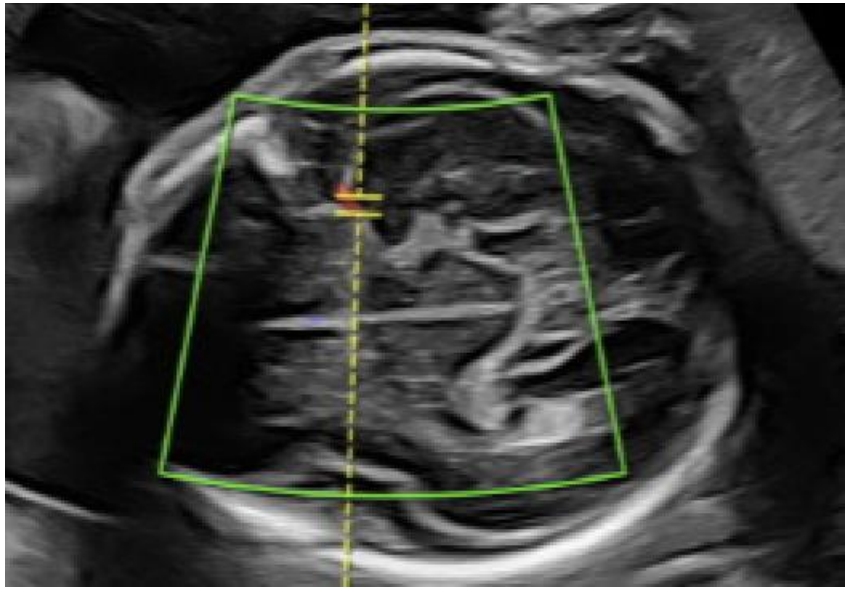
Practical exemples

CLINICAL INFORMATION

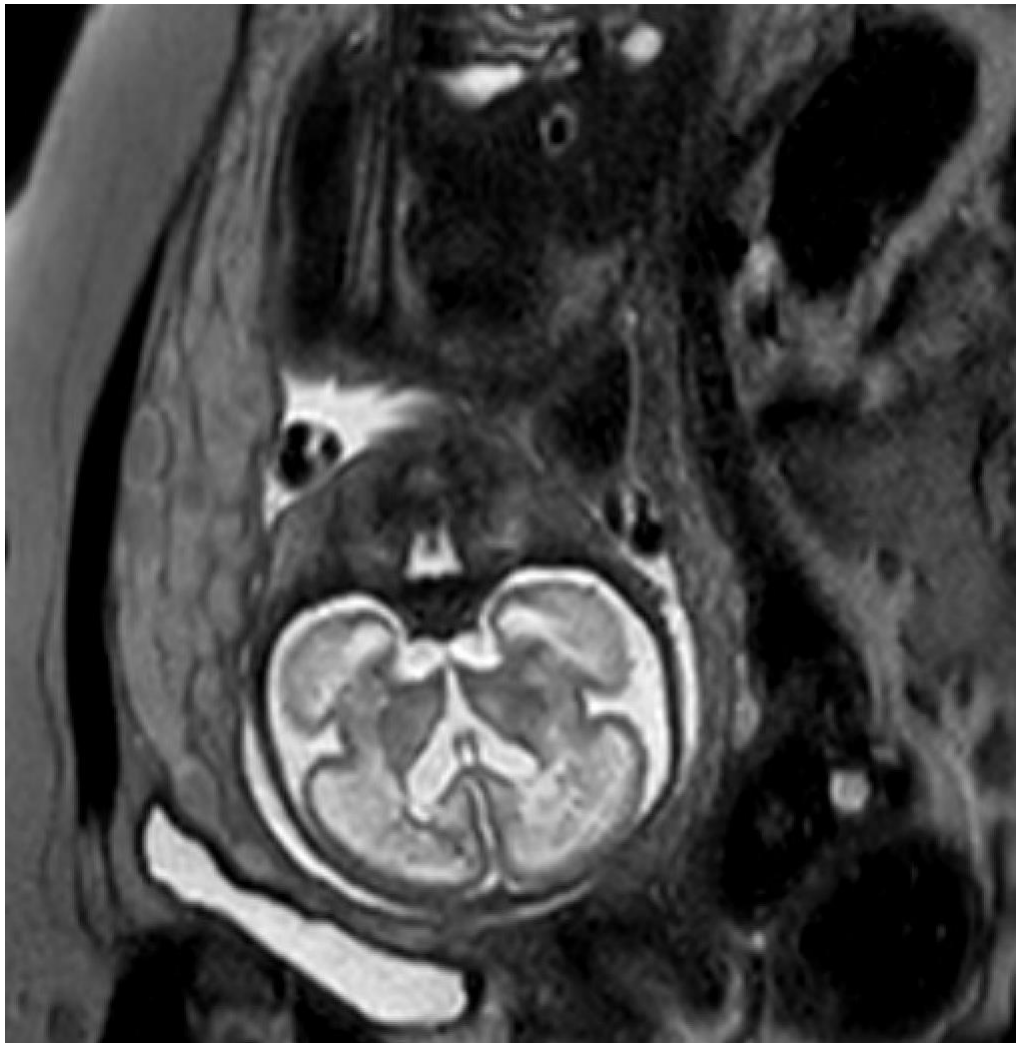
- Healthy mother, 38 Y, 1 healthy child

- Uneventful pregnancy until referral at 23 GW
- US 23 GW: bilateral very mild hydronephrosis, polyhydramnios
  - Brain normal on US



CLINICAL INFORMATION

- MRI 27 GW
  - Hyperintensity paraventricular bifrontaal + hypointensities
  - Irregular cortical mantle, suspicious for Polymicrogyria
  - **Mild** ventriculomegaly
  - Abnormal cerebellar hemipheres



CLINICAL INFORMATION

- MRI 27 GW
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  - Irregular cortical mantle, suspicious for Polymicrogyria
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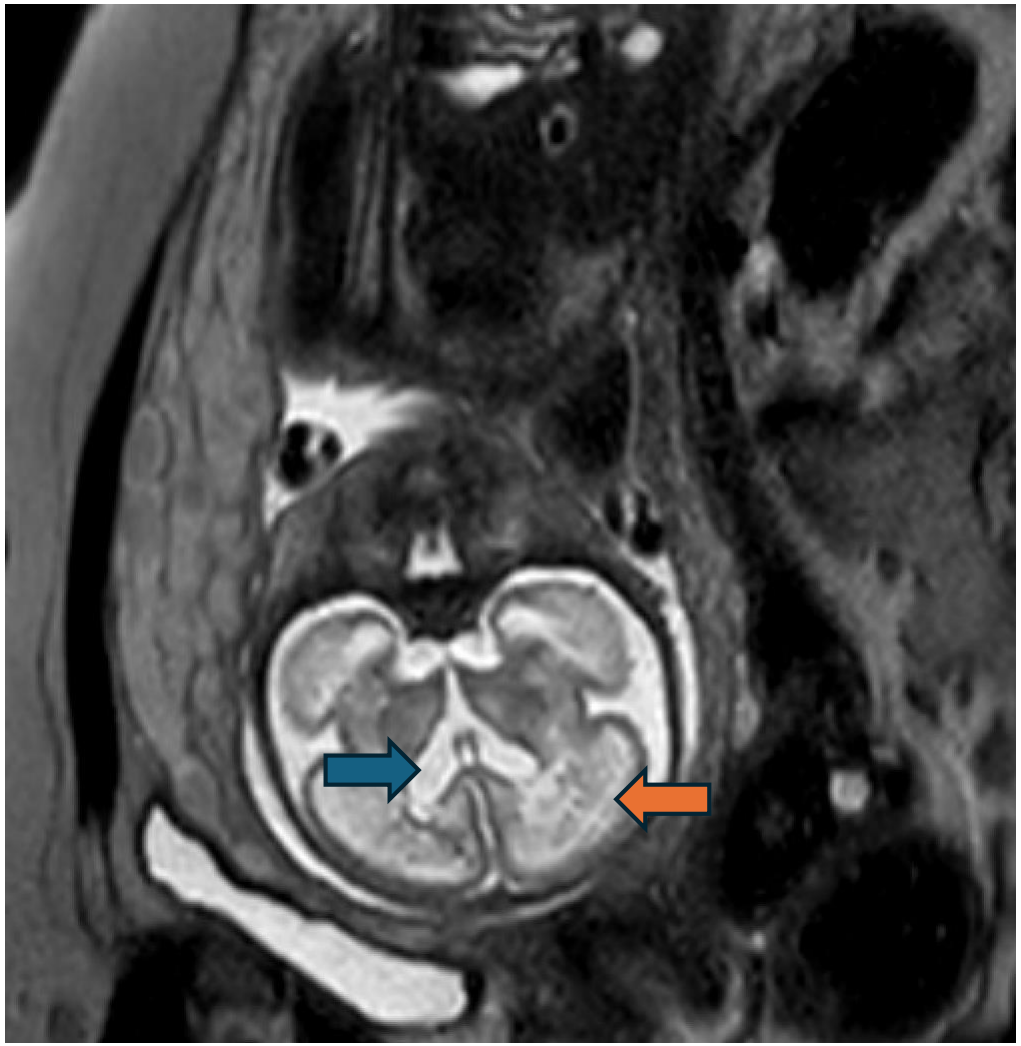
  - Abnormal cerebellar hemipheres



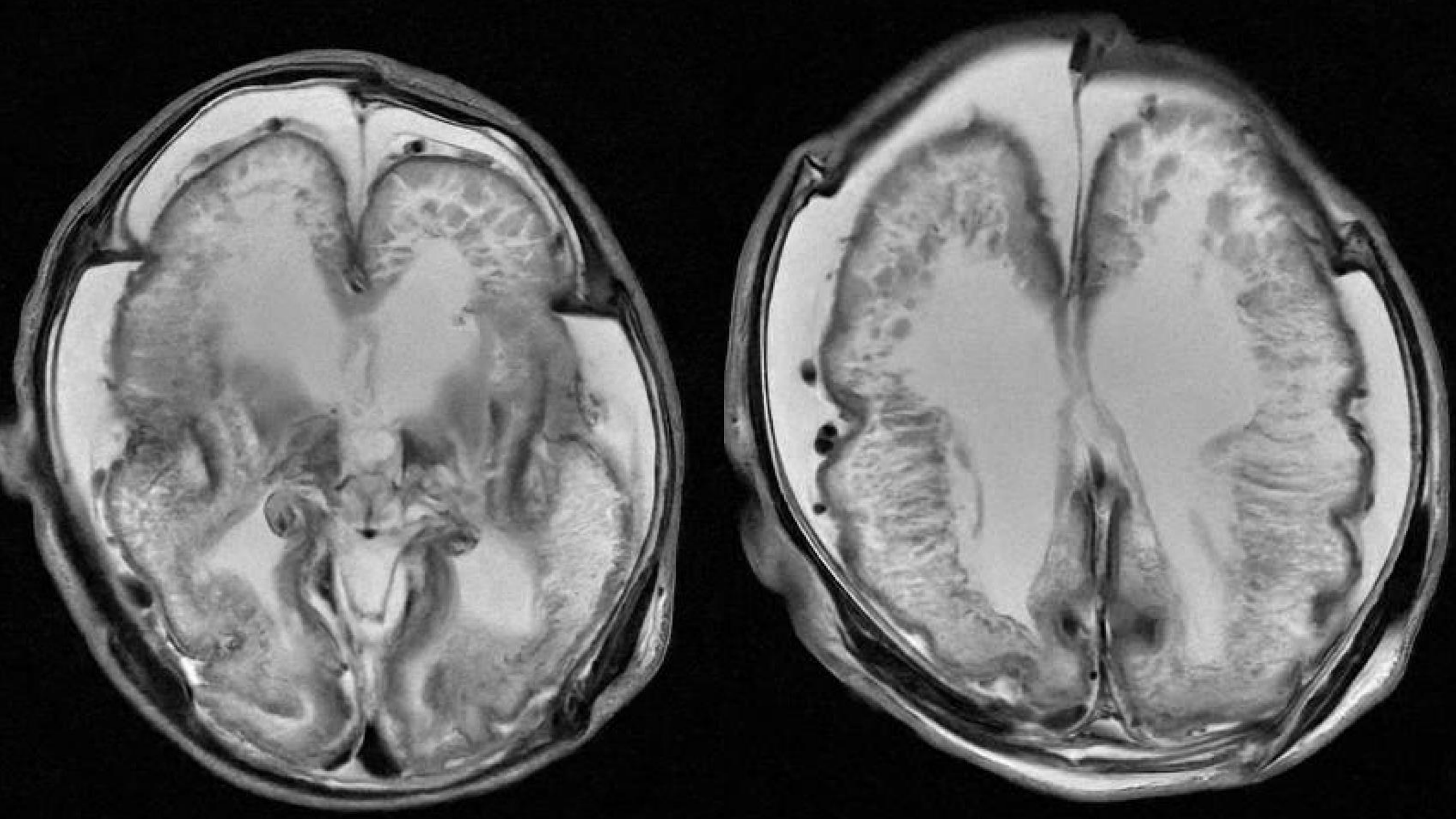
CLINICAL INFORMATION

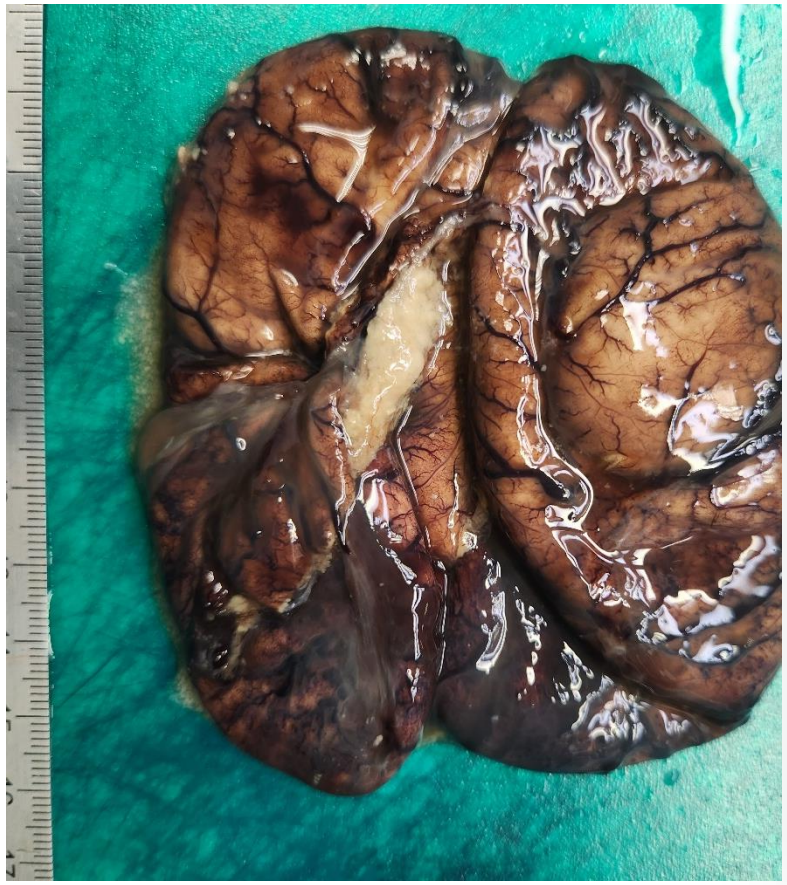
- Referal at 23 GW
- US: bilateral hydronephrosis, incomplete cardioscreening, polyhydramnios

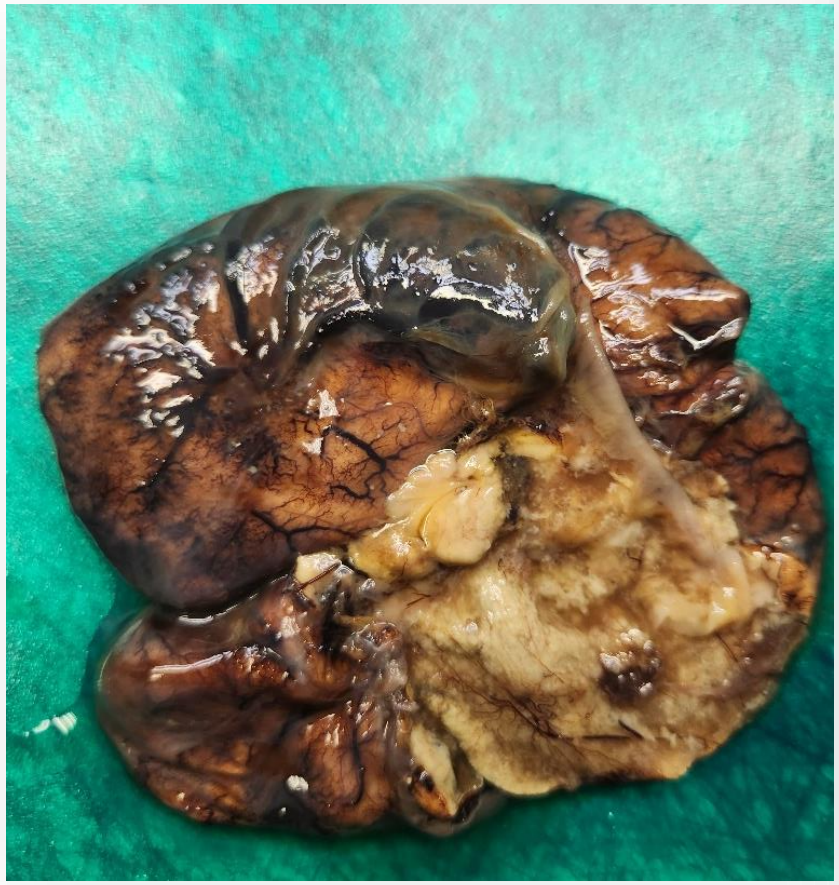
- MRI 27 GW
  - Hyperintensity paraventricular bifrontaal + hypointensities
  - Irregular cortical mantle, suspicious for **PMG**
  - Mild ventriculomegaly.
  - Abnormal cerebellar hemipheres

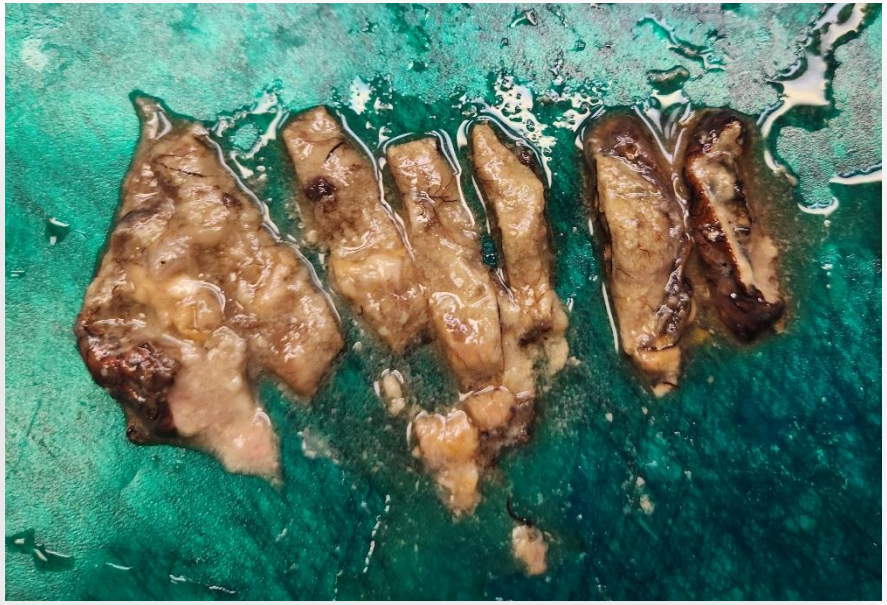
- US 28w → 29 w : evolutive panventricular hydrocephaly

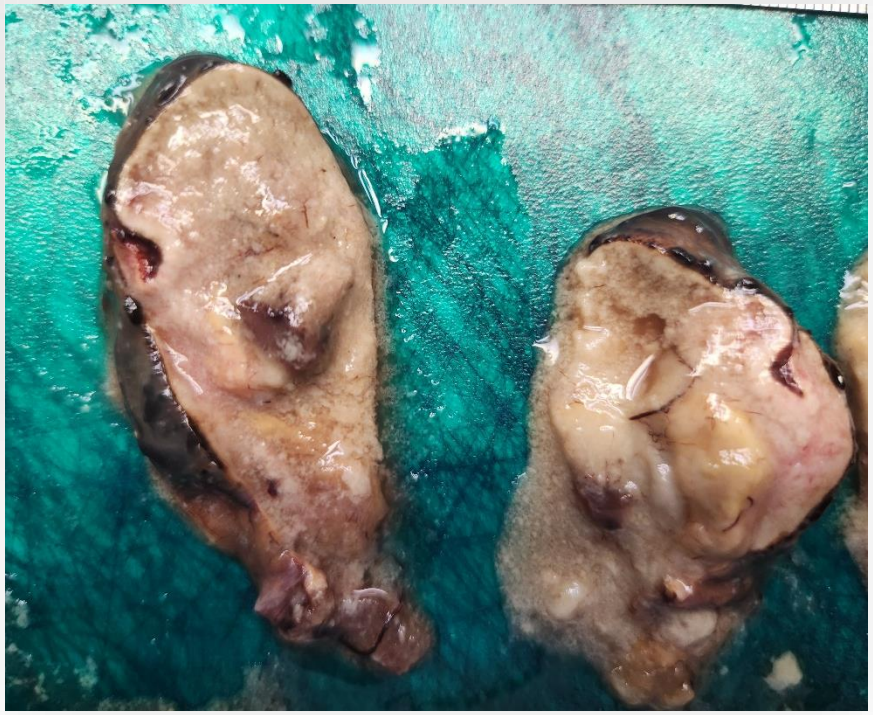
- TOP 30 GW : Autopsy: No external abnormalities, hepatosplenomegaly



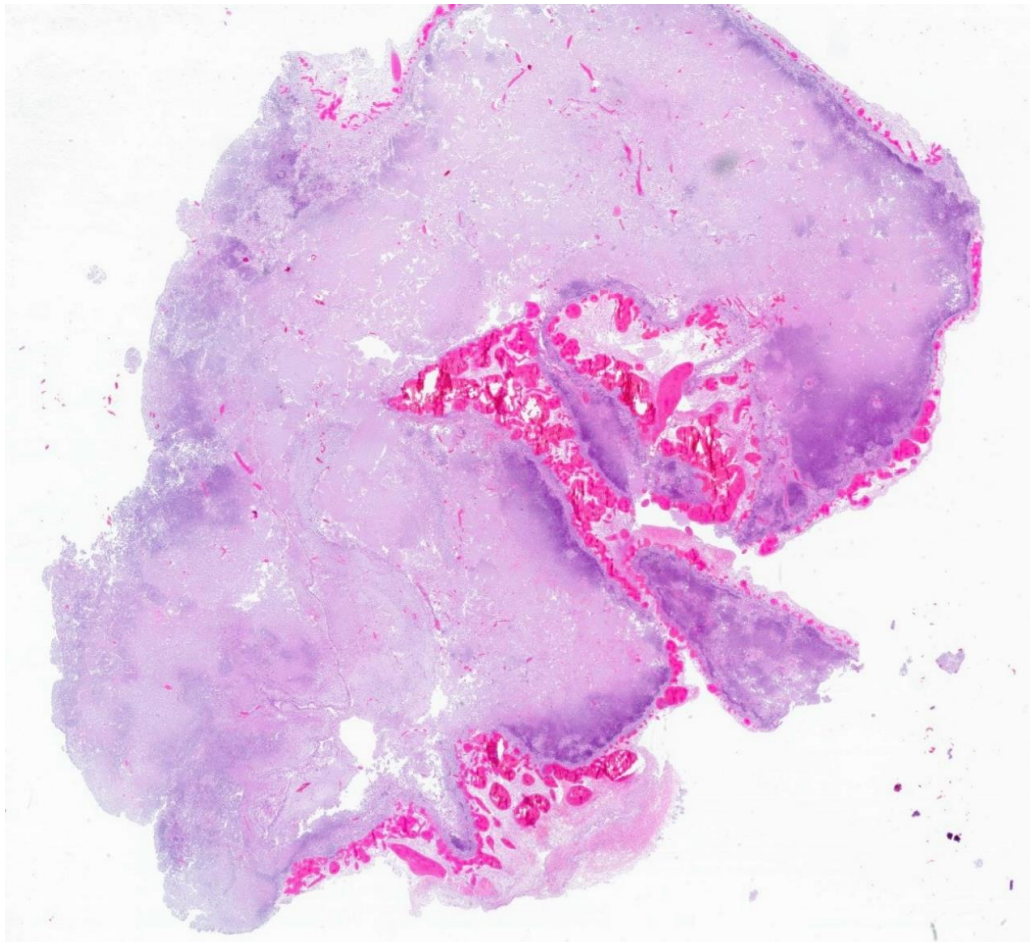




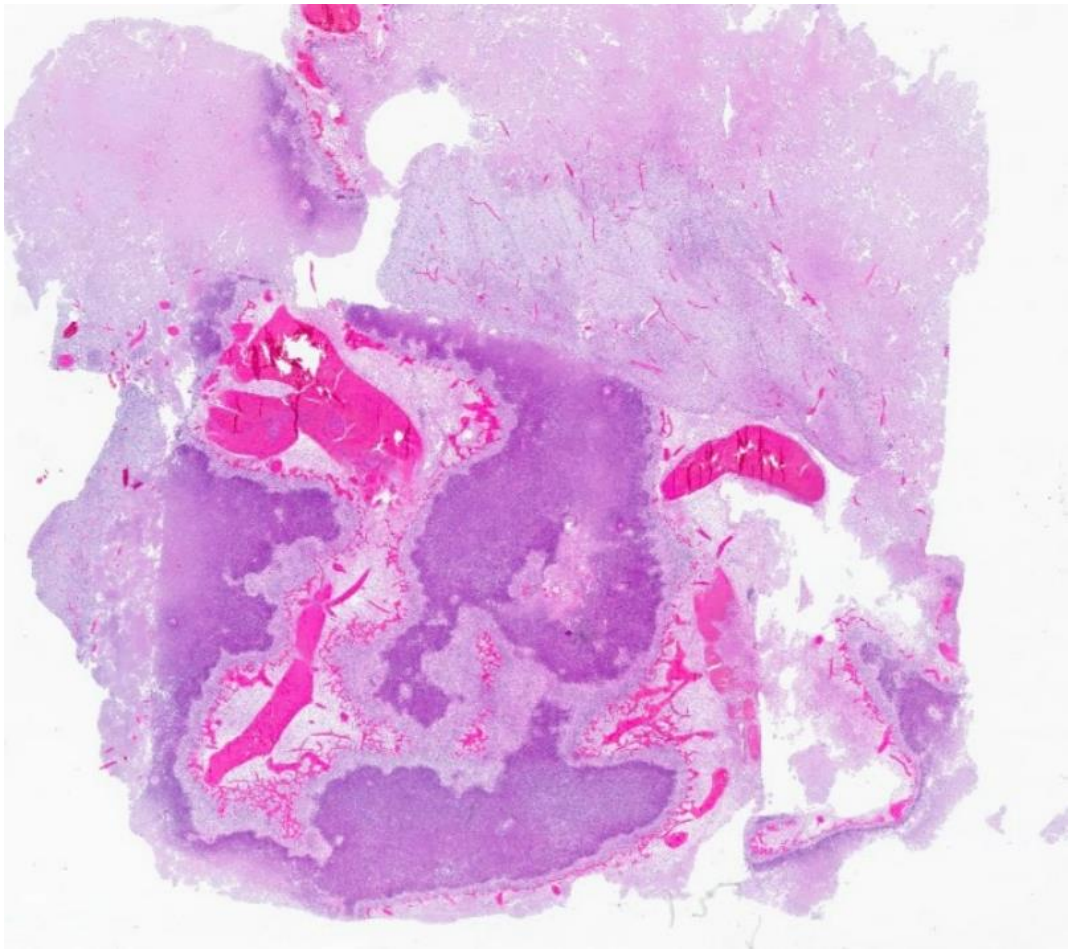


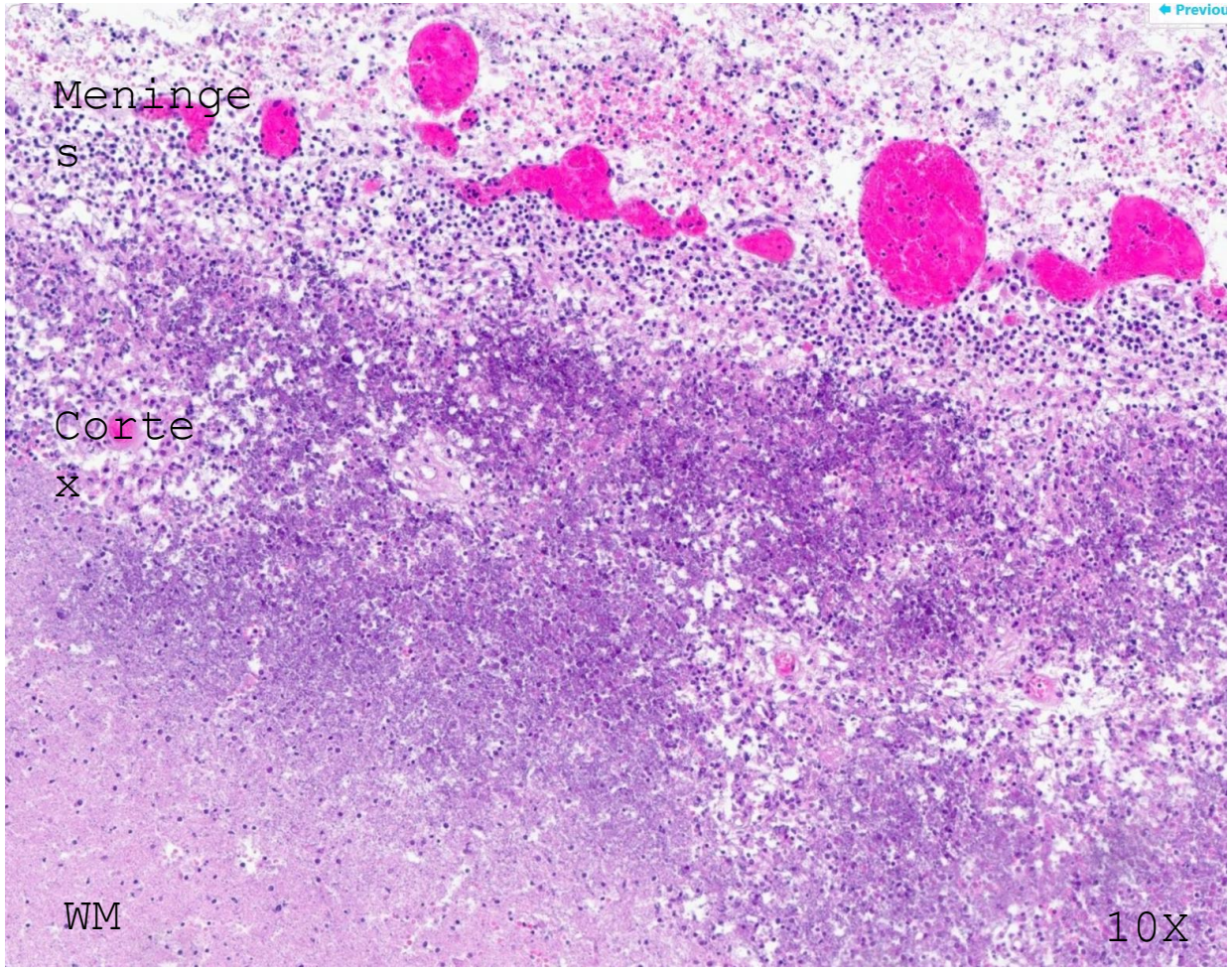


- Frontal Right



- Frontal Left




Meninge
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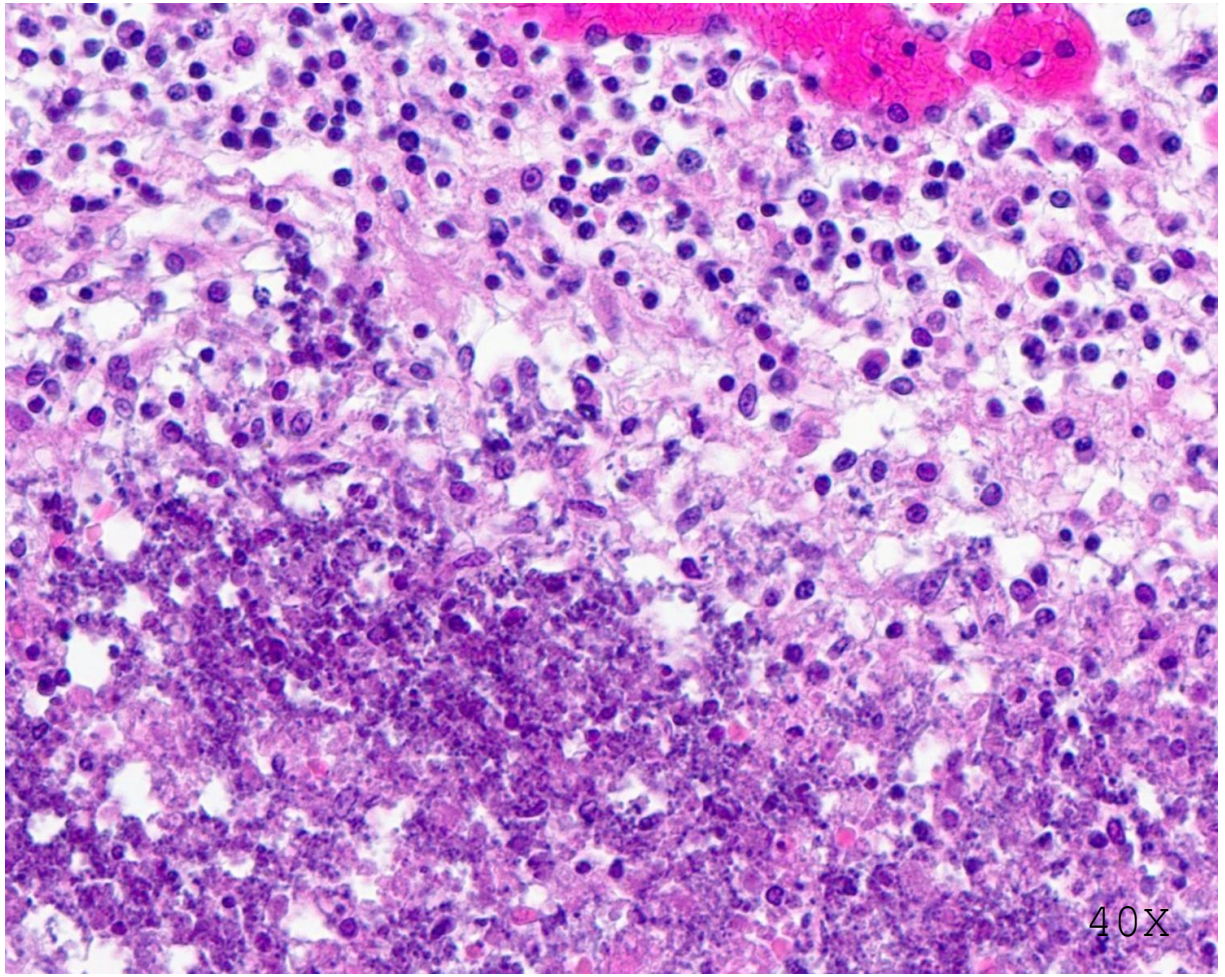
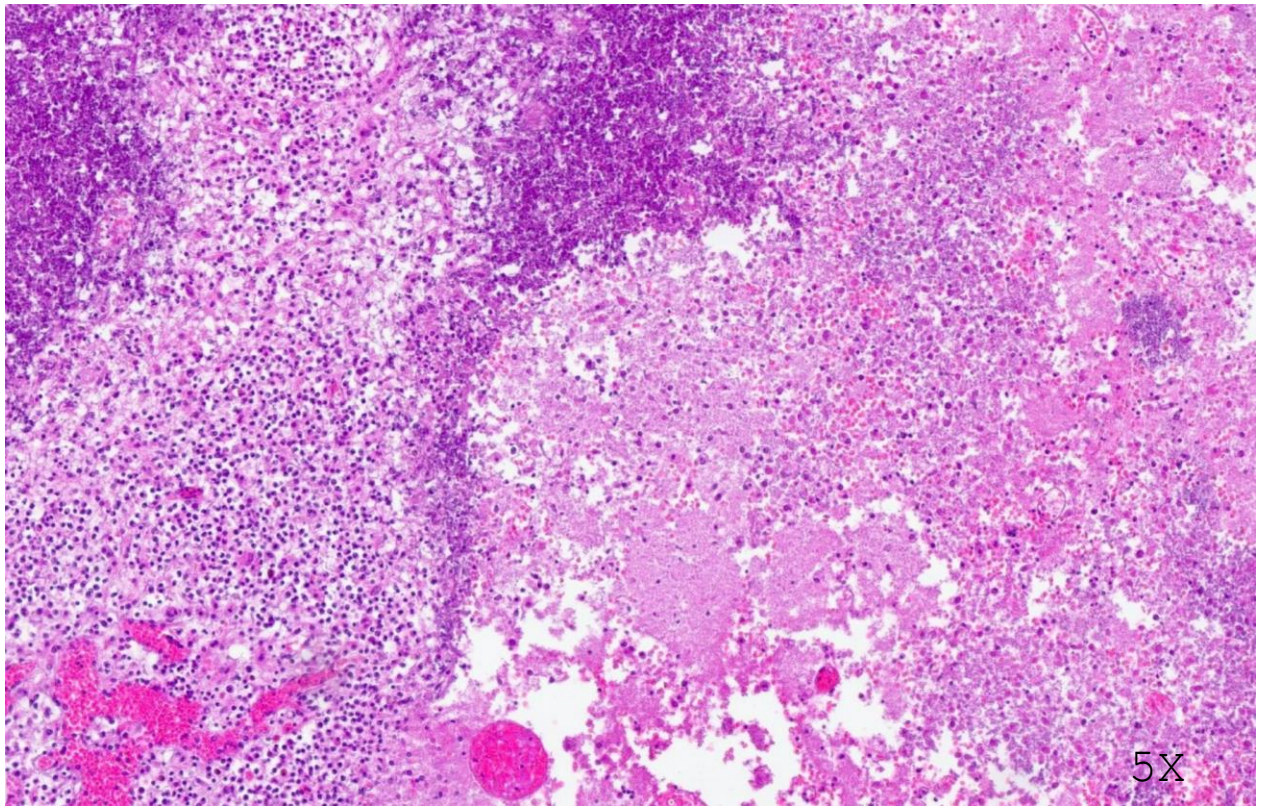

40X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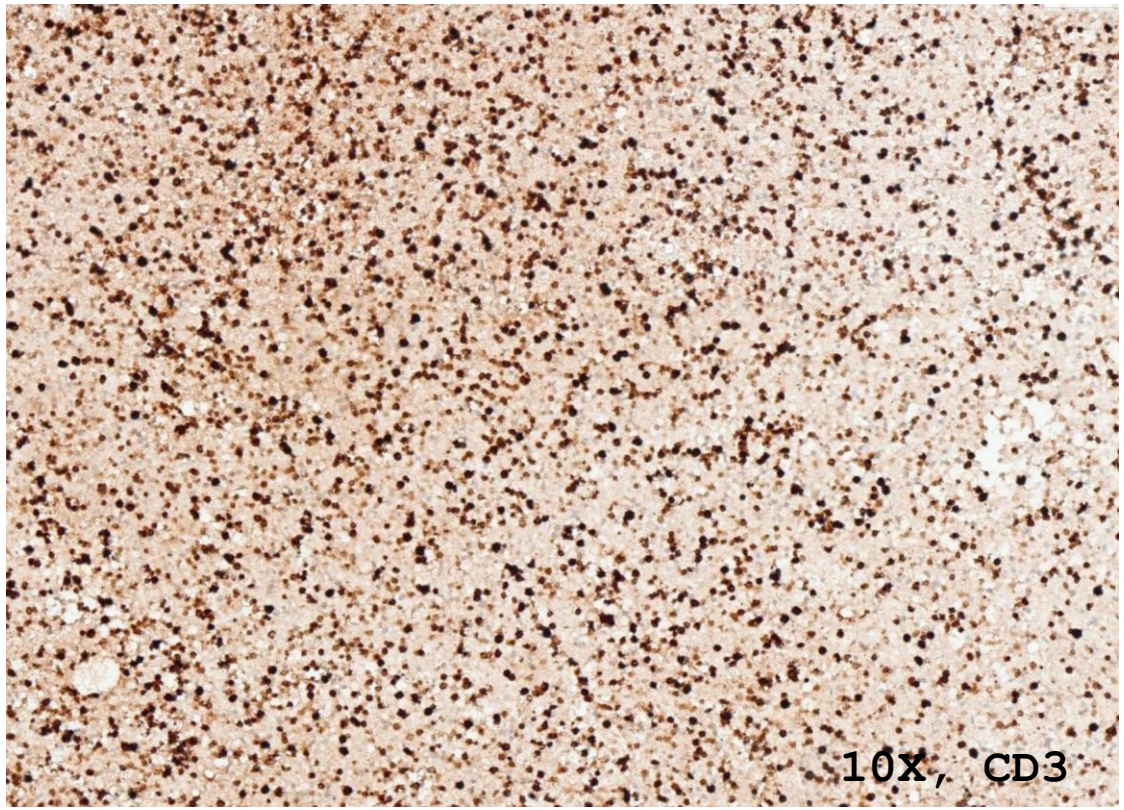
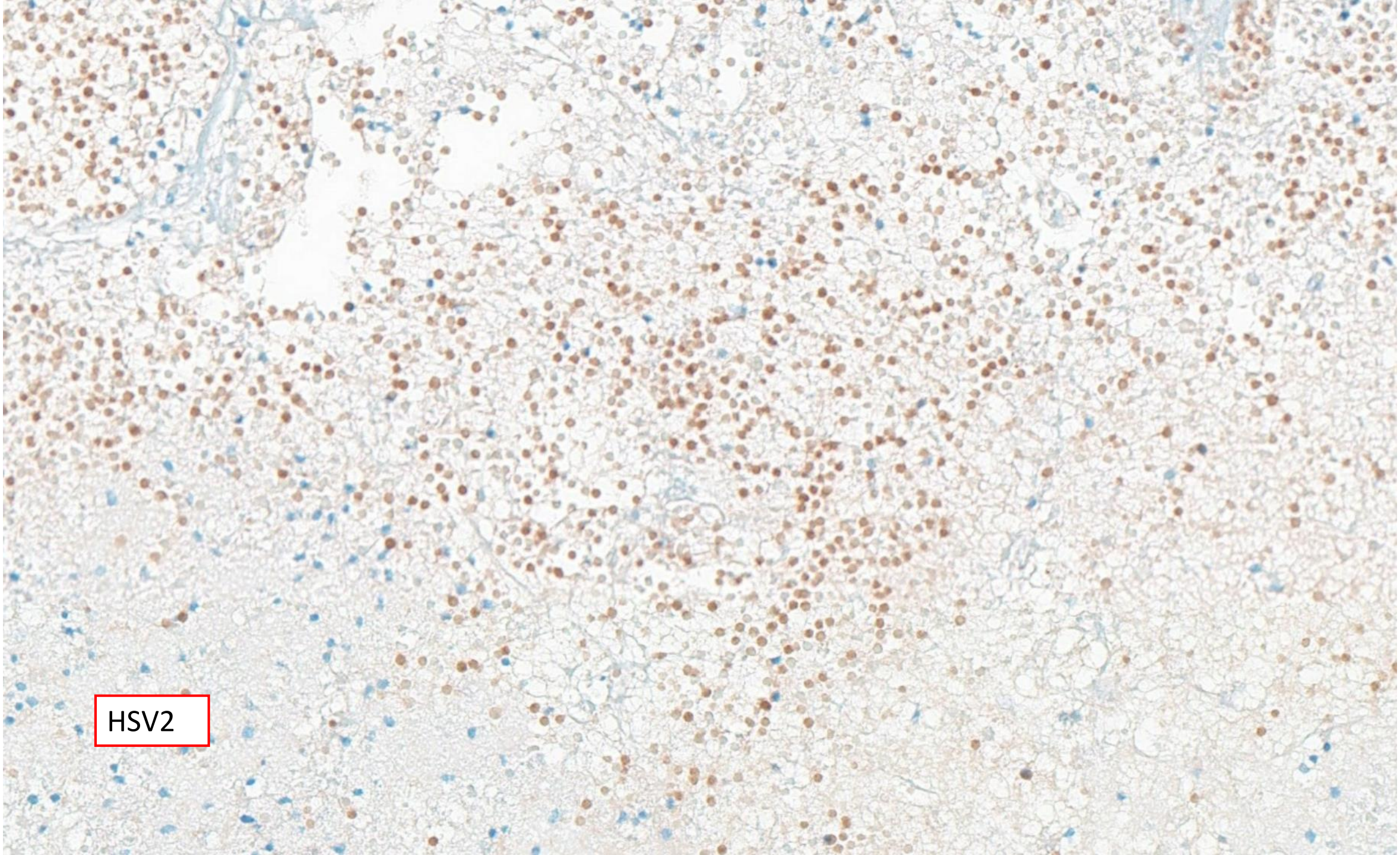

10x, CD3


HSV2

Microbiologie
Amnionvocht
Herpes simplex virus - PCR
Positief voor het herpes simplex virus type II

Placenta

- Hypotrofic placenta (p3)
- FVM
- Acute + chronic chorioamnionitis
- No villitis
- HSV IHC focally weakly positive but no viral inclusions seen

Diagnosis: Congential **HSV2 infection in utero.**

- Mother-to-child transmission can occur ***in utero*** (5%)
  - *E*stimated transmission rate of 1 in 300,000 deliveries
- Peripartal (85%) and postnatal transmission (10%) are more common
- Found to occur with both primary and recurrent maternal HSV infections
- Nearly 80% of women who deliver an HSV-infected infant **have no known history of genital HSV lesions**

J Pediatric Infect Dis Soc. 2014 Sep;3(Suppl 1):S19–S23. doi: 10.1093/jpids/piu050

Mother-to-Child Transmission of Herpes Simplex Virus

Scott H James [1], Jeanne S Sheffield [2], David W Kimberlin [1]

A Report of Three Cases and Review of Intrauterine Herpes Simplex Virus Infection

Lucila Marquez [*], Moise L Levy [*,†,‡,§], Flor M Munoz [*,¶], Debra L Palazzi [*]

HSV infection

- *In utero* HSV: distinct clinical entity characterized by the **triad** of :
  - cutaneous findings,
  - neurologic manifestations present at birth.
  - eye abnormalities

- Disseminated form : hemorragic necrosis, lymphocytic infiltration, destruction, calcifications
  - liver, adrenals, lungs, brain, and heart. Hemorrhagic necrosis is the predominant

Congenital infections

- Major cause of premature birth, maternal and fetal morbidity and mortality

- Can be bacterial, viral, fungal or parasitic
- TORCHES: toxoplasmosis, rubella, CMV, herpes, syphillis

- Fetal infection can occur by:
  - Hematogenous spread
  - Extension from urogenital tractus or iatrogeneous spread

Table 22.7 Viruses that may cause congenital or perinatally acquired infection or disease

DNA viruses
- Cytomegalovirus
- Herpes simplex virus types 1 and 2
- Varicella-zoster virus
- Human parvovirus B19
- Hepatitis B virus
- Variola virus (smallpox virus)
- Human papilloma viruses

RNA viruses
- Rubella virus
- Mumps virus
- Measles virus
- Enteroviruses (coxsackie virus, echo virus, polio viruses)
- Hepatitis C virus
- Lymphocytic choriomeningitis virus
- HIV

ZIKA

Covid 19

Congential infection

- When to think about it?:

- IUGR
- Cutaneous lesions
- Hepatosplenomegaly, thymus hypoplasia
- Calcifications or necrosis
- CNS abnormalities
- Etc.

- Importance of Placental examination !!!

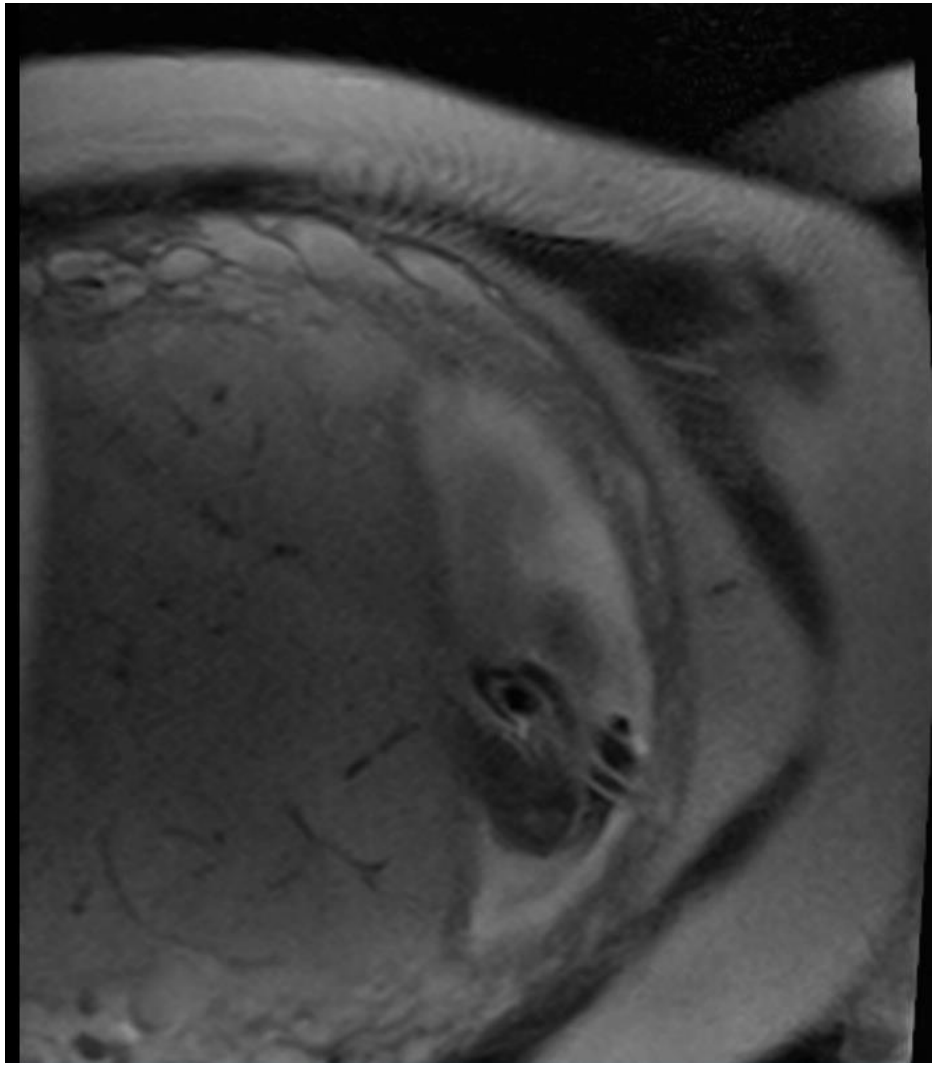
Clinical case

- 29-year-old Polish
- G1P0
- Well controlled hypothyroidism
- 2nd opinion for multiple complex congenital malformations

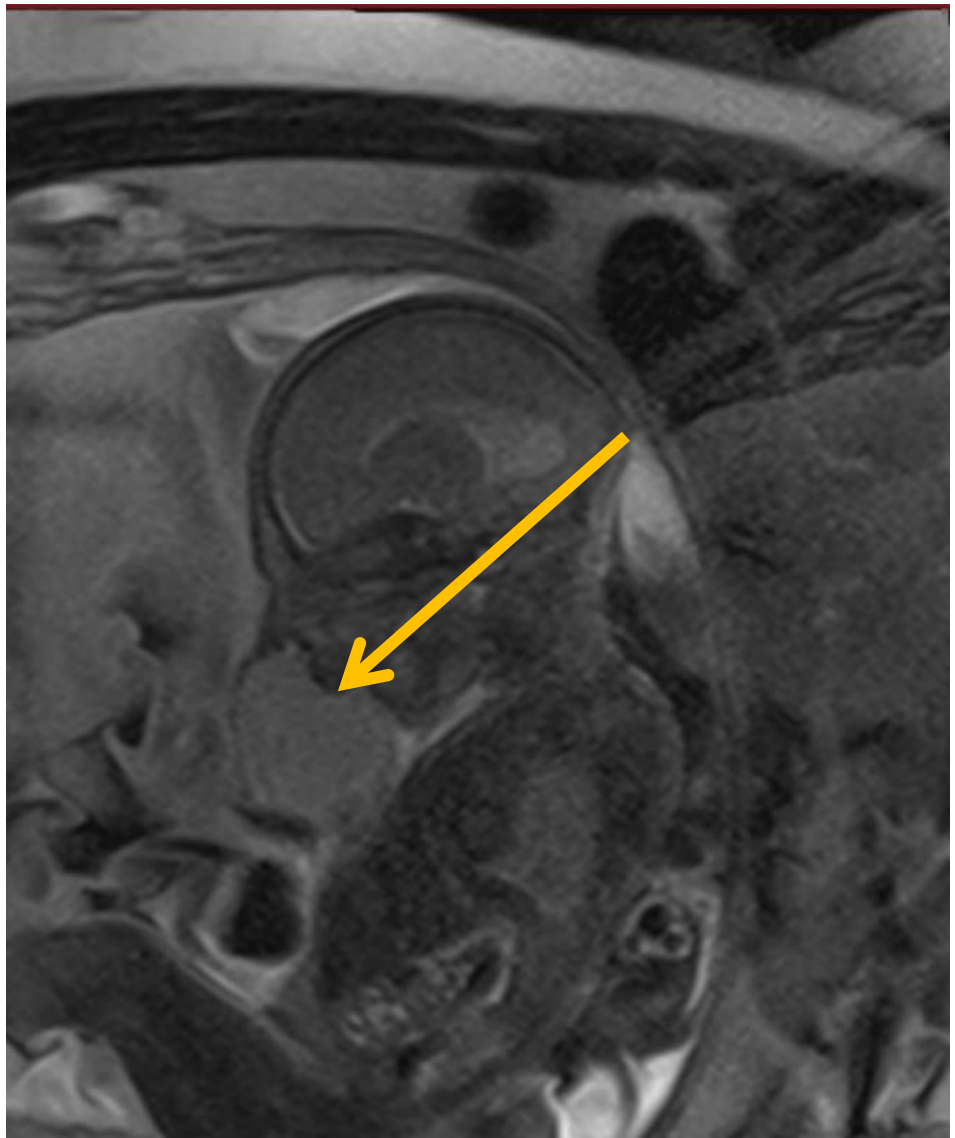
Clinical Case

- 1st trimester scan and NIPT : normal
- 2nd trimester scan 21 WG:
  - Large anechoic cystic structure with internal solid elements
  - Protruding from the fetal mouth
  - Appeared to be connected to the intracranial space
  - Via a defect in nasopharynx.

Pre termination MRI 28WG



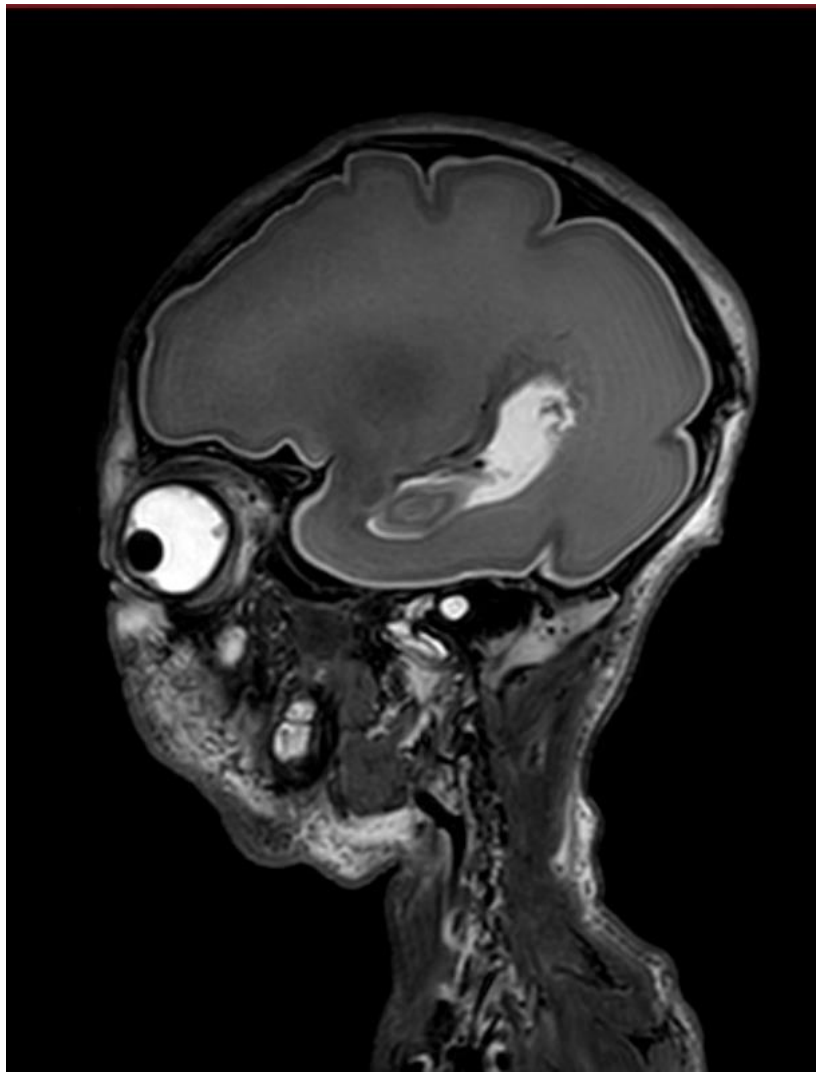
Pretermination MRI



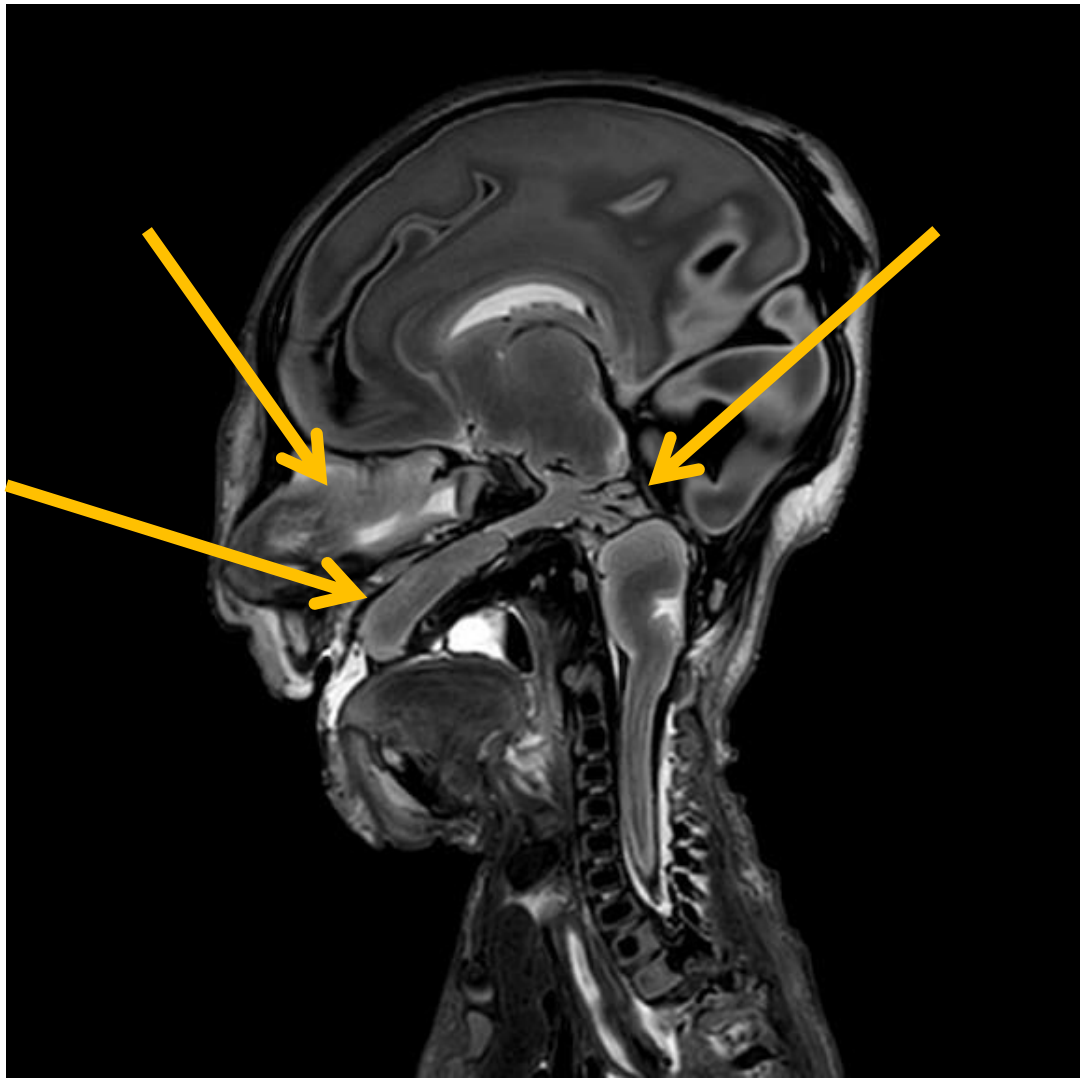
Clinical case

- Other abnormalities
  - Polyhydramnios
  - Cleft palate
  - Micrognathia
  - Hypoplastic and abnormally positioned cerebellum
  - Thin corpus callosum

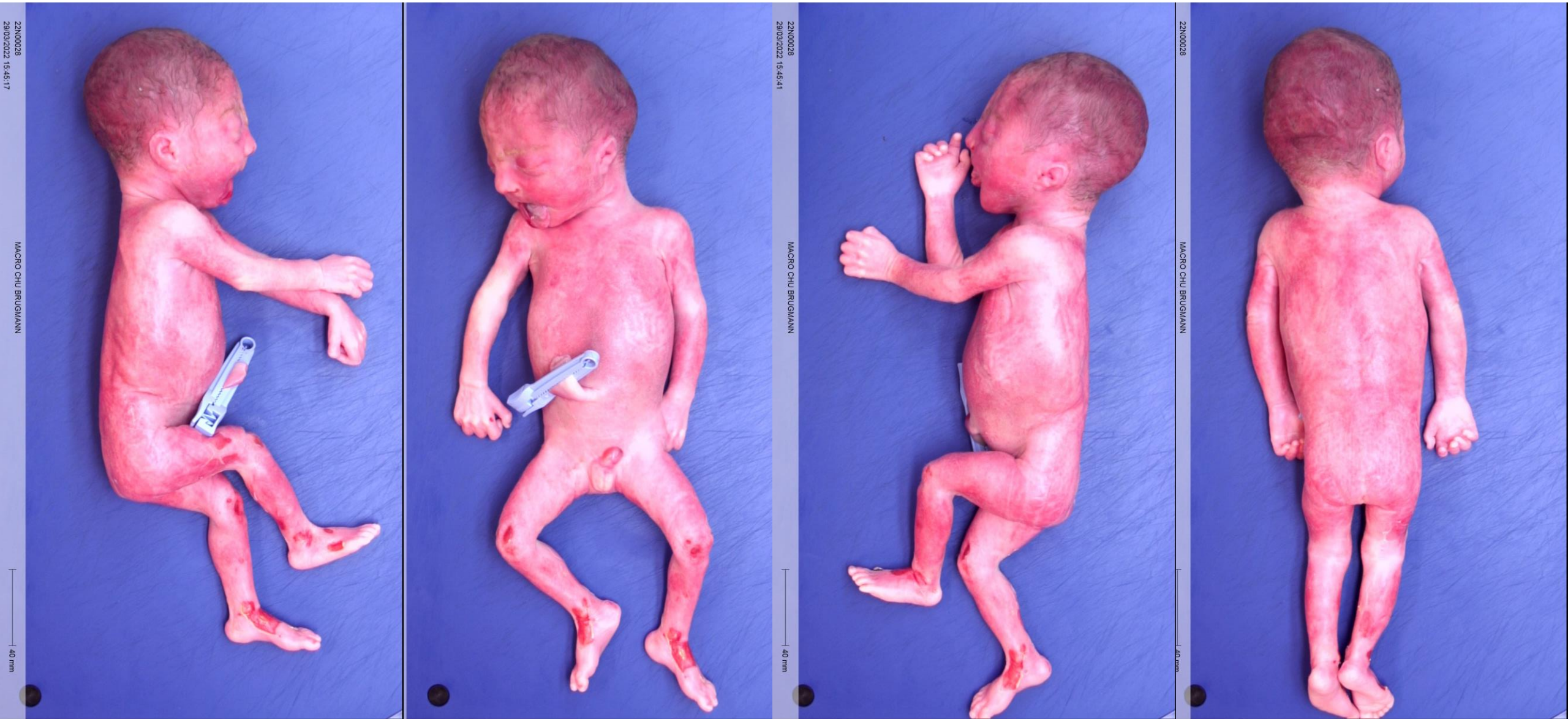
Postmortem MRI



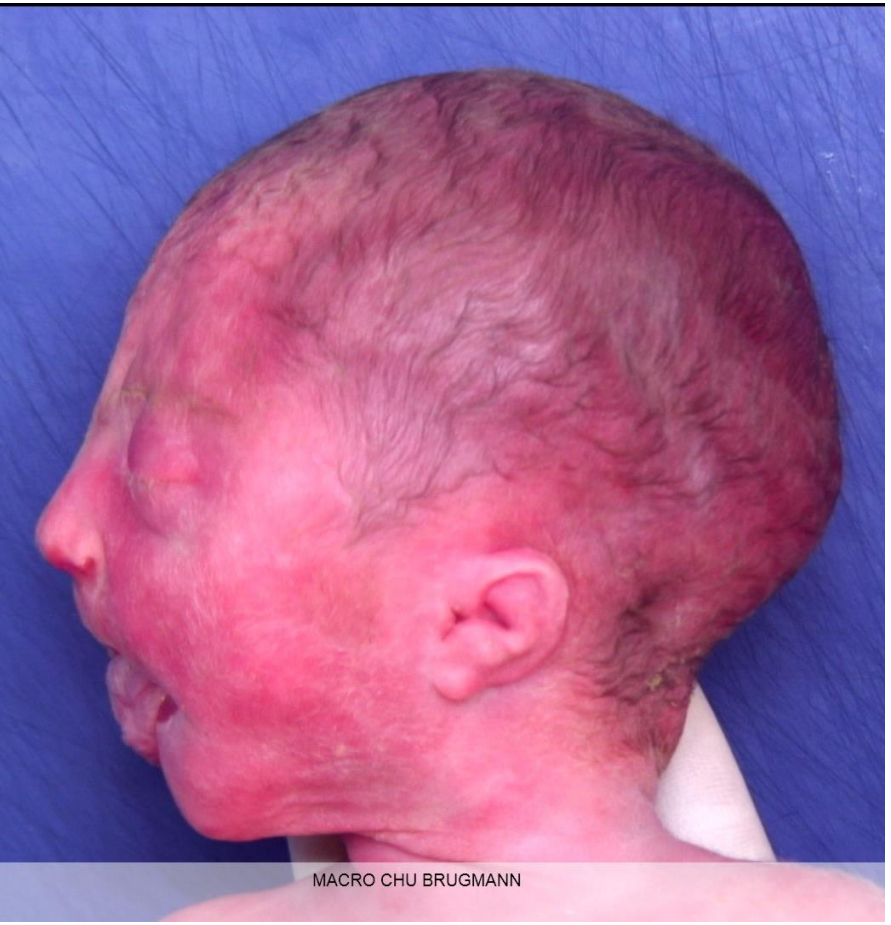
Postmortem MRI

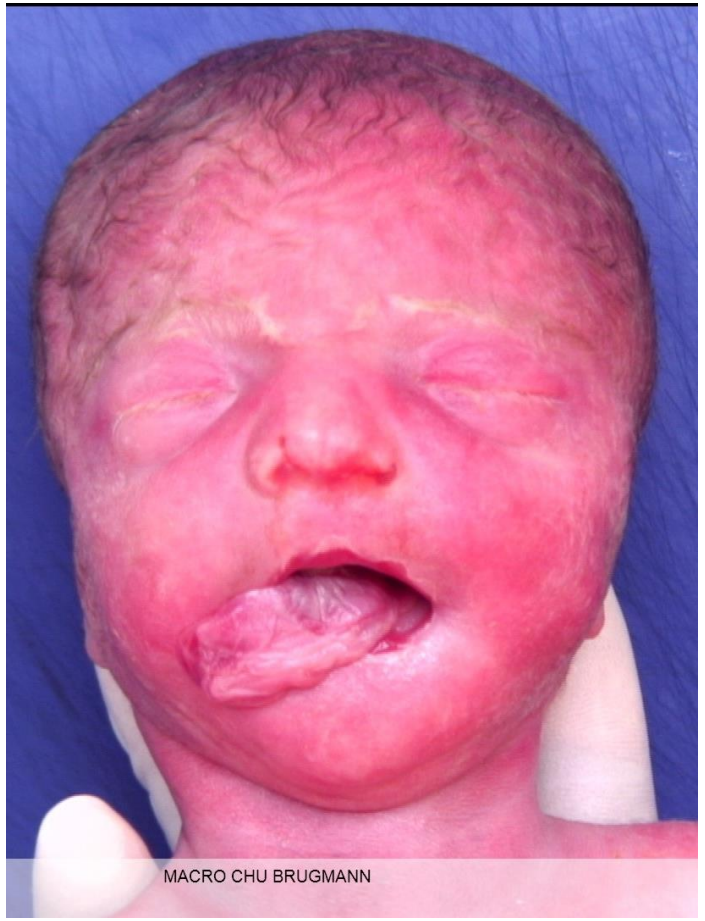


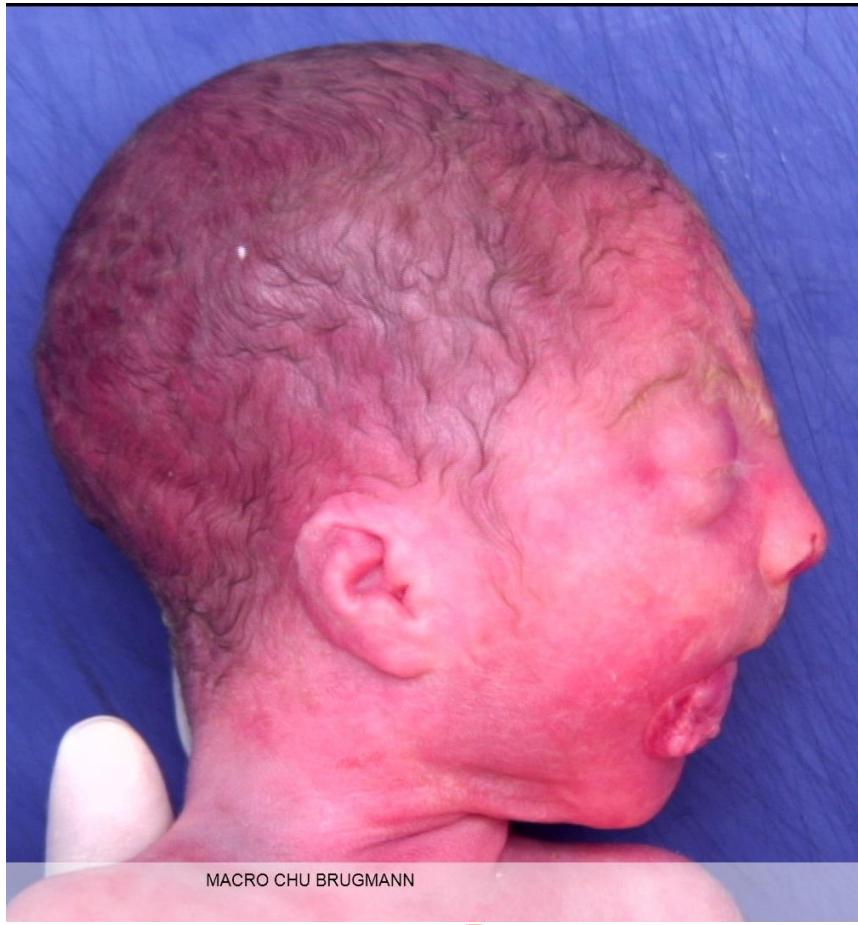
External examination



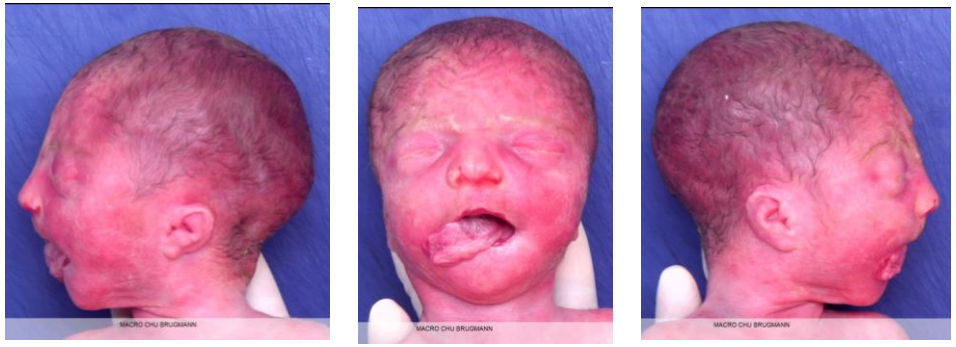
External examination





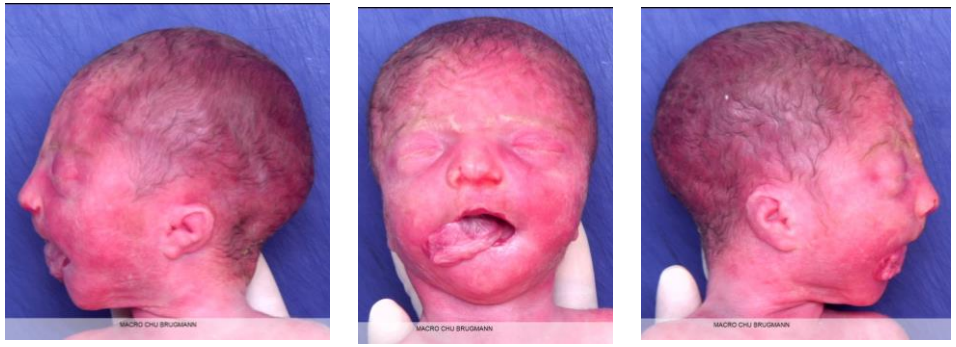


External examinatio

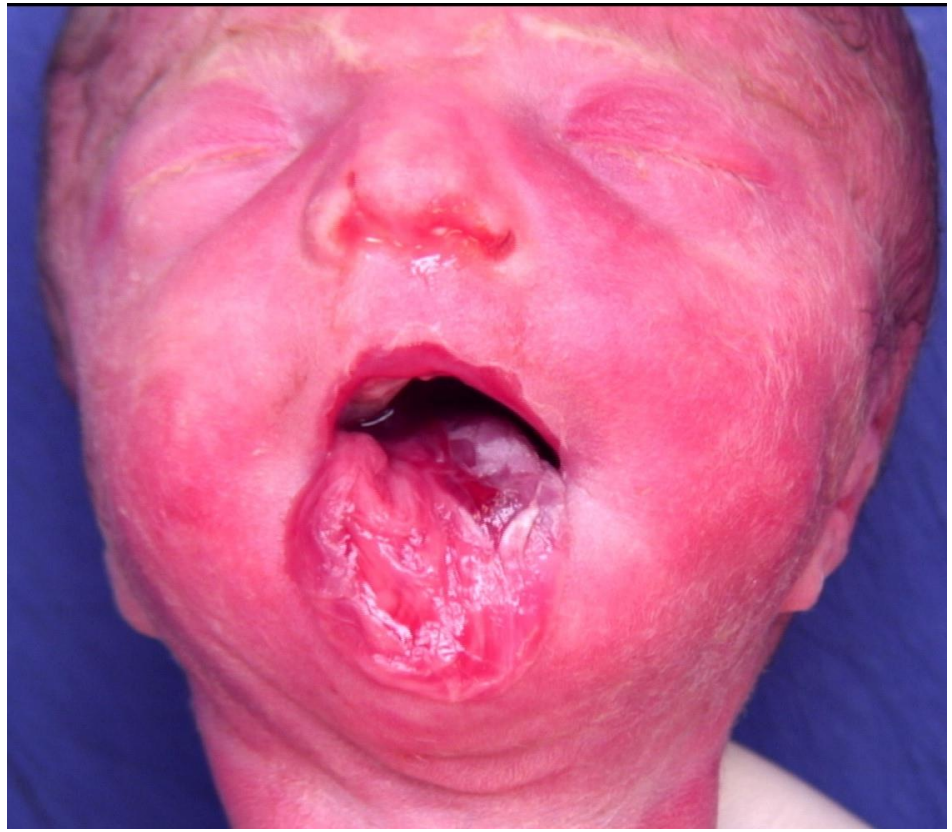


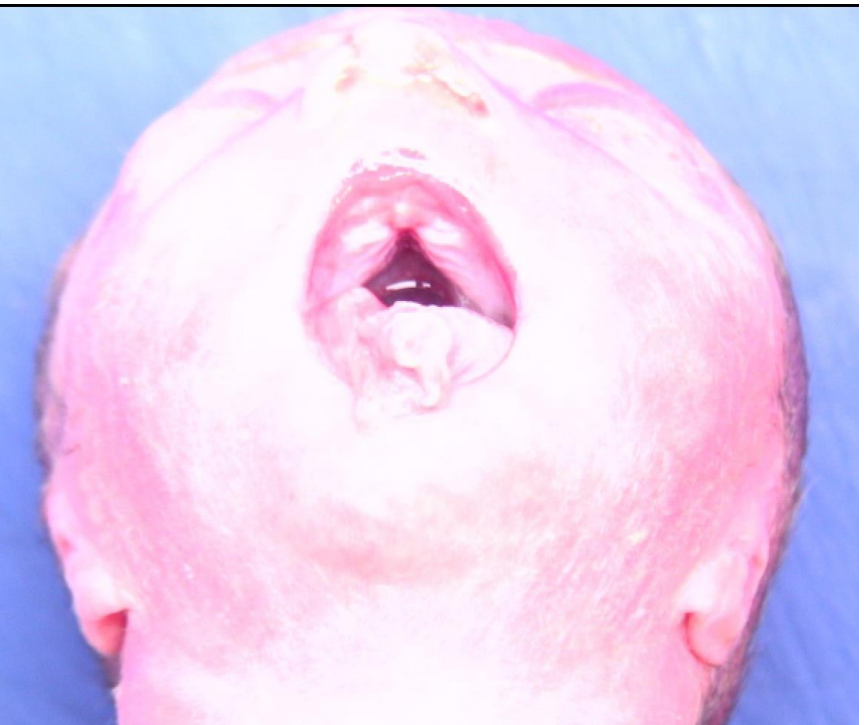
- Sloping forehead HP:0000340
- Low set ears, posteriorly rotated HP:0000368
- Hypertelorism HP:0000316
- Exophtalmia HP:0000520
- Large based nose HP:0012811
- Long philtrum HP:0000343
- Microretrognatia HP:0000308
- Microglossia HP:0000171

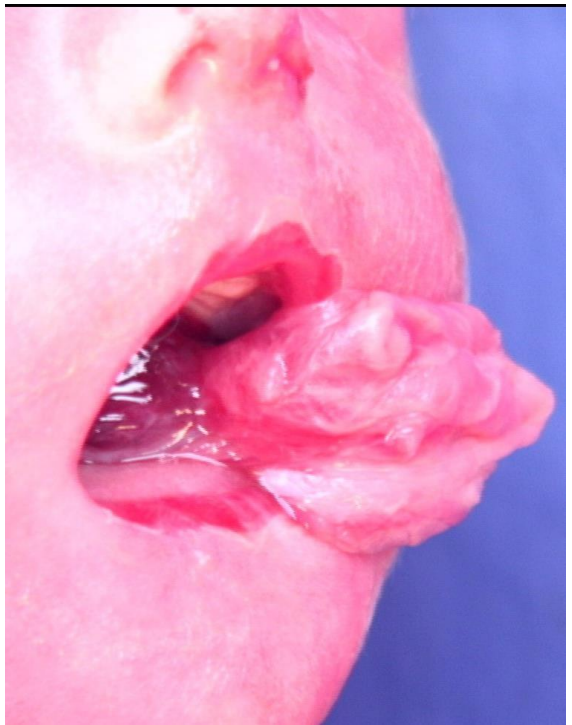
External examinatio



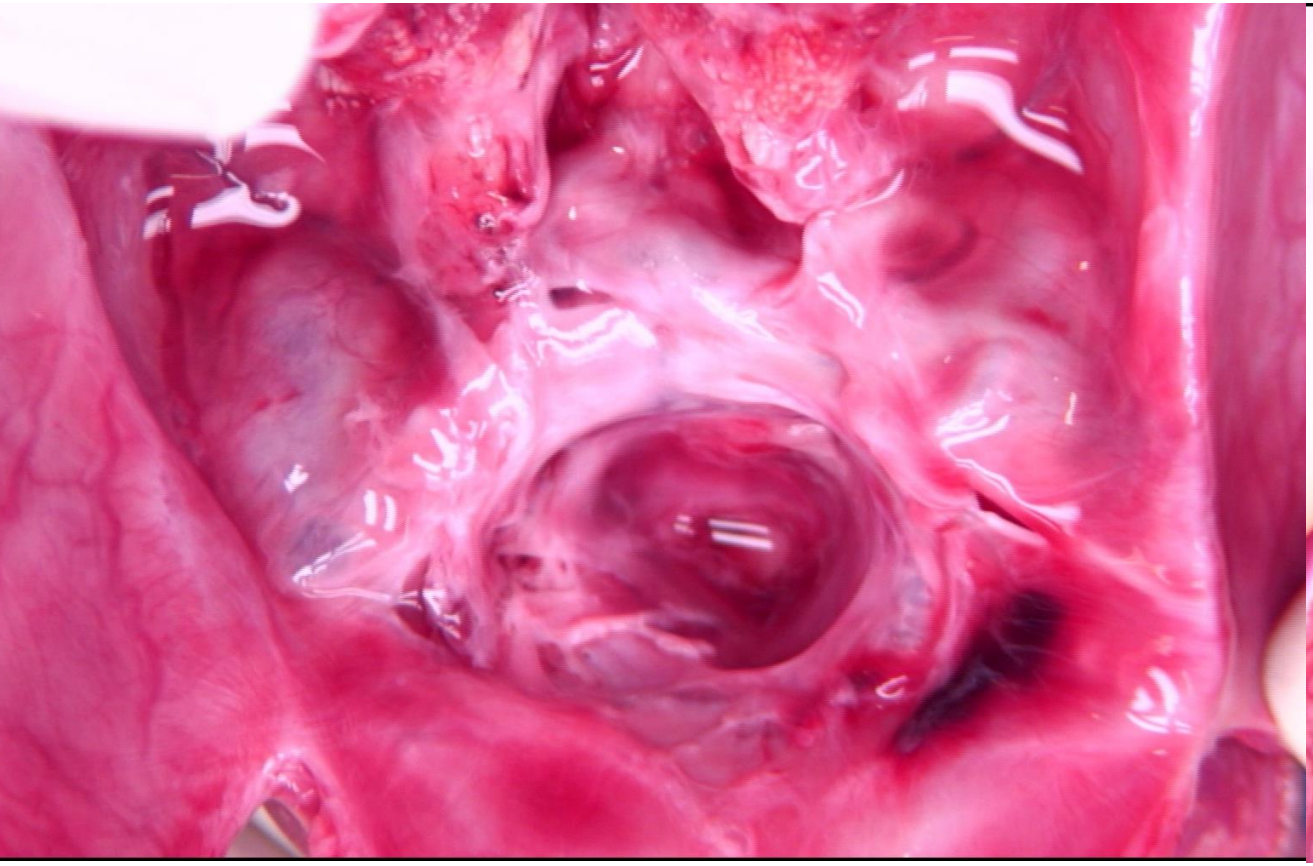
- Intranasal mass HP:6000997
- Cleft palate HP:5201003
- Abnormal midnasal cavity HP:0010641

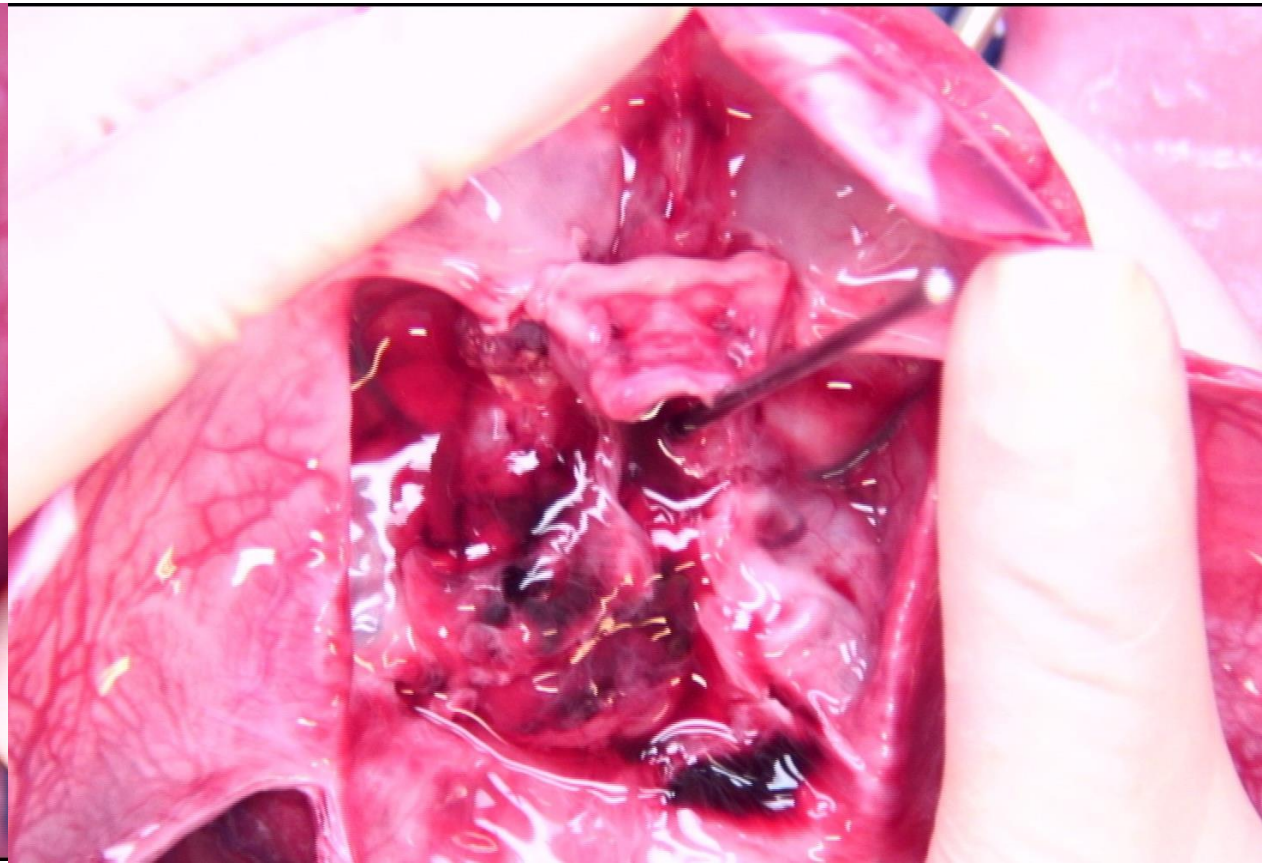




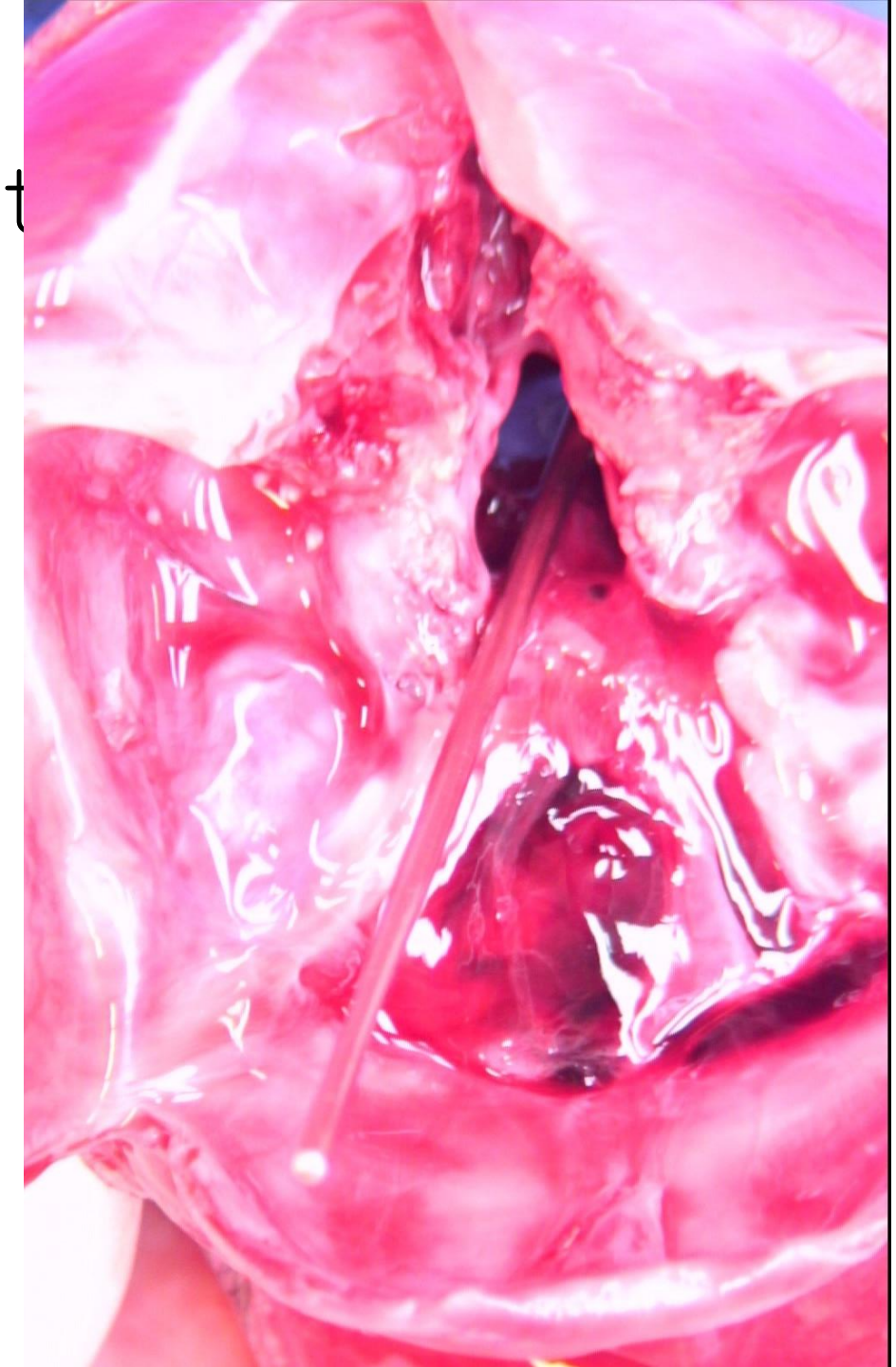


Skull examination





Skull examinat



Other findings

- Arachnodactylie HP:0001166
- Cryptorchidism HP:0000028
- Long eyelashes HP:0000527

Trans-sphenoidal meningo(encephalo/myelo)coeles

- Cephalocoeles = herniations of cranial contents through skull defects
- Incidence of 1 in 3500-5000 live births
- M/F : 1/1
- Associated with other abnormalities in 30% of cases
- Classification according to their contents and location.

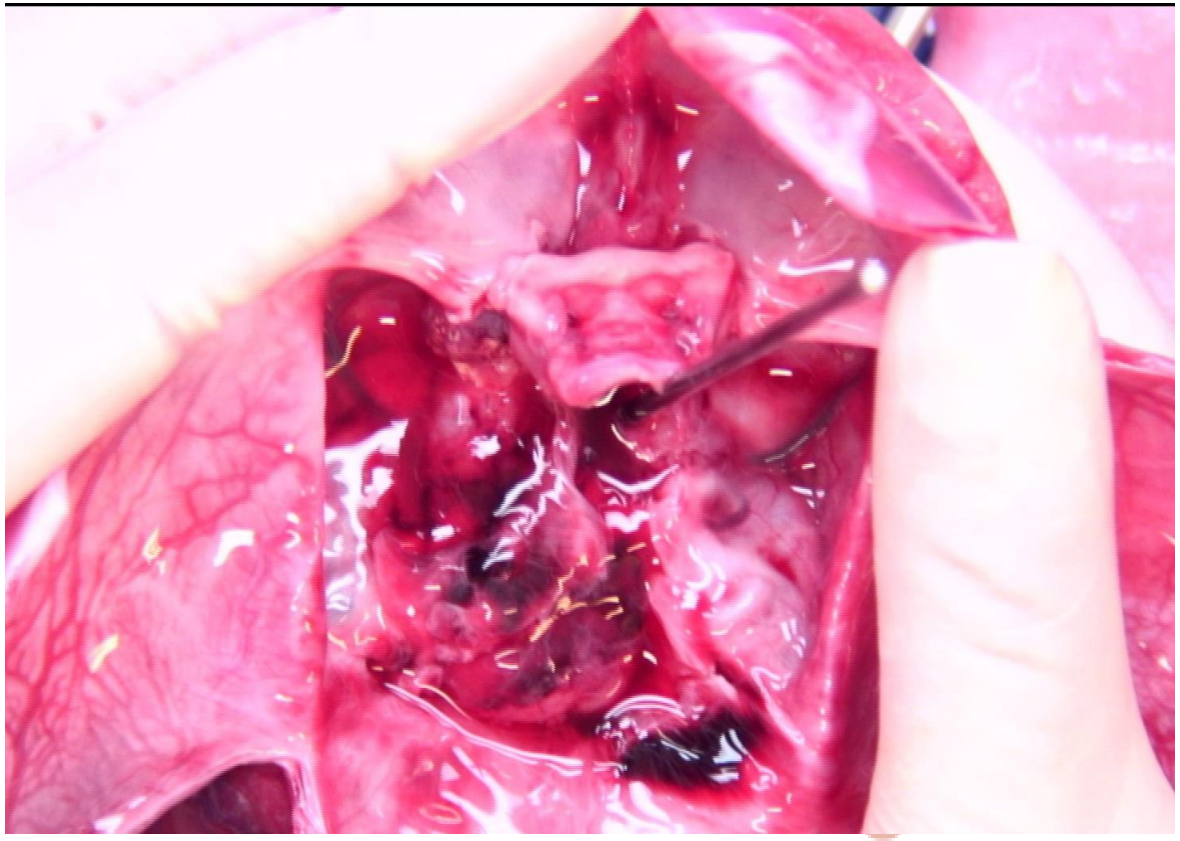
Trans-sphenoidal meningo(encephalo/myelo)coeles

- Cranial meningocoeles = meninges
- Meningoencephalocoeles = meninges and brain tissue
- Meningoencephalomyelocoeles = meninges and brain tissue and spinal cord

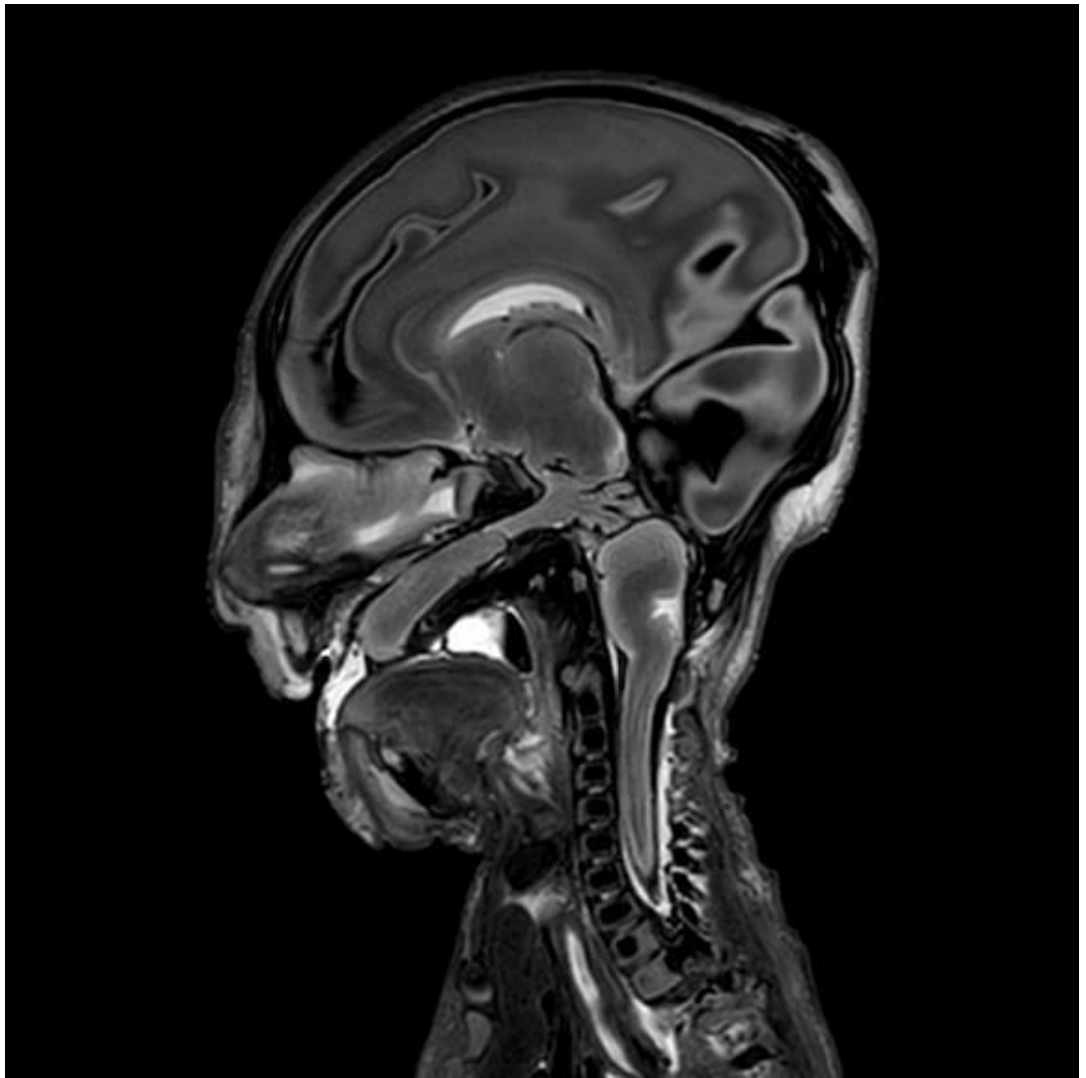
Trans-sphenoidal meningo(encephalo/myelo)coeles

- The modified classification system of Suwanela

- Based on location
  - Occipital (70%, the most
  - Frontal
  - Ethmoid
  - Basal subtypes
    - Transsphenoidal (1/700.000
    - Spheno-orbital
    - Sphenomaxillary
    - Spheno-ethmoidal



Postmortem MRI



Report:
MTP at 26 WG for anterior meningoceole

Malformations

- Sloping forehead HP:0000340
- Arachnodactylie HP:0001166
- Cryptorchidism HP:0000028
- Long eyelashes HP:0000527
- Intranasal mass HP:6000997
  - Transphenoidal meningo/encephalo/myelocoeles
- Low set ears, posteriorly rotated HP:0000368

Deformations

- Hypertelorism HP:0000316
- Exophtalmia HP:0000520
- Large based nose HP:0012811
- Long philtrum HP:0000343
- Microretrognatia HP:0000308
- Microglossia HP:0000171
- Cleft palate HP:5201003
- Abnormal midnasal cavity HP:0010641

Genetics

- Amniocentesis revealed a normal molecular karyotype

- No abnormal variants detected on whole exome sequencing (WES).

TOM

- Use and abuse of post mortem imaging
- Always keep in mind that death and/or delivery can modify your findings at the autopsy
- Be cautious when writing your report

CHU | UVC
BRUGMANN

The hidden mole

DR. MARIE-LUCIE RACU (CHU-BRUGMANN)

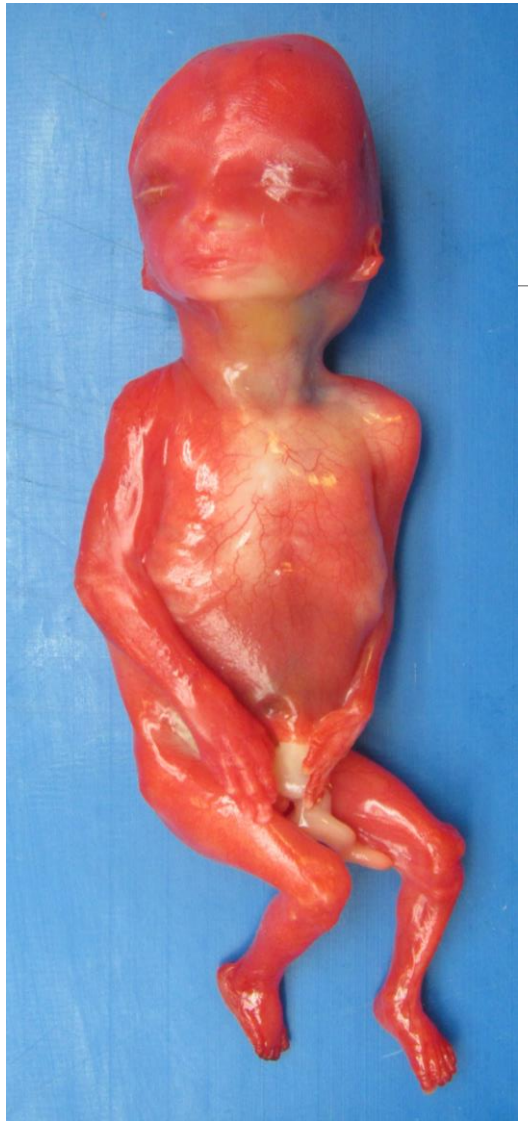
Clinical history

25 year old ♀

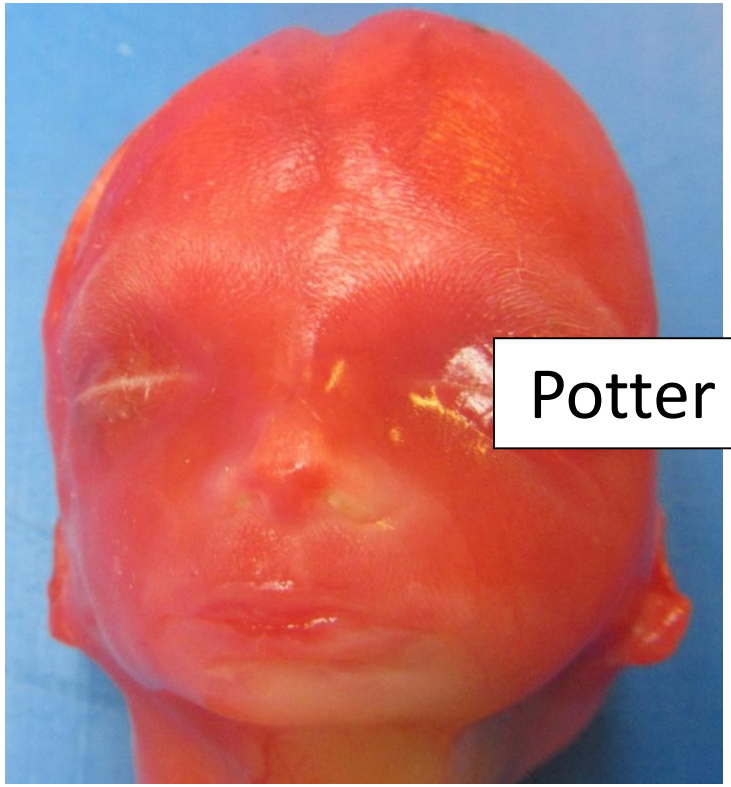
- G2P1 (1 vaginal birth)
- Brought in by the emergency services because of heavy bleeding with abdominal pain
- Currently 16 weeks pregnant (T1 US nl)
- Light bleeding for the last two weeks → under 200mgx2/day of progesterone
- Fetal US : oligoamnios with suspicion of premature rupture of the membranes (PROM), image of marginal placental abruption involving a 4^{th} of the placental surface

Interruption of pregnancy at 17 weeks

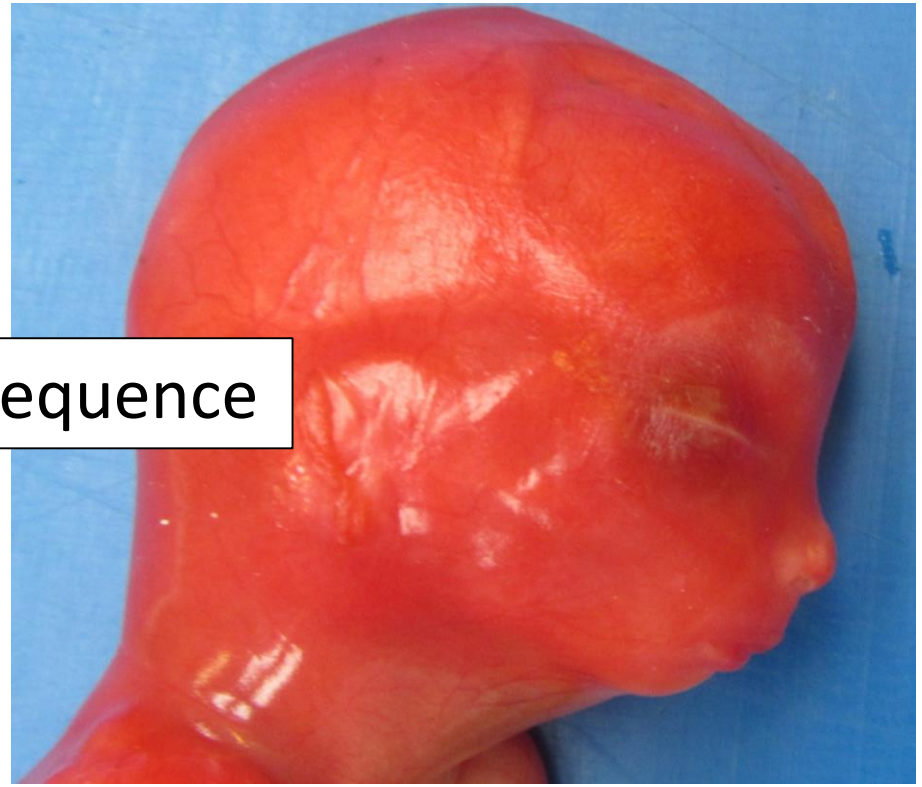
Fetal external exam



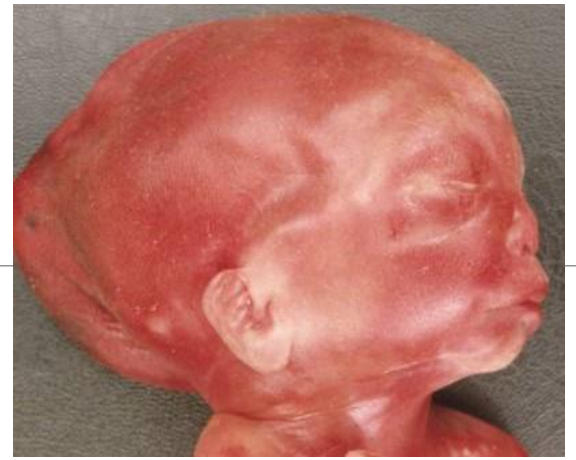
Male 15-16w



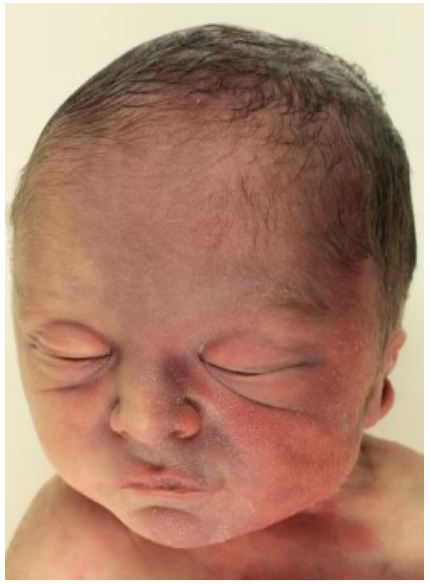
Potter sequence



Potter sequence



- Short neck
- Dolichocephaly
- Excess of skin
- High and wrinkled forehead
- Marked infraorbital folds +/- upslanting palpebral fissures
- **Large and flat nose**
- **Microretrognatia**
- **Low set ears, posteriorly rotated**, flattened, misfolded
- Excess skin on the lower part of the face (cheeks)



Khung Suonavy

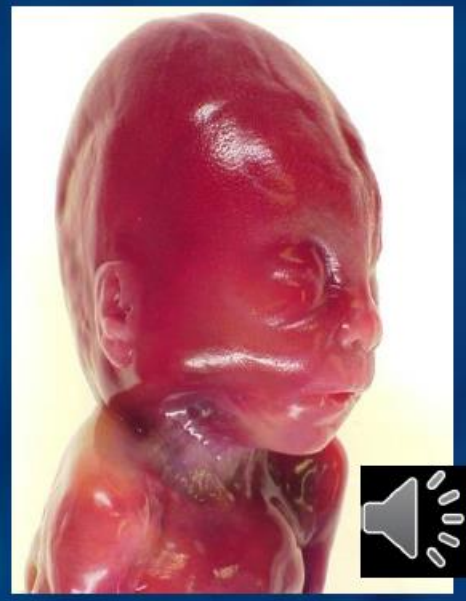
La dysmorphie de Potter

https://www.youtube.com/watch?v=rHsGA2KcHyo

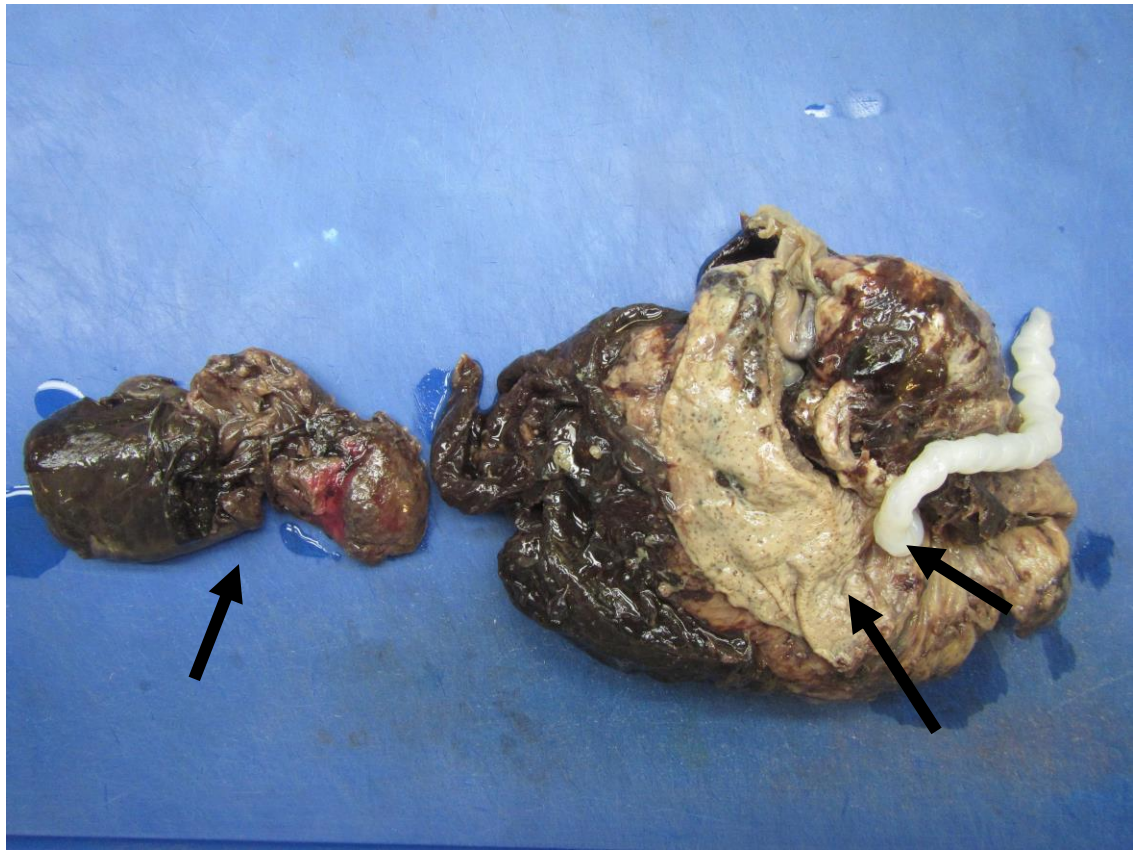
« Aller le plus loin possible avec un collant sur la tête »

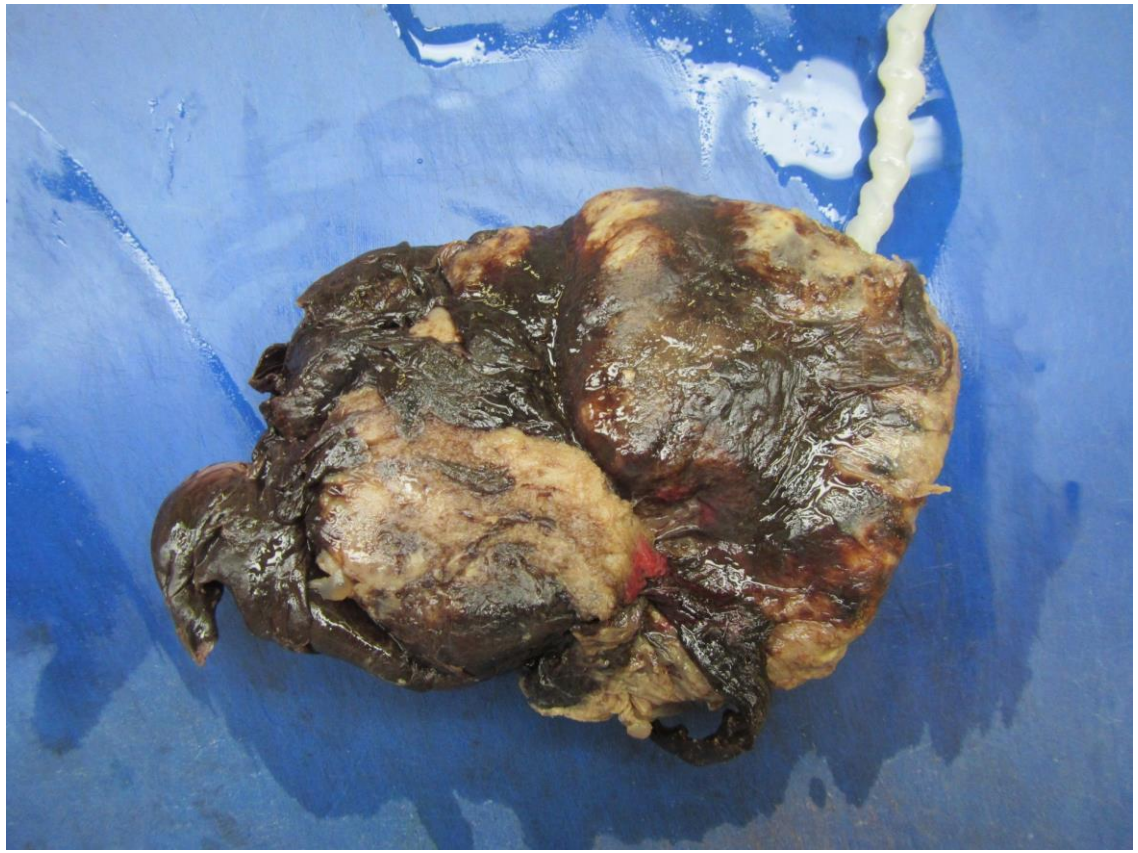
+

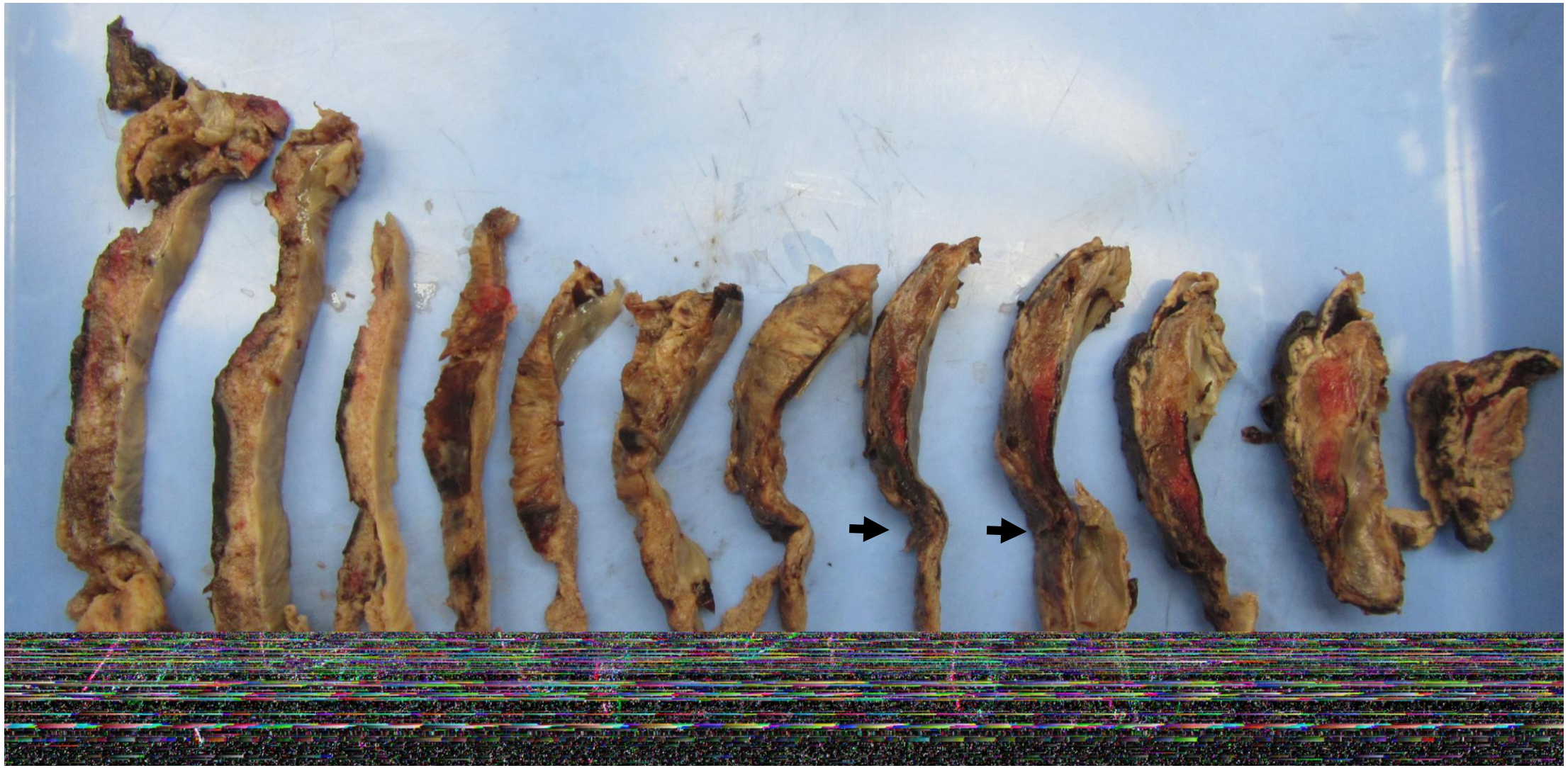
=



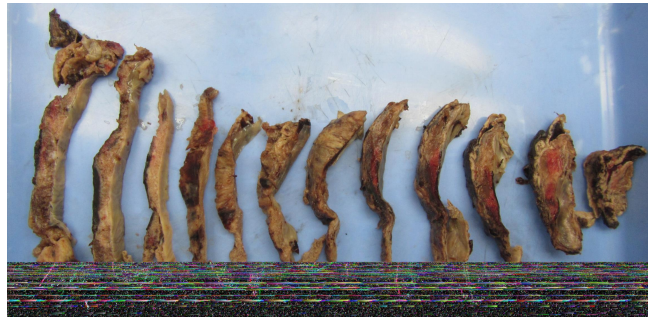
Placenta analysis

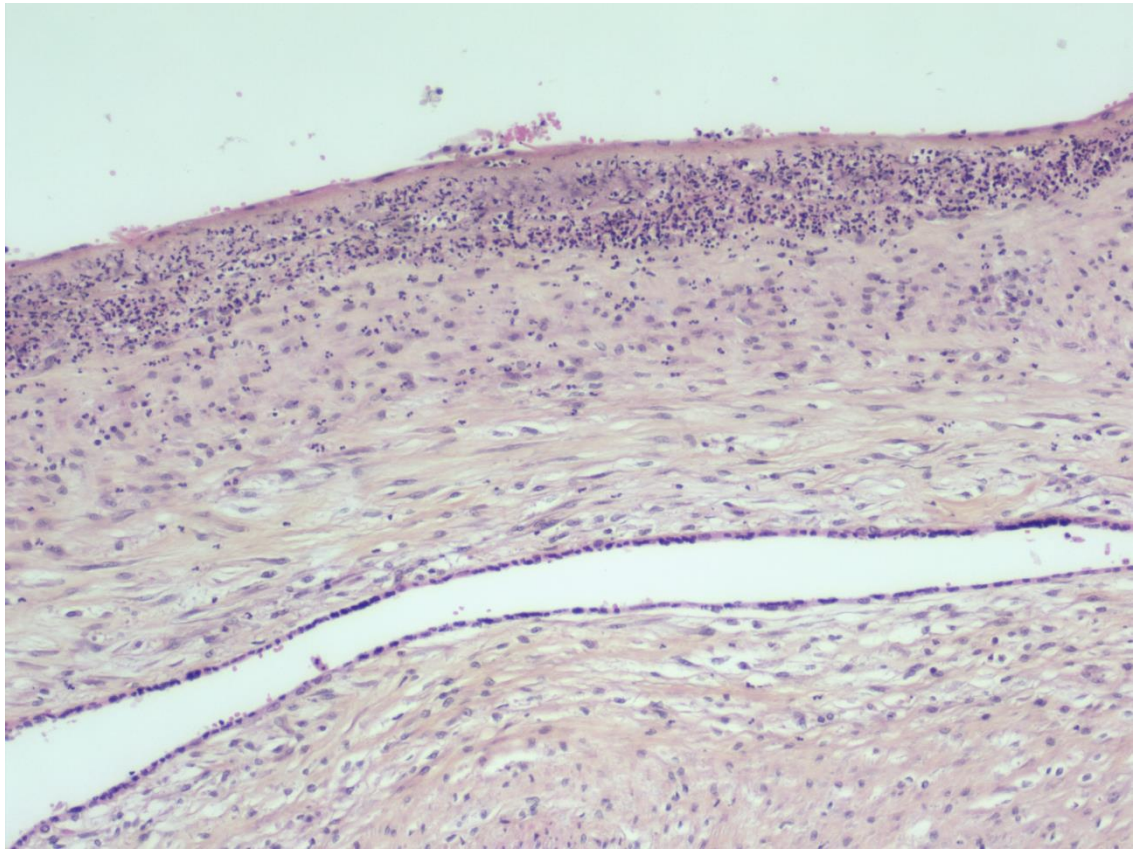




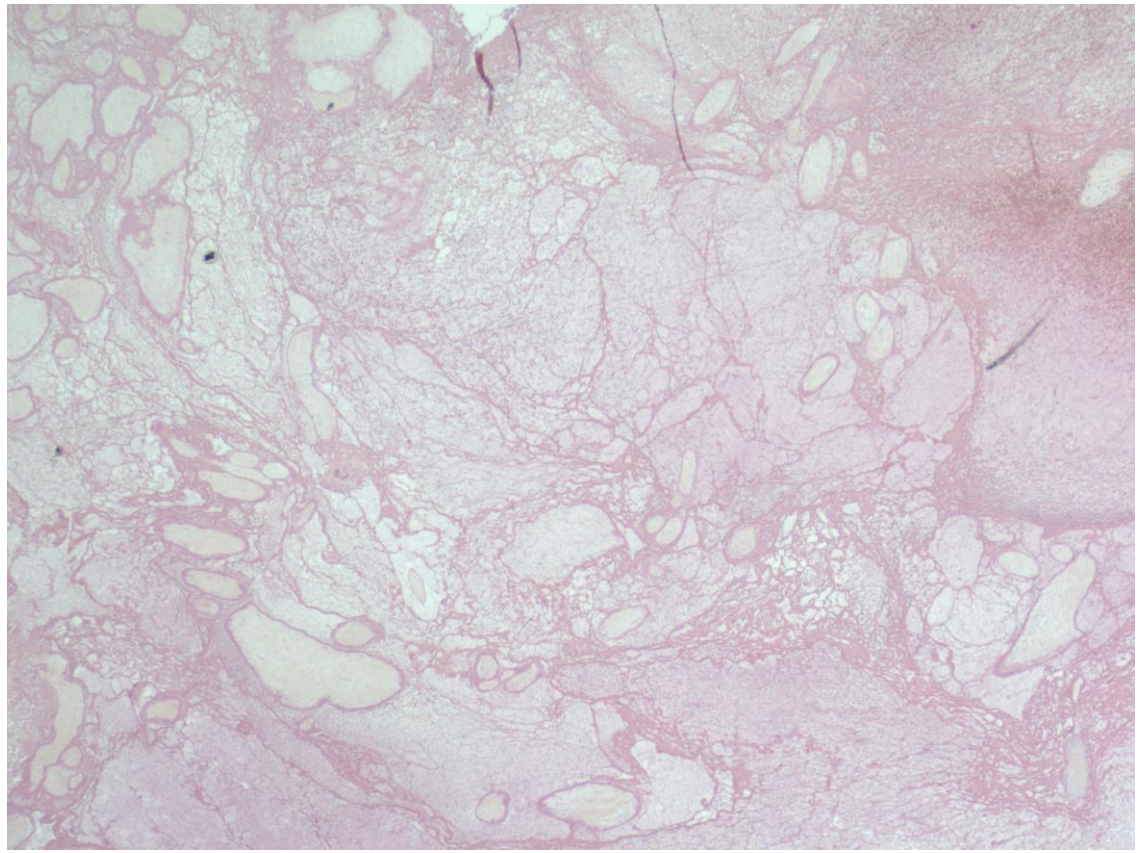


Microscopic analysis

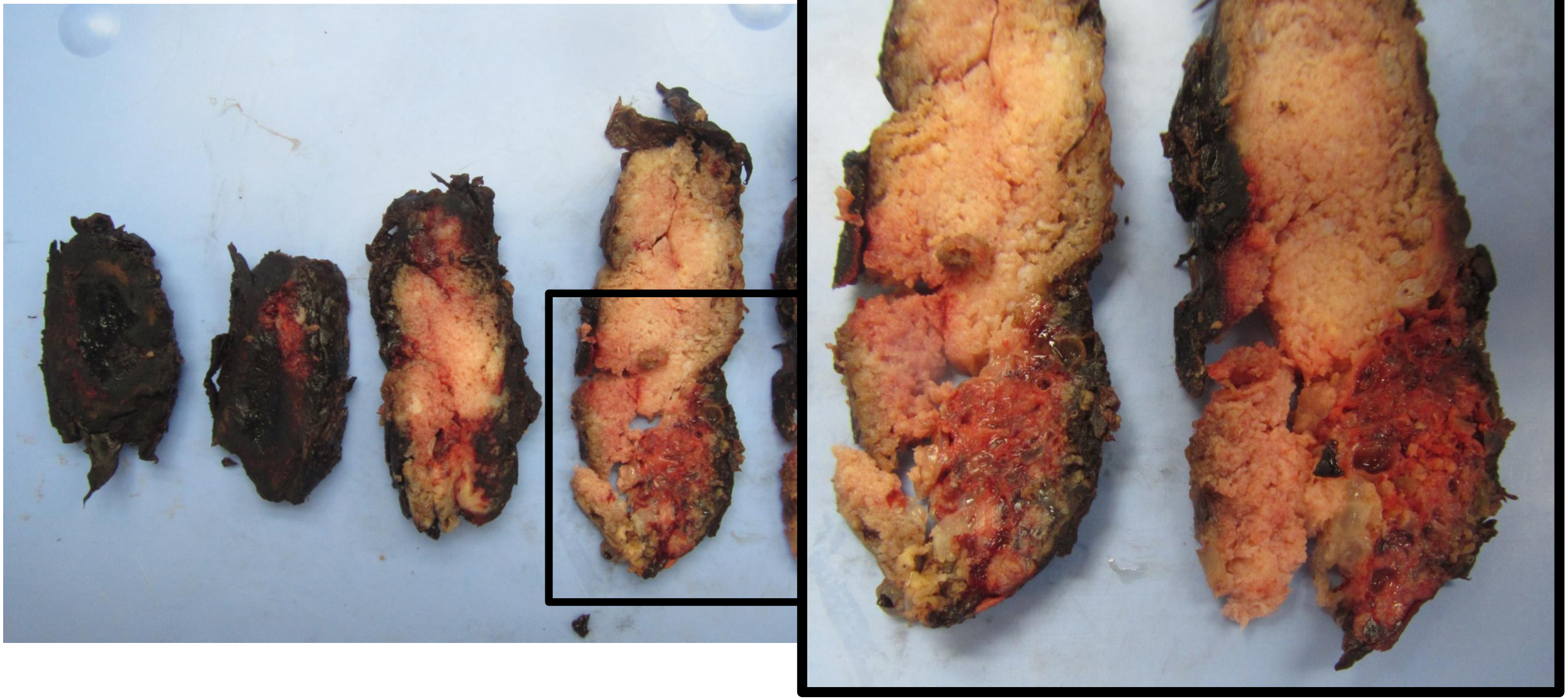




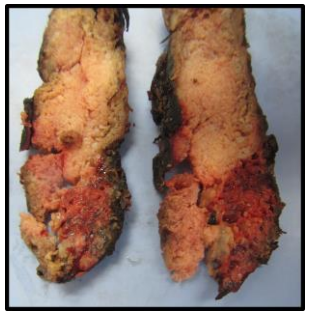
Acute chorioamniotitis

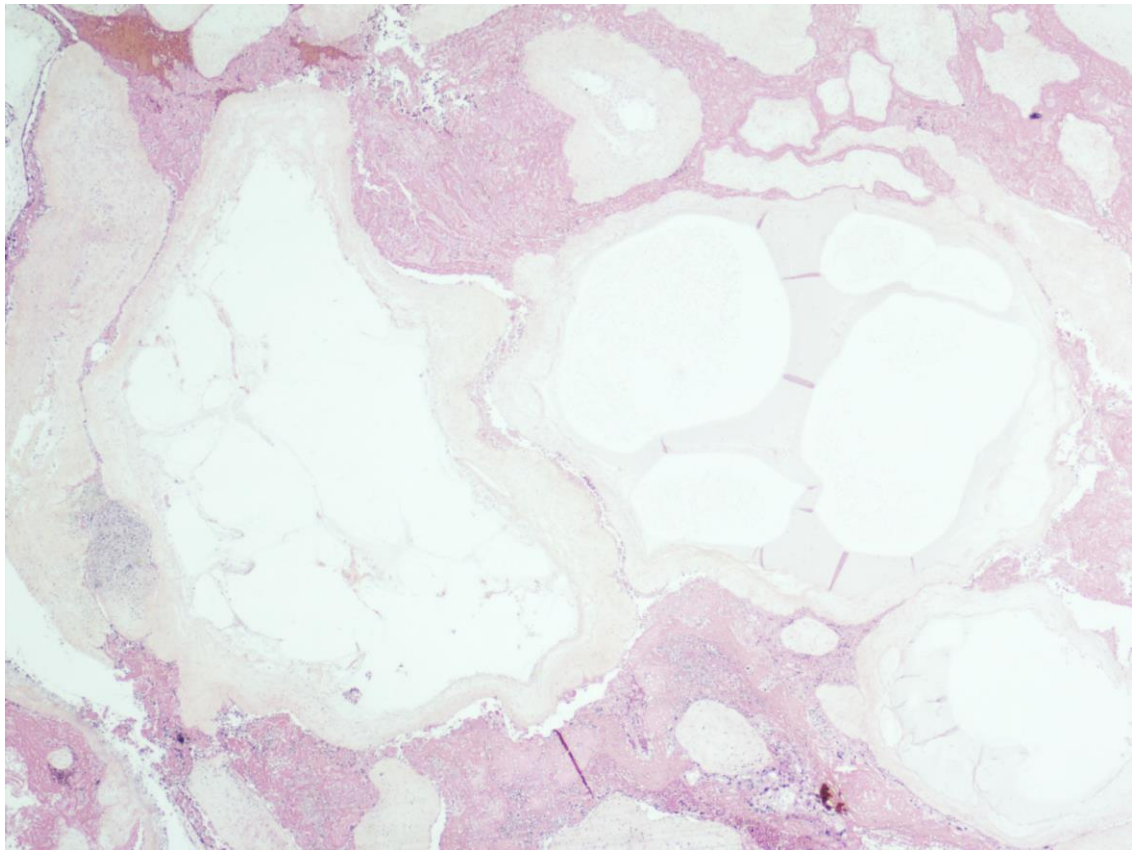


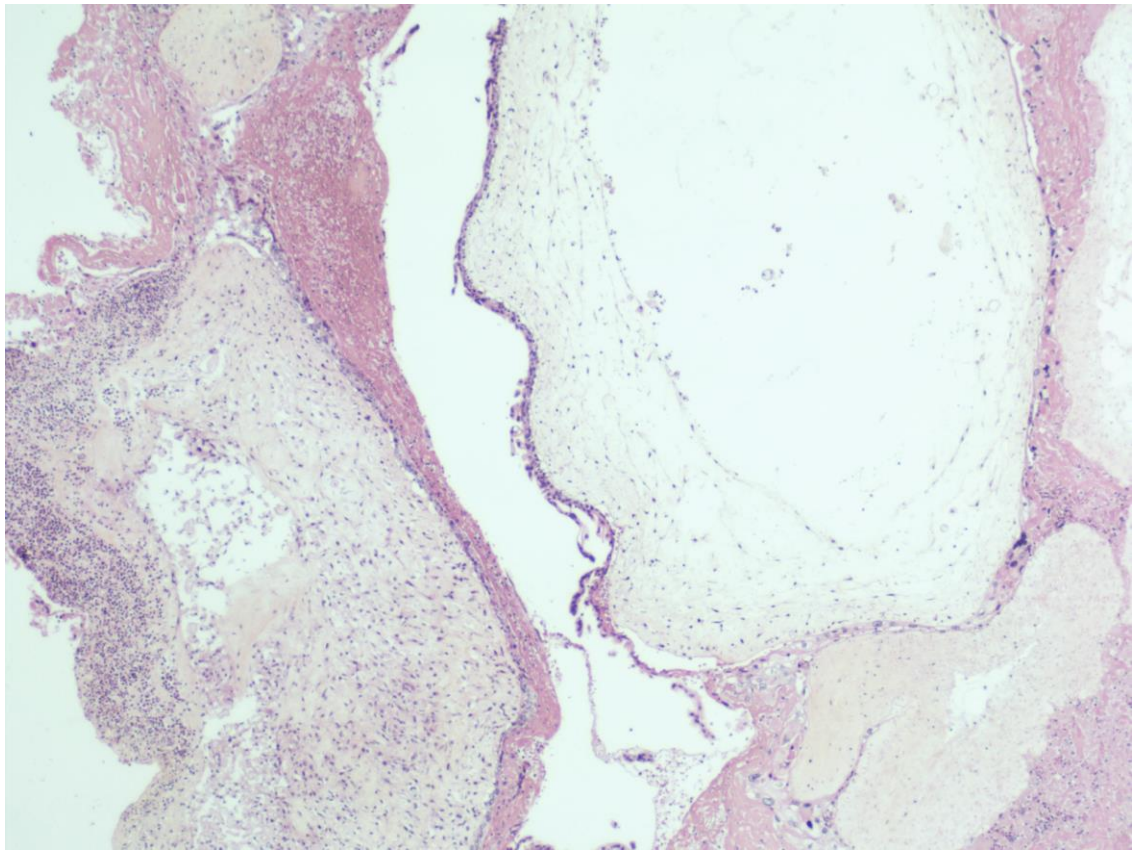
Large infarction of the placenta



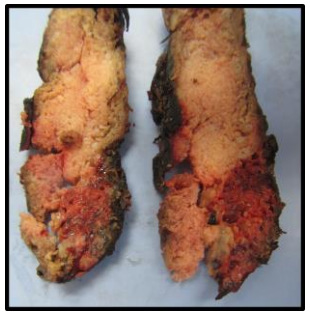
Microscopic analysis

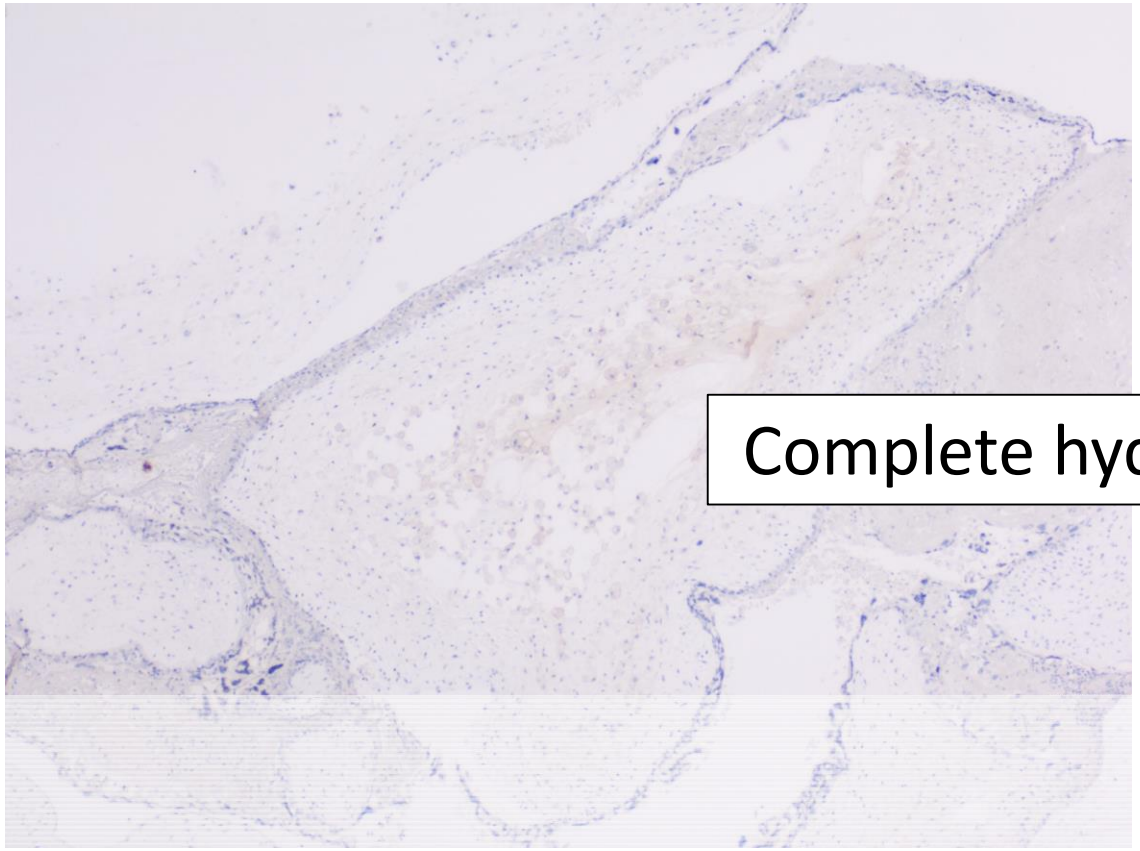


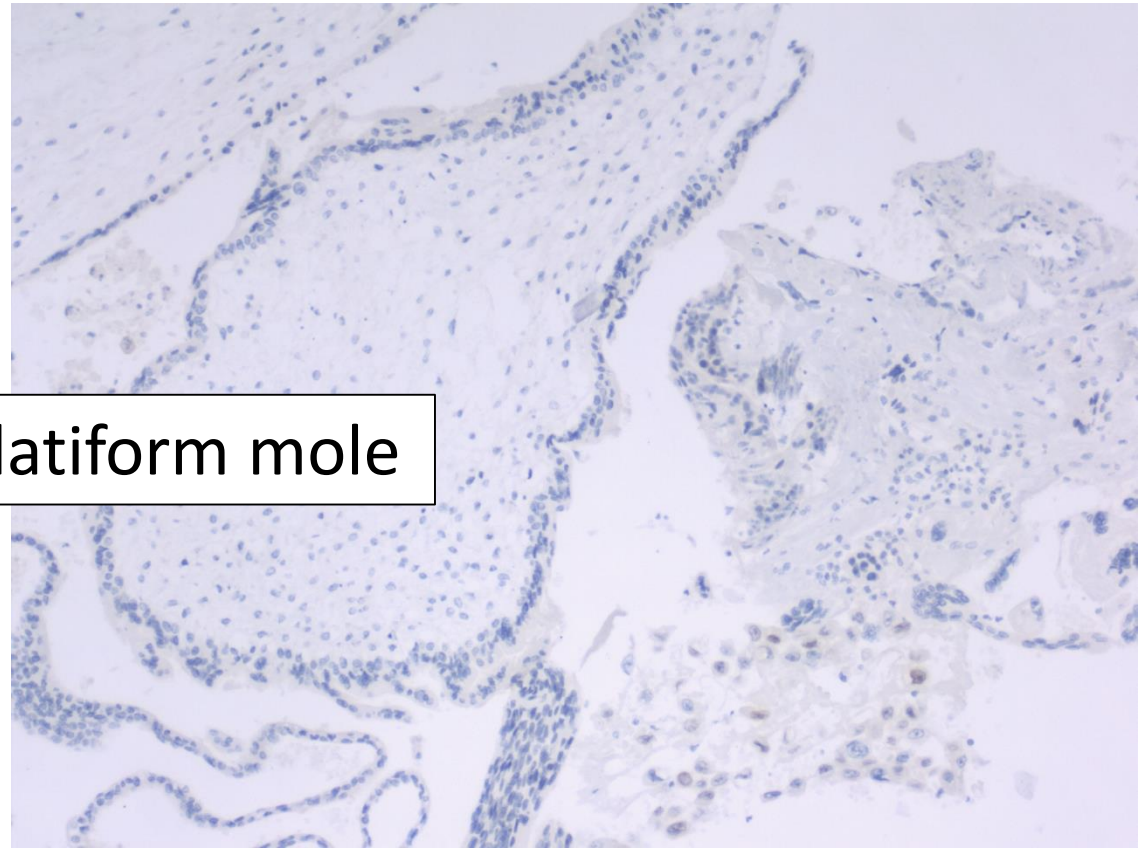




Microscopic analysis







Complete hydatiform mole

Negative p57 immunohistochemistry

Conclusion

Male fetus, 15-16w:

- Potter sequence in the context of oligoamnios << PROM

Placenta:

- **Twin pregnancy with a complete mole**
- Placental abruption with retroplacental hematoma and infarction of the parenchyma
- Associated signs of chronic hypoxia
- Acute chorioamniotitis with villitis >< PROM

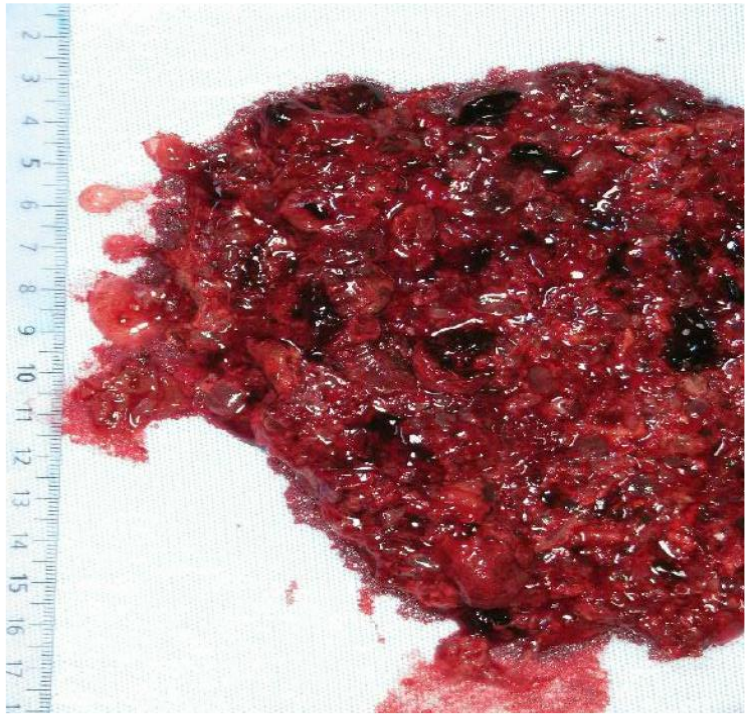
Complete hydatiform mole (CHM)

Diploid 46 XX or 46XY

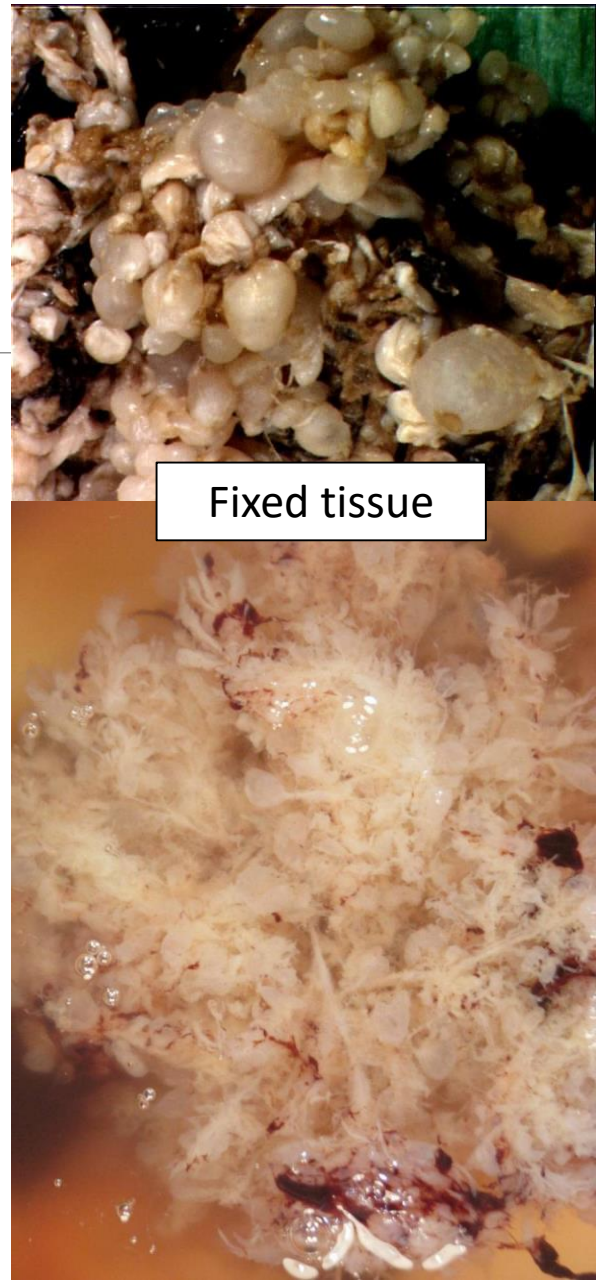
All chromosomes are **paternal in origin → NO EMBRYON**

Clinical presentation:

- Uterus too big for gestational age
- HCG too high for gestational age
- US: « snowstorm », heterogenous, multilacunar
- Usually diagnosed at 6-8w
- Hemorrhage 11-25w
- **Rarely an incidental finding**



Fresh tissue

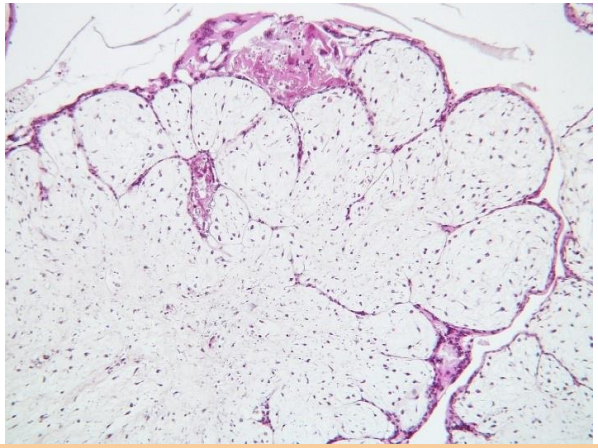


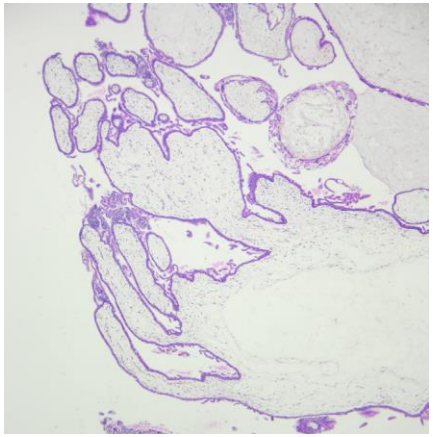
Fixed tissue

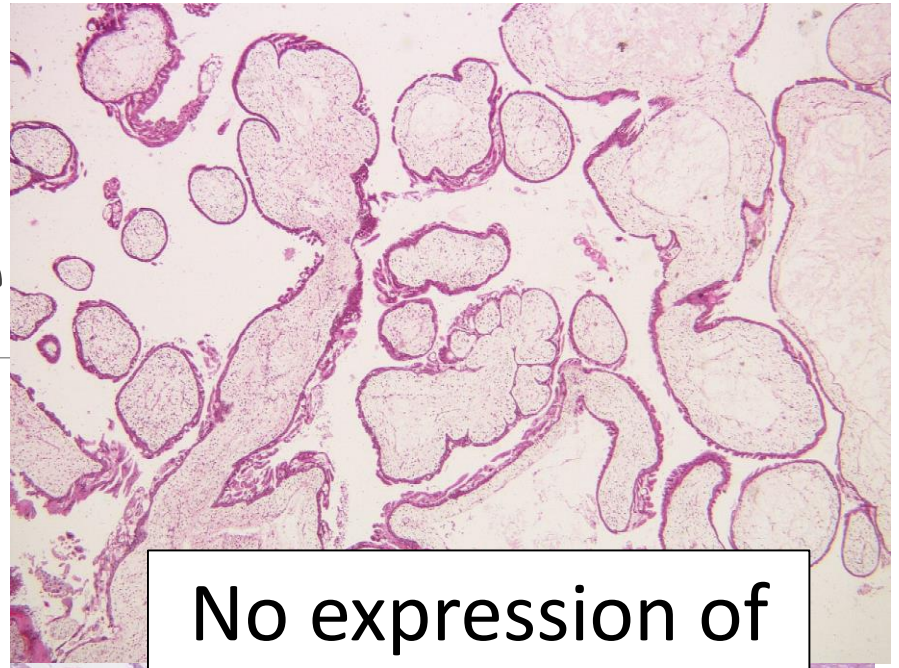
Complete hydatiform mole

Microscopic exam:

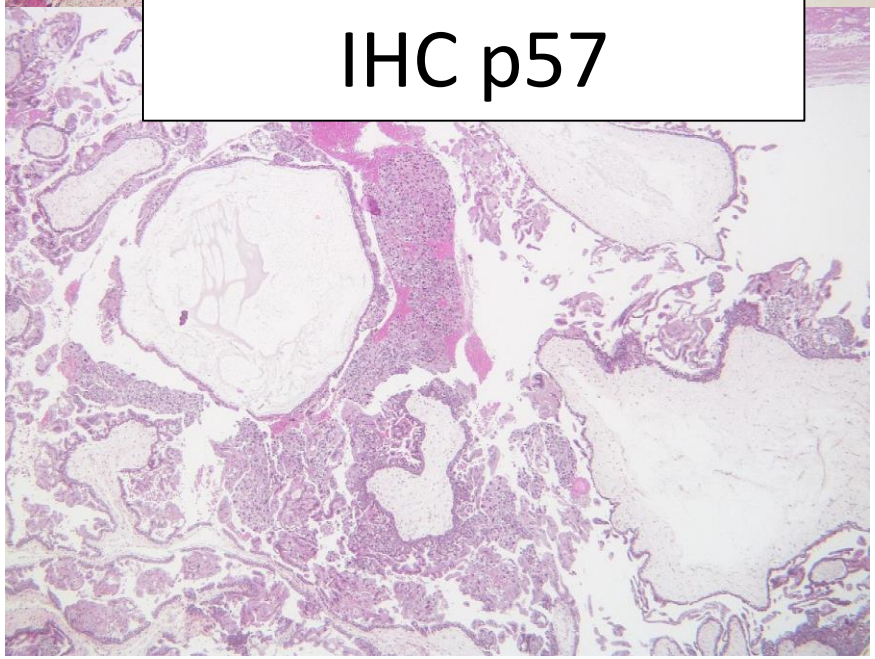
- One population of large type villi
- Oedema of stroma with a pseudocystic aspect
- No signs of embryonal development (no nucleated blood cells, no embryonic tissue…)
- Irregular villi (cauliflower, polypoid)







No expression of IHC p57



Evolution and prognosis

Recurrence risk for developing subsequent molar pregnancy after first CHM : 1-2% (10-20x higher than normal risk!)

- After 2 : 25%

Increases risk of gestational trophoblastic disease (GTD) and neoplasm (GTN):

- When trophoblastic activity persists after aspiration : 15-20% with CHM (<1% with partial mole !)
- 2-3% of CHM evolve into choriocarcinoma/50% of choriocarcinoma follow CHM

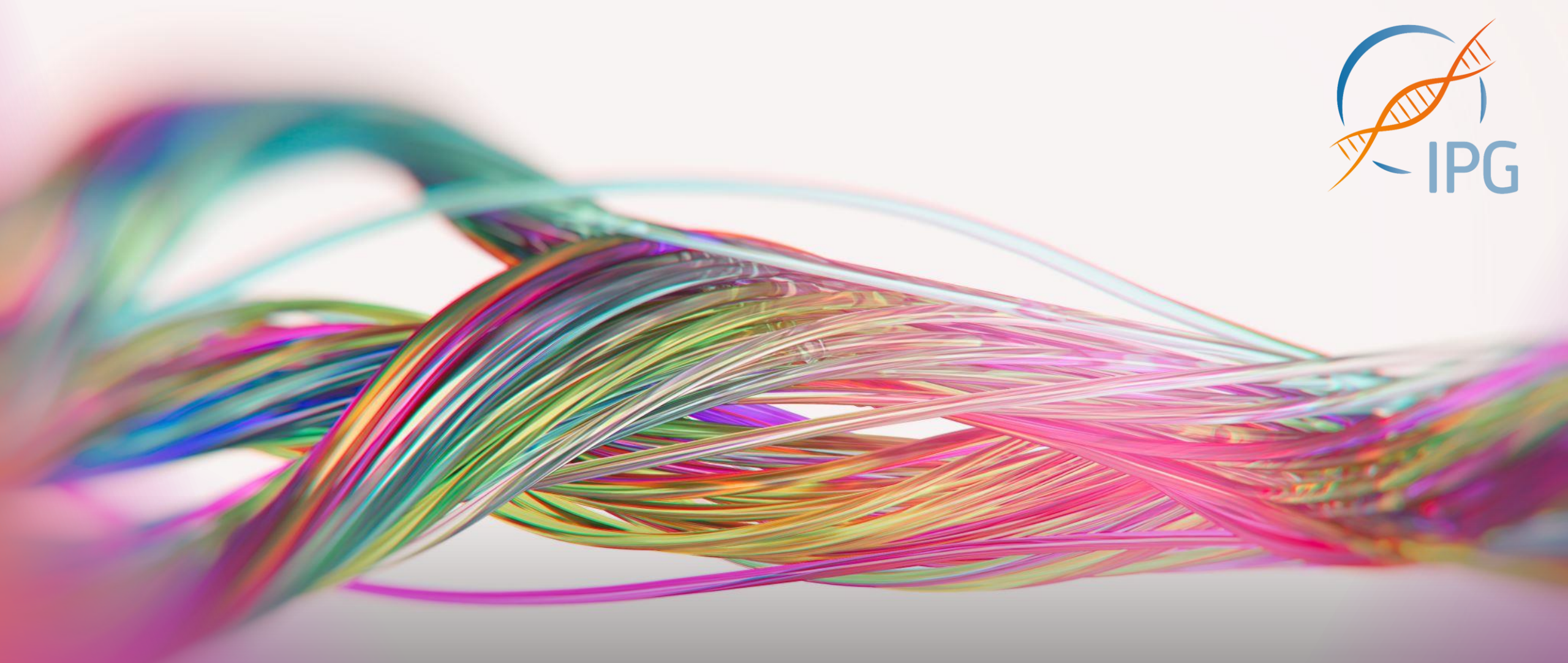
Most regress after aspiration and HCG levels decrease

95% of cases will have a low risk of GTD/GTN, 100% survival

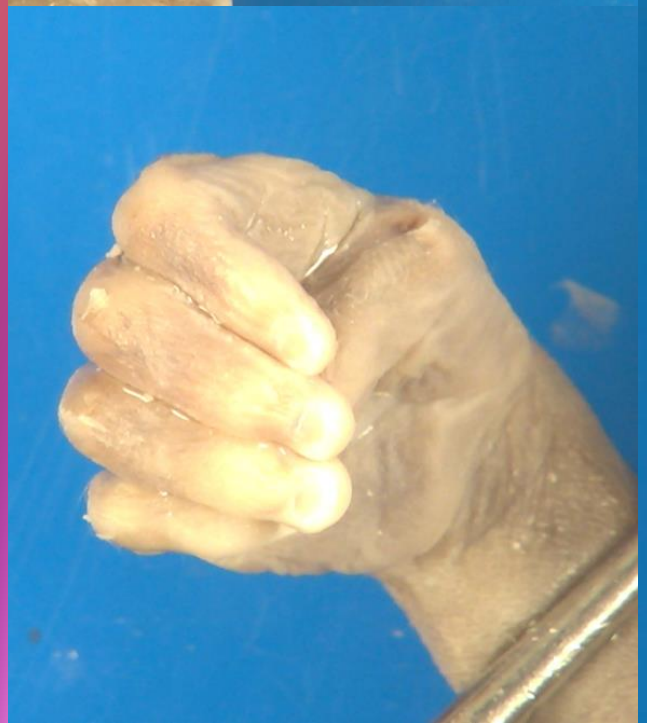
Twin pregnancy with complete mole

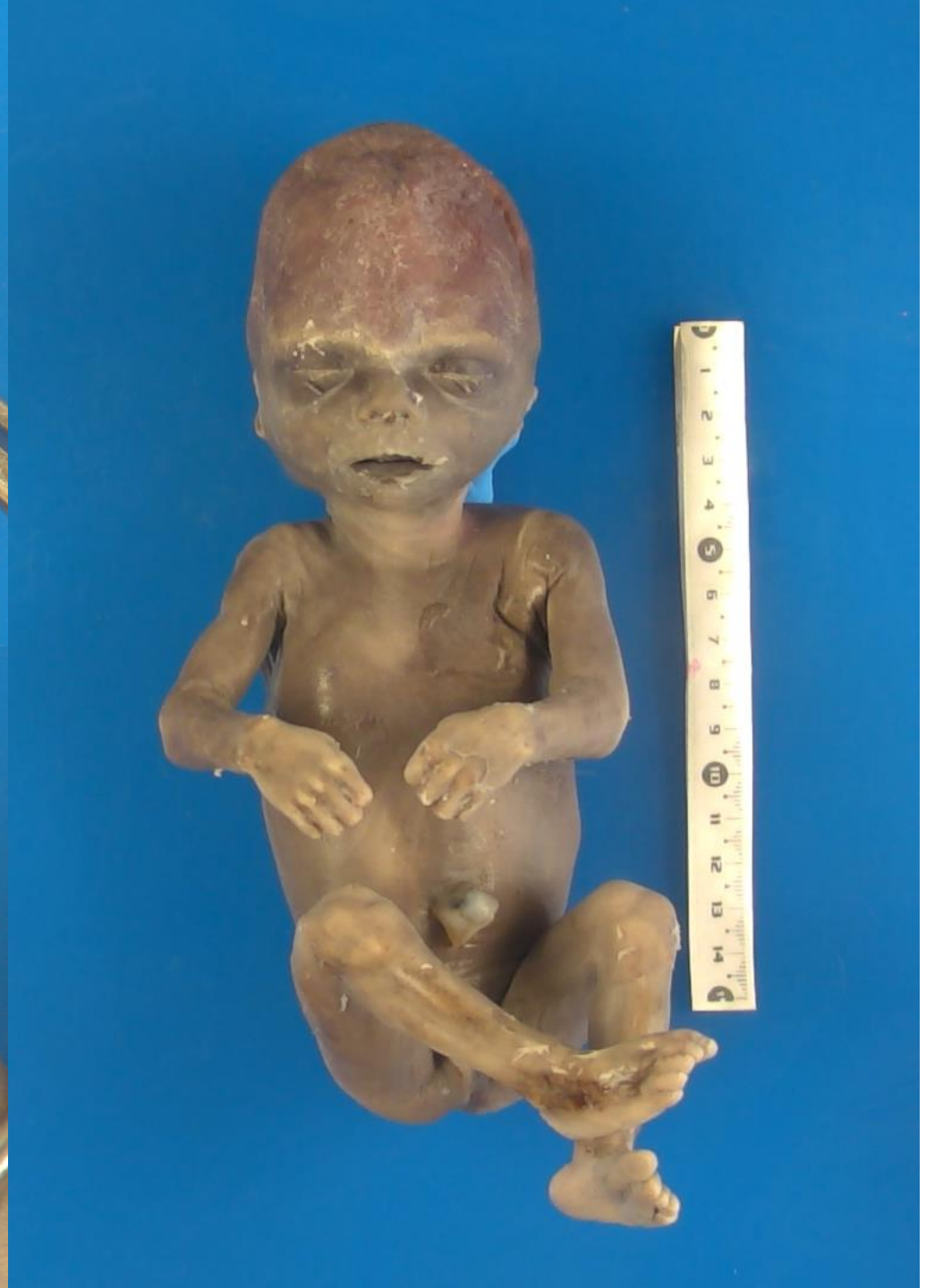
- **Rare (1/20 000 to 100 000 pregnancies)**
- Coexisting complete mole and a living fetus
- Usually missed
- Typical complications of late complete moles → increased fatal complications:
  - Hemorrhage
  - Pre-eclampsia
  - Hyperthyroidism
  - 55% incidence of GTN, 22% of metastatic disease
- DD: partial mole, placental mesenchymal dysplasia

Thank you
Questions?



X-linked hydrocephaly

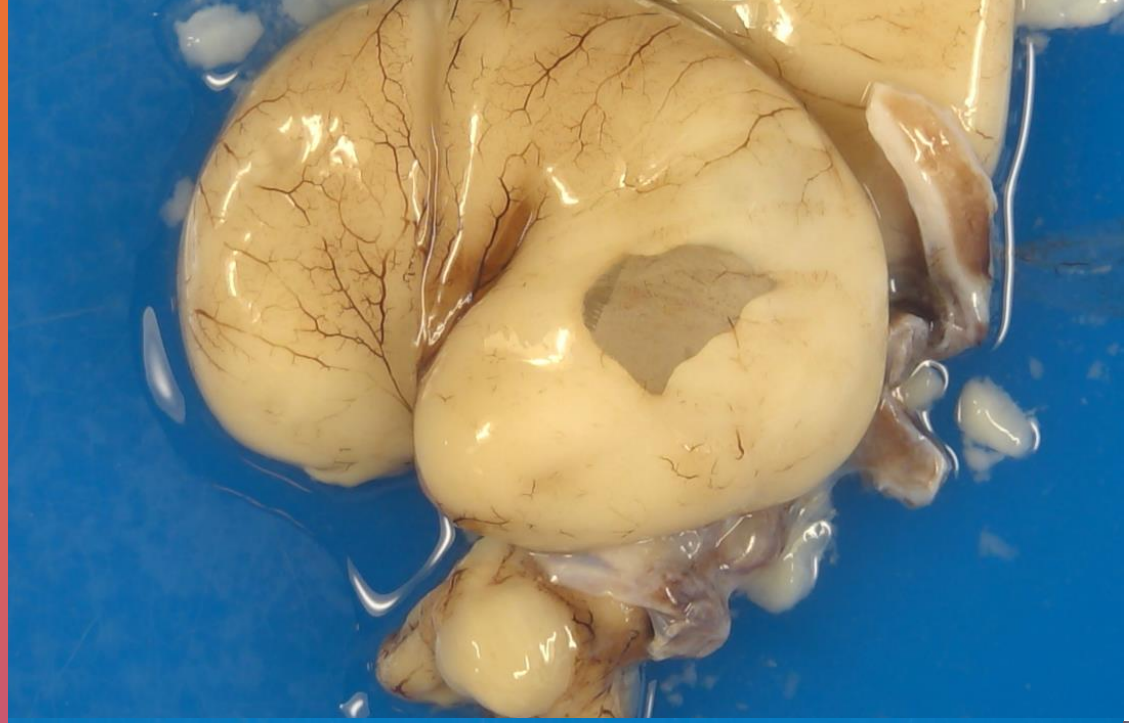




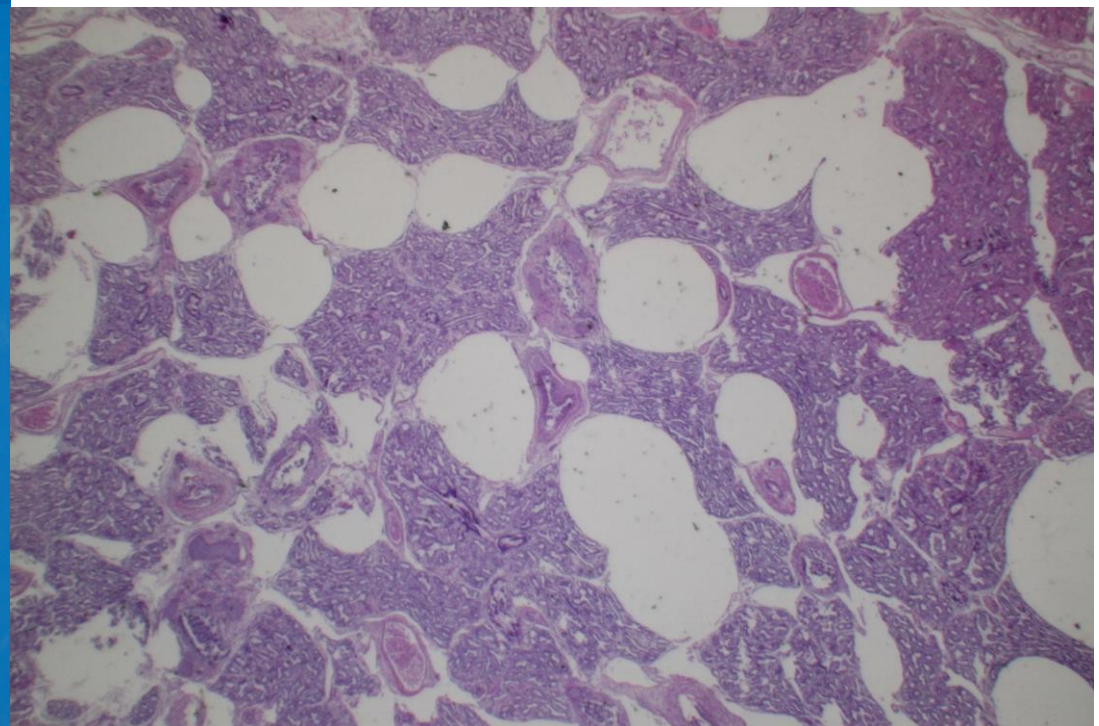
- US : triventricular dilatation (17mm).
- Corpus callosum agenesis.

- TOP 23 WG
- Eutrophic male fetus

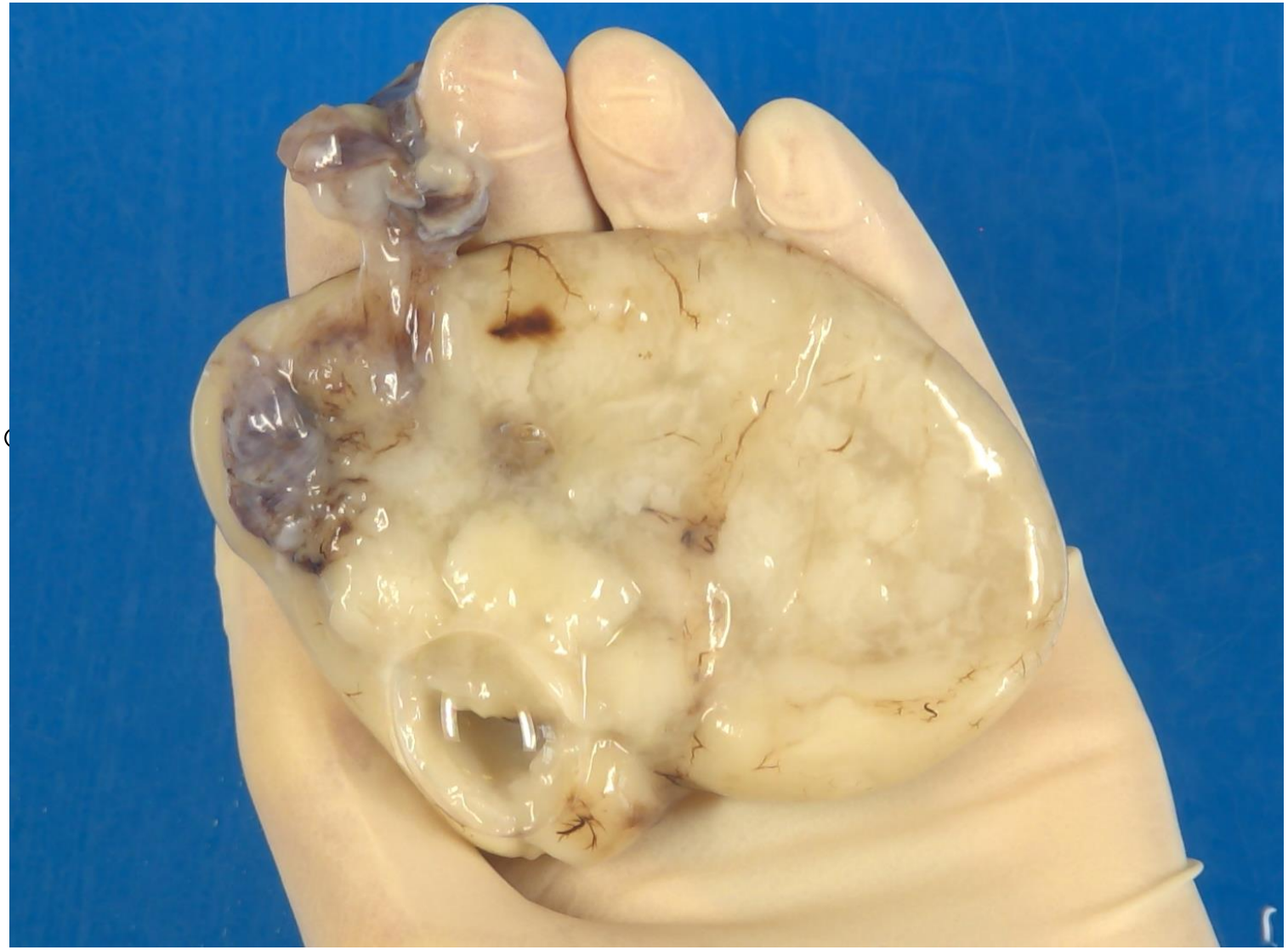
- Adductus thumbs

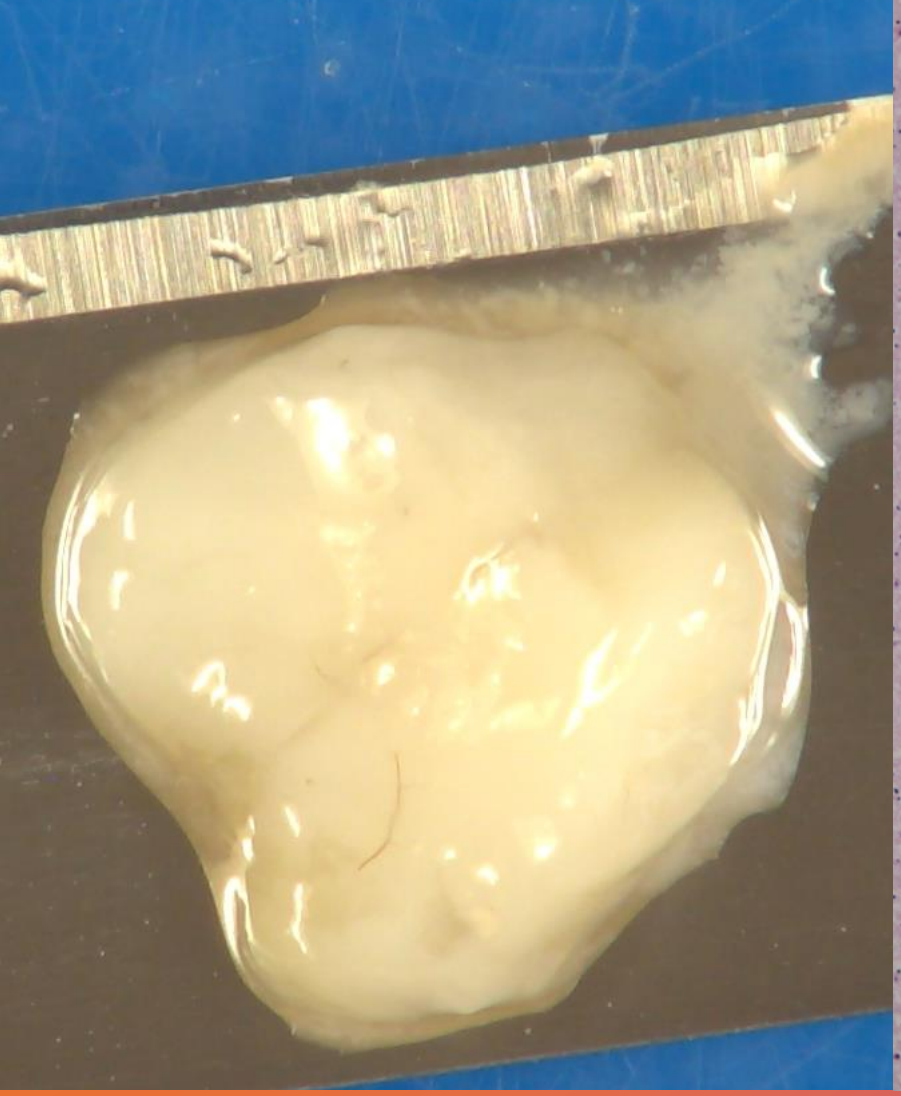
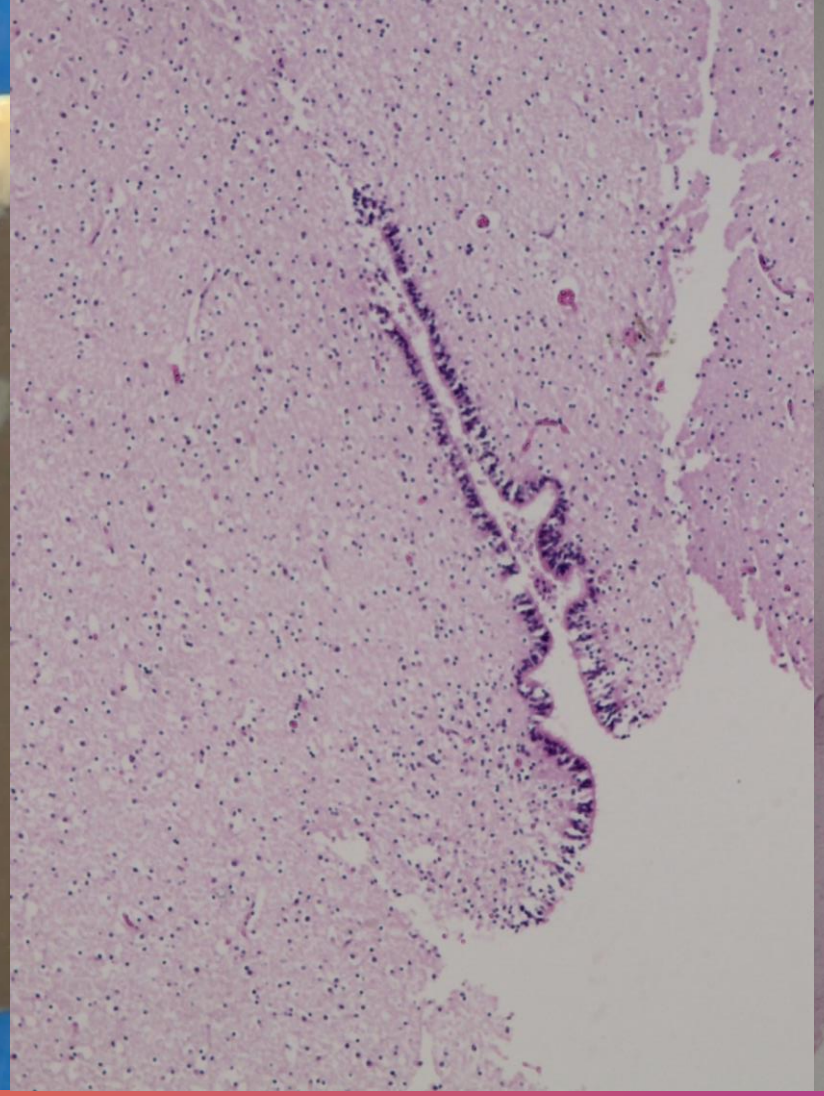
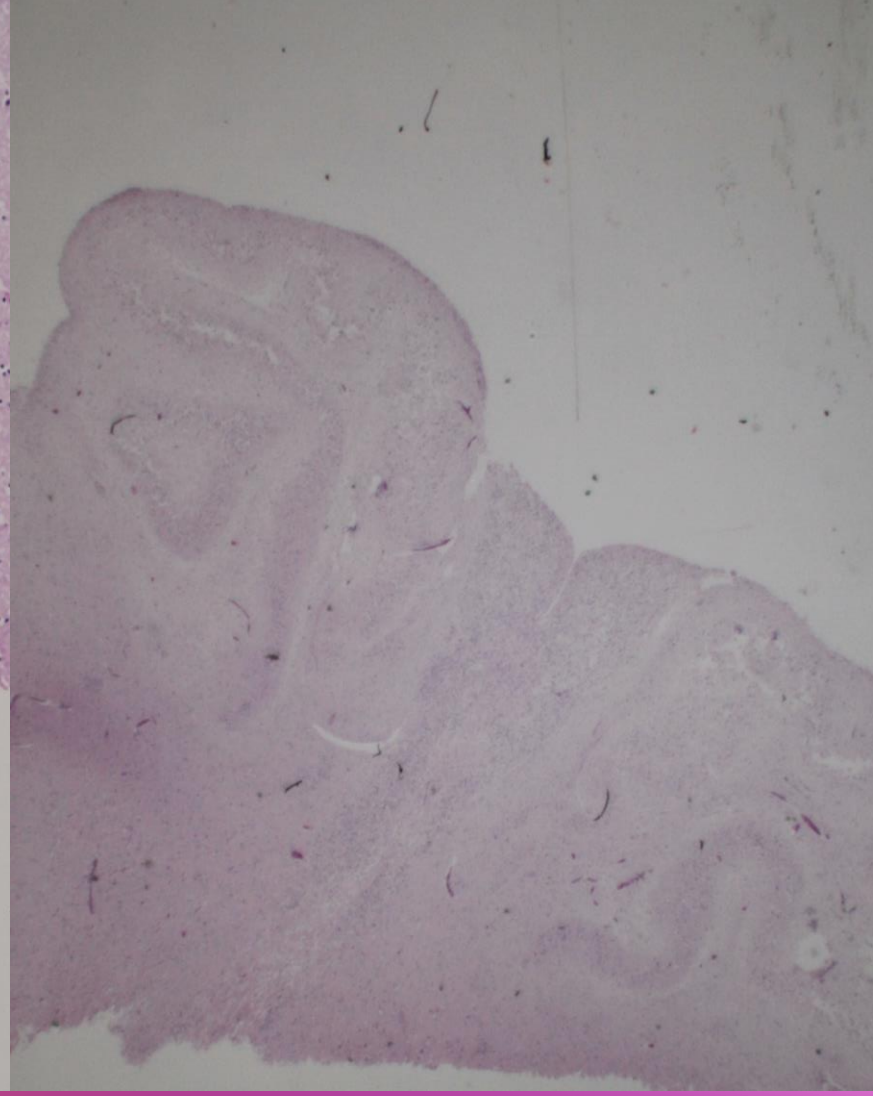


TOP with intra cardiac air injection……



- Corpus callosum??
- No corpus callusum neuro
at microscopy, but…

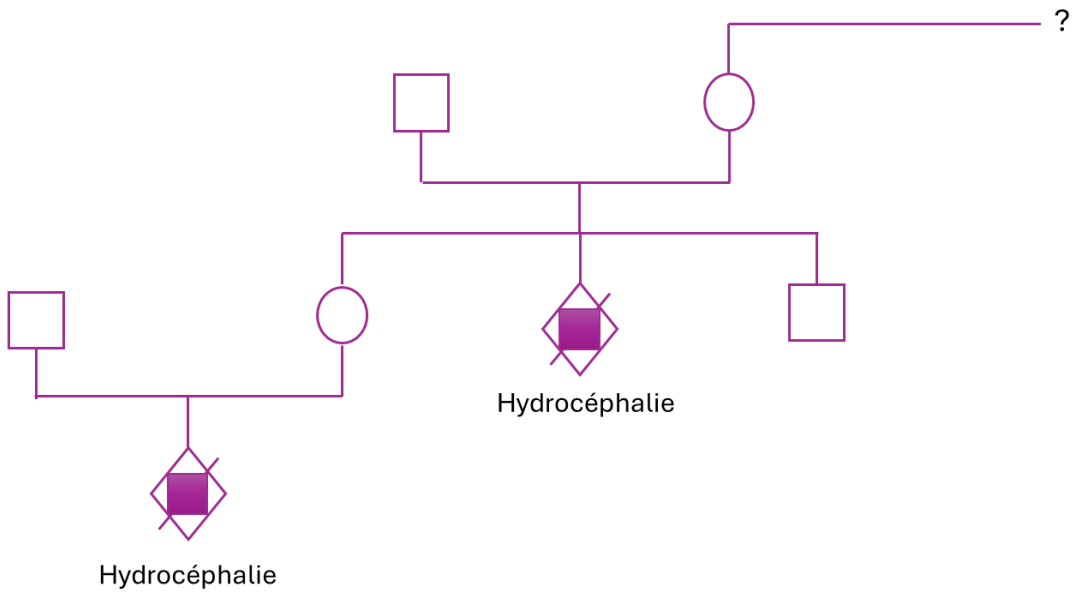


Mesencephalon : small aqueduct of Sylvius

Microscopy : pyramids hypoplasia

- Male fetus
- Hydrocephaly
- Adductus thumbs
- Aqueduct of Sylvius stenosis
- Pyramidal agenesis
- Corpus callosum agenesis

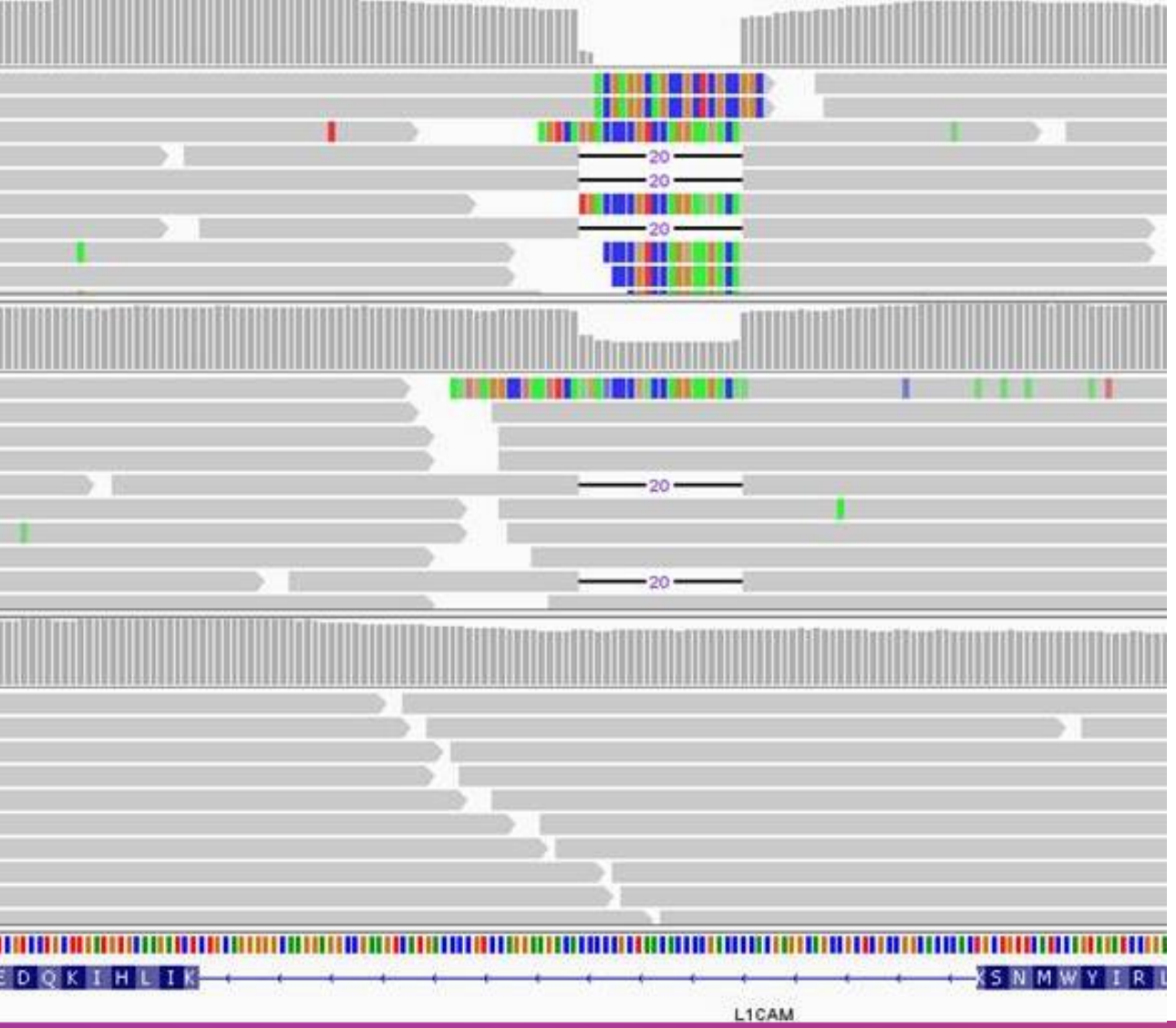


L1CAM

Genetic analysis

- Spastic paraplegia panel
- No pathogenic variant in *L1CAM*

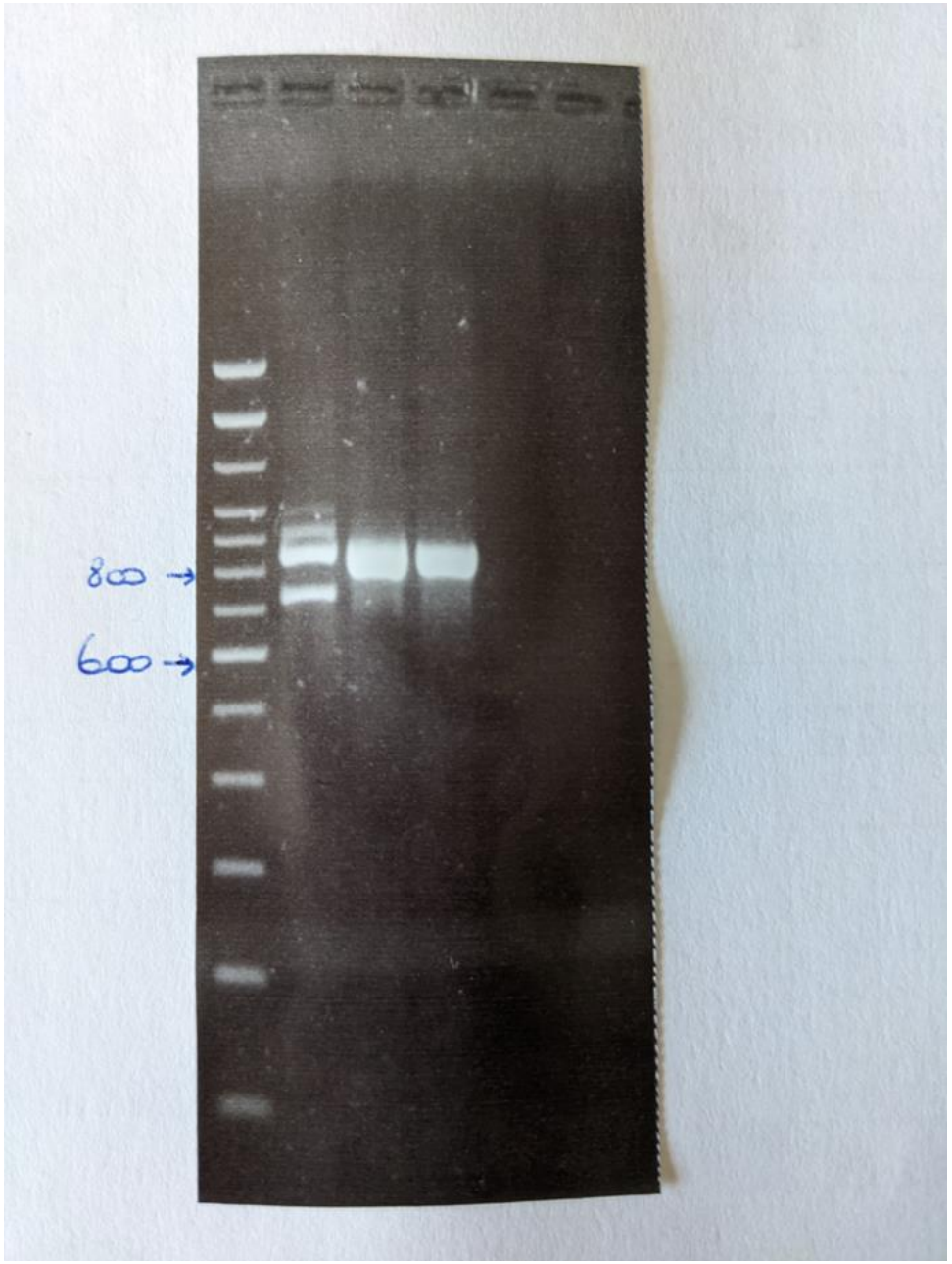
- WES
- No pathogenic variant in *L1CAM*
- No other pathogenic variant



Deep intronic deletion *L1CAM* (20pb)
NM_001278116.1: c.523+30_524-48del (classe 3)

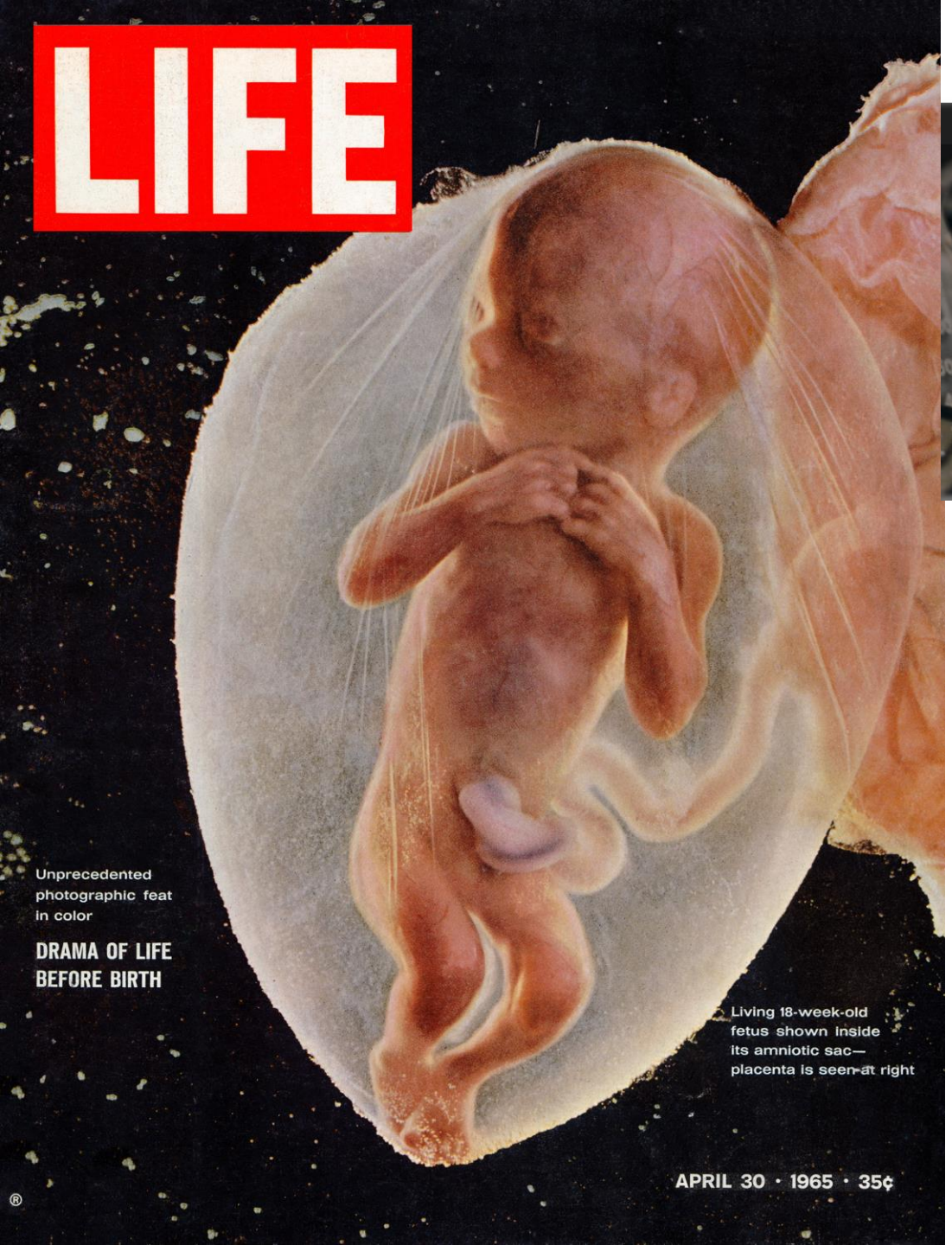
Transcript analysis

splicing defect with a shorter transcript, absent in controls



Deep phenotypic necessary in multiomics era

Help to understand pathophysiological mechanism involved in rare diseases



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