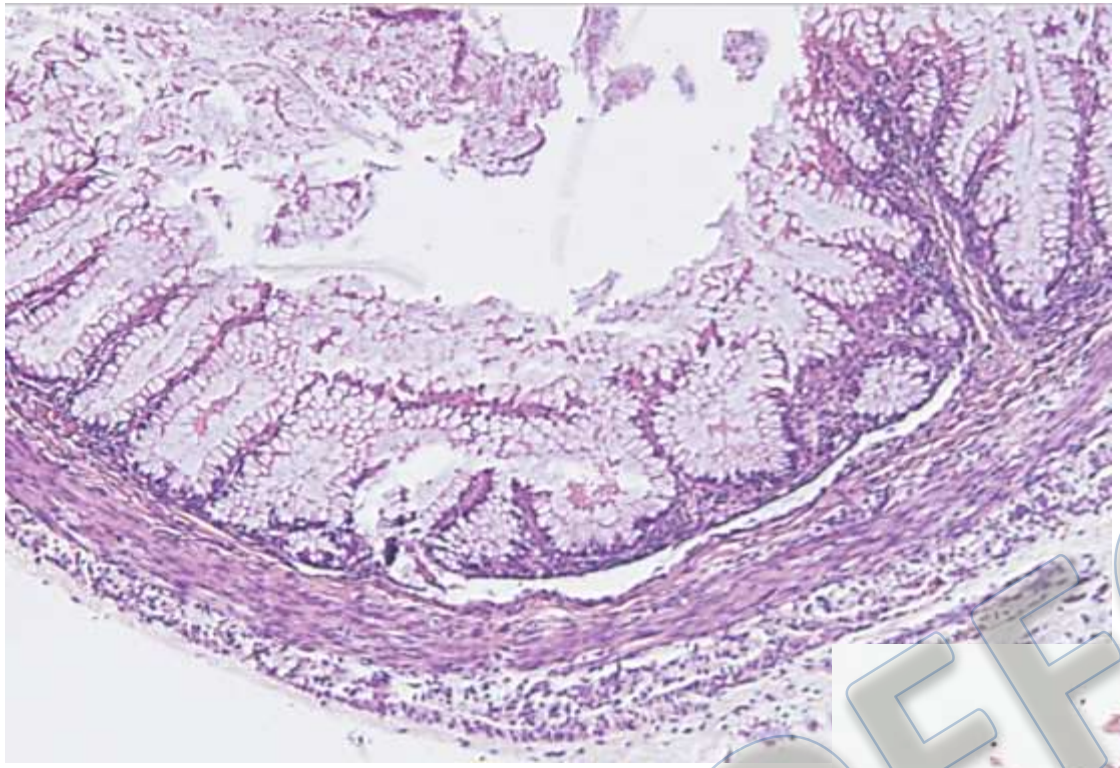


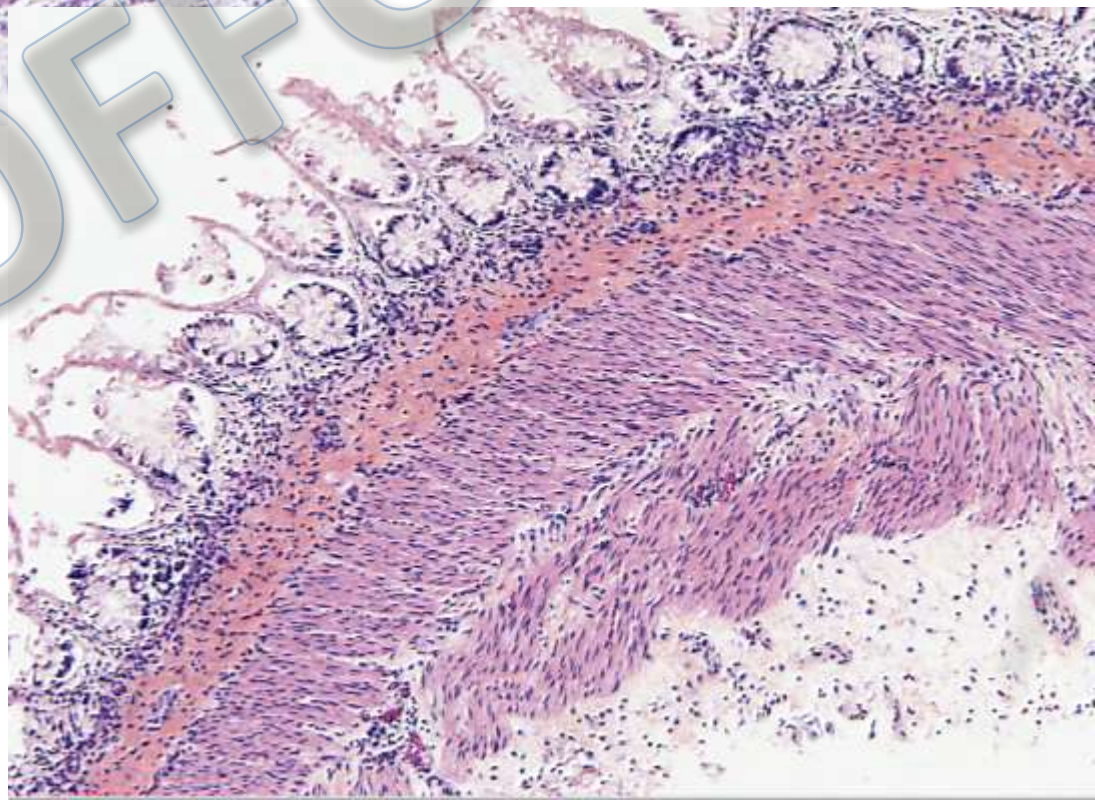
Histology





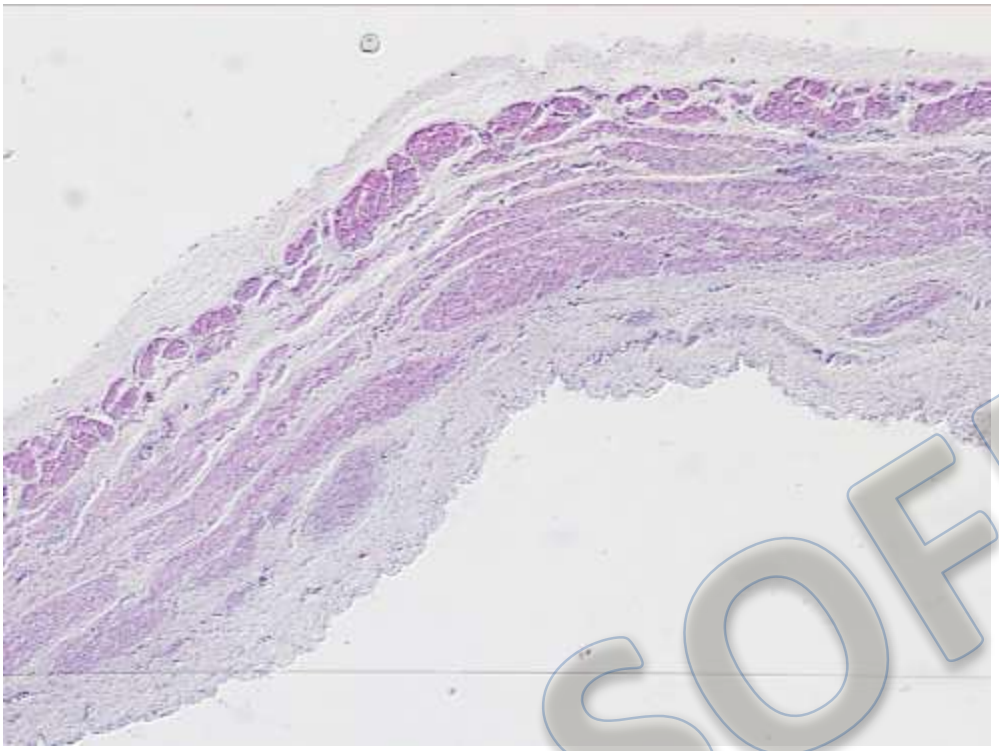


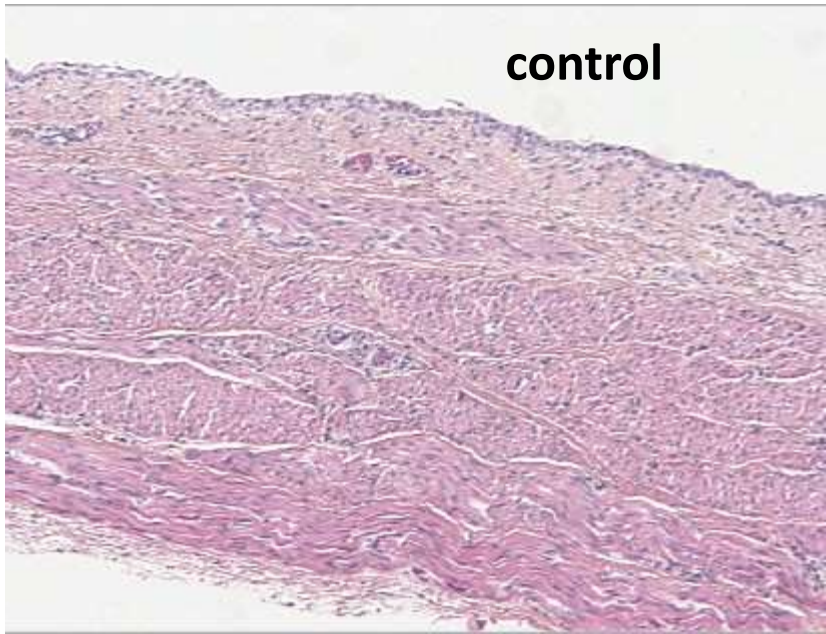


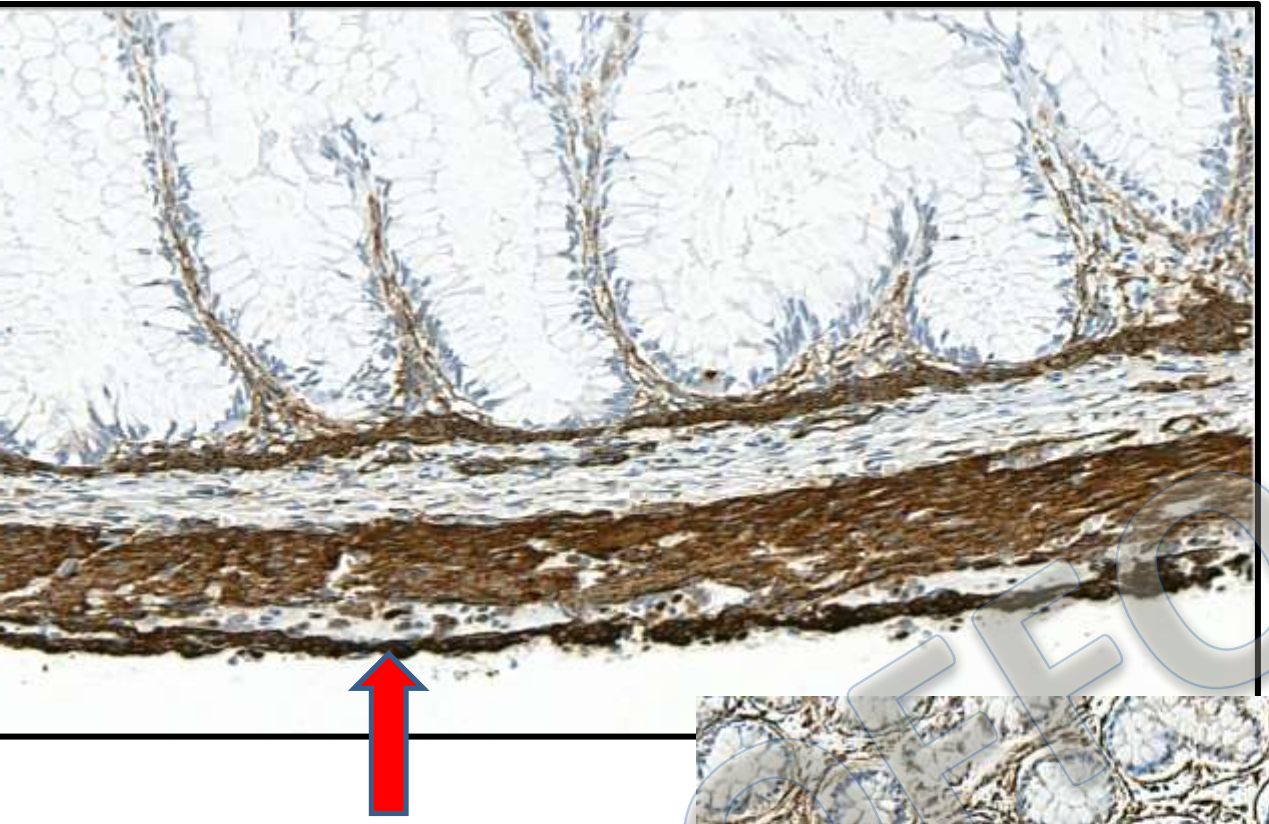


control

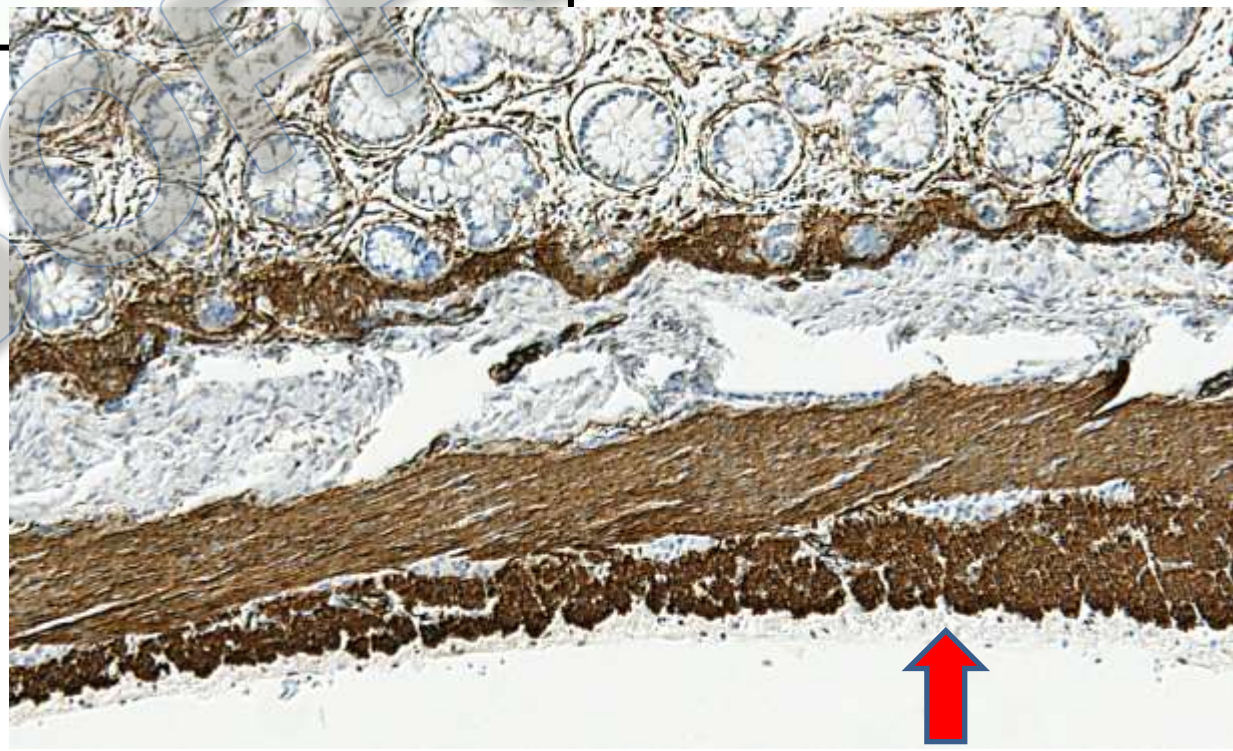
Histology: bladder







SM Actin: weak expression in muscular longitudinal external layer



control

Fetal megacystis: differentials

- **Posterior urethral valves** 57%
- Urethral atresia/stenosis 7%
- Prune-belly syndrome 4%
- **Megacystis Microcolon Intestinal Hypoperistalsis Syndrome 1%**
- Cloacal anomalies 0.7%

- Radiologist proposed the diagnosis of Megacystis Microcolon Intestinal Hypoperistalsis syndrome : MMIHS

- Post mortem findings favour diagnosis
- Molecular analysis of *ACTG2* gene showed

de novo missense mutation

exon 6, c.532C>T, p.Arg178Cys, heterozygous

Pathogen recurrent variant

(dr Rendu, Grenoble University Hospital)

Megacystis Microcolon Intestinal Hypoperistalsis syndrome (**MMIHS)**

- OMIM 155310
- Rare congenital anomaly
- First described in 1976 by Berdon
- Characterised by:
  - largely distended non-obstructed bladder causing abdominal distension
  - Microcolon with decreased or absent peristalsis
- Female predominance

MMIHS: genetics

- Between 50 and 70% of MMIHS have a heterozygous pathogenic variant in gene ***ACTG2*** (actin gamma 2) located on 2p13.1
- Missense mutation
- Identified by Lehtonen et al. in 2012
- *ACTG2* encodes for smooth muscle actin
- Autosomal dominant inheritance or de novo
- De novo mutation responsible for severe phenotype **MMIHS**

ACTG2 disorders

- Visceral myopathy
- Spectrum of disease, multiple phenotypes
- Intestinal hypoperistalsis as common denominator
- Variable involvement of bladder and intestine
- MMIHS is the most severe form
- Prune-belly syndrome
- Chronic Intestinal Pseudo Obstruction (CIPO)

ACTG2 disorders

- No phenotype/genotype correlation
- Complete penetrance
- Inter and Intrafamilial variability
- Whittington et al. reported a case
  - Woman with history of CIPO
  - 5 prior surgeries on her intestine and colon
  - Gave birth to a child with MMIHS
  - Same new mutation of ***ACTG2***

Case Rep Genet, 2017

Prognosis of MMIHS

- Poor
- Urinary tract infection and bowel obstruction
- Death generally occurs before the age of 6 months
- Patients require total parental nutrition and urinary catheterization

- Prenatal surgical procedures such as in utero drainage are useless
- Termination of pregnancy

Prenatal findings MMHIS

- 50 cases (Tuzovic, 2014)
  - Prenatal diagnosis made at second trimester in 26% of cases
  - Half of these had a previously affected sibling
  - **Fetal megacystis +/- hydronephrosis 88%**
  - Gastrointestinal abnormalities in 24% of pregnancies
  - Amniotic fluid normal :69 % ; increased 27%.

Conclusion

- MMIHS is a rare condition
- Should be considered in the setting of fetal megacystis
- Gastrointestinal abnormalities are present
- Poor prognosis
- Termination of pregnancy
- *ACTG2* analysis not done prenatally
- Other genes have to be identified

Merci de votre attention!

Avez-vous un cas (avec génétique)? Suis intéressée !

BIENVENUE A ROUEN !