SOFFOET BEST OF MEETING

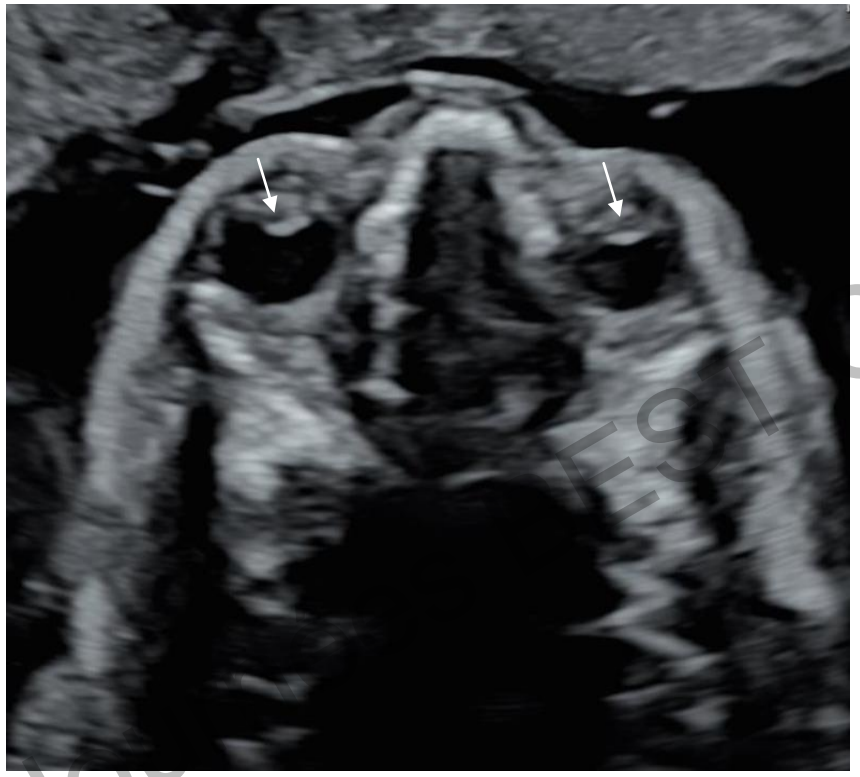
PRENATAL DIAGNOSIS OF LOWE SYNDROME: EXPANDING THE GENOTYPIC AND PHENOTYPIC SPECTRUM

ANA GRANGEIA[1], SARA TAVARES[2], SANDRA SECO[3], RITA QUENTAL[1], RENATA D'OLIVEIRA[1], TERESA CARRACA[3], CARLA RAMALHO[3], ANA COSTA BRAGA[4]

[1]DEPARTMENT OF MEDICAL GENETICS, UNIVERSITY HOSPITAL CENTER OF SÃO JOÃO (UHCSJ); [2] ALGARVE PRIVATE HOSPITAL; [3]DEPARTMENT OF OBSTETRICS, UHCSJ; DEPARTMENT OF PATHOLOGICAL ANATOMY, UHCSJ, PORTUGAL.

OCTOBER THE 15TH,2021

CASE REPORT



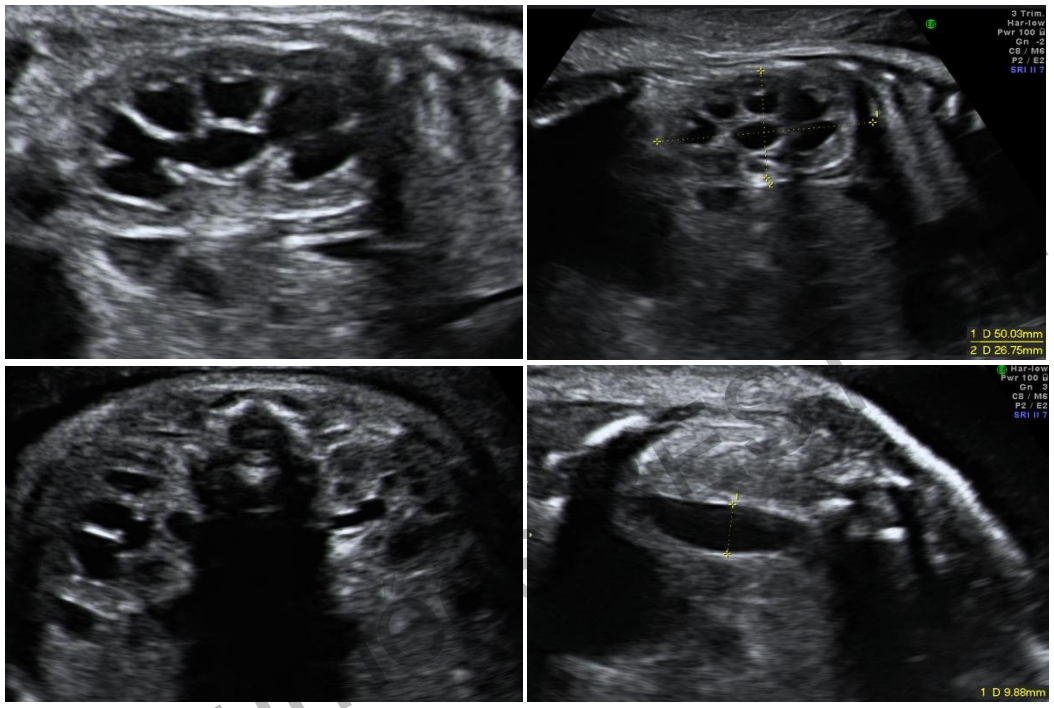
Bilateral lens opacity (arrows) observed on 2D ultrasound image at 21 weeks of gestation.

- First pregnancy of a non-consanguineous healthy Portuguese couple.
- Prenatal ultrasound revealed a male fetus with bilateral lens opacity suggesting bilateral cataract.

CASE REPORT

- Amniocentesis was performed and molecular study by next-generation sequencing panel including 144 genes associated with lens anomalies was requested.
- A **novel** likely pathogenic variant was identified in hemizygosity, c.1694_1697dup, p. (Leu566Phefs*12) in the *OCRL* gene, not previously reported in the literature or in population (GnomAD) or disease (ClinVar) databases.
- This is a frameshift variant that change the ribosome reading frame leading to a premature stop codon, being expected to have a deleterious impact.

CASE REPORT



2D ultrasound imaging at 30 weeks of gestation

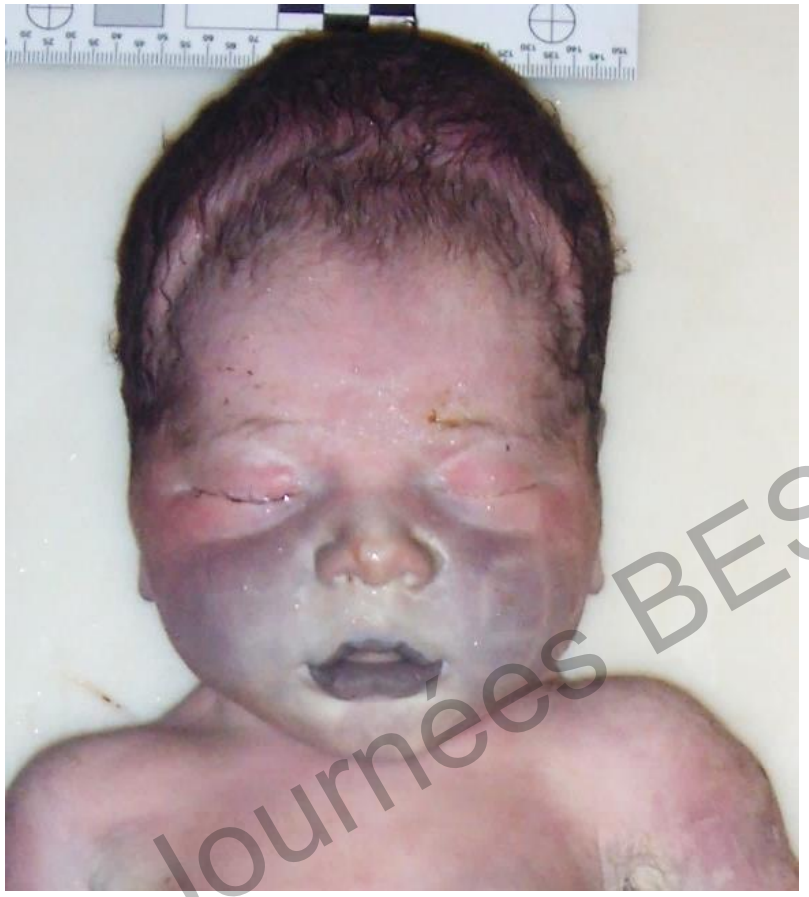
- Subsequent ultrasound evaluation identified bilateral ureteral dilation, right kidney dilatation and hydronephrosis.

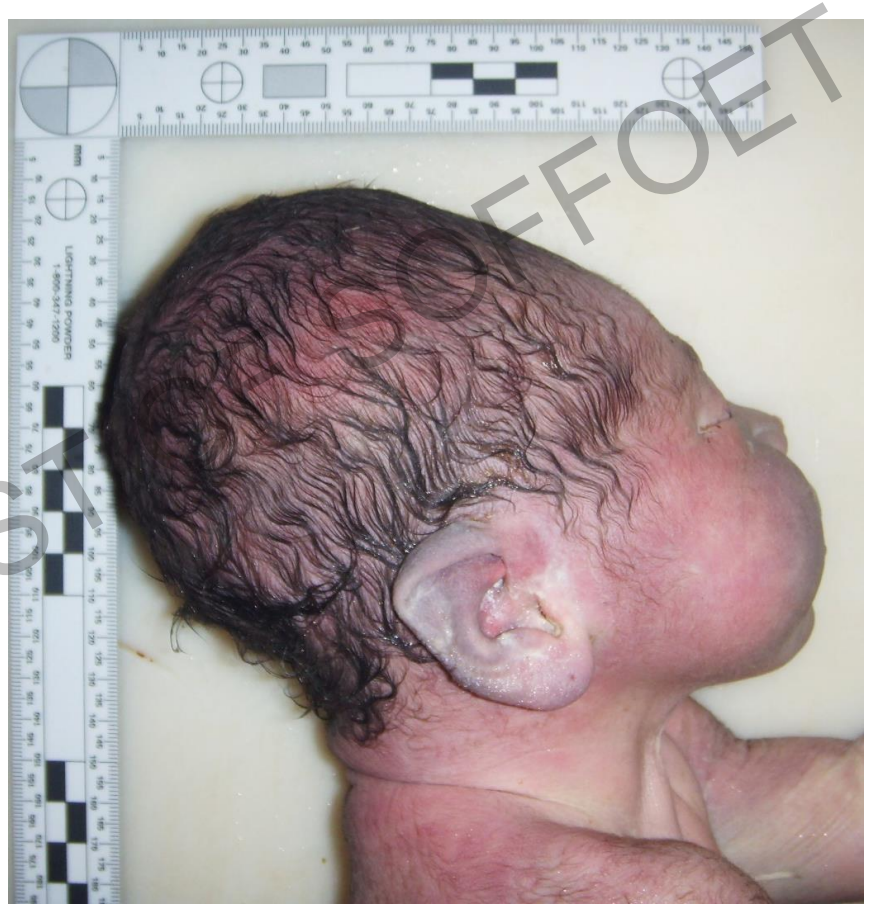
These findings were compatible with the diagnosis of **Lowe Syndrome** and the couple requested medical termination of pregnancy.

Lowe Syndrome, also named Oculocerebrorenal Dystrophy (OCRL), is caused by pathogenic variants in the *OCRL* gene with recessive X-linked inheritance. It is characterized by congenital cataracts, motor development delay, intellectual disability, short stature, rickets and proximal renal tubulopathy.

Imagen Font: Lowe Syndrome Trust

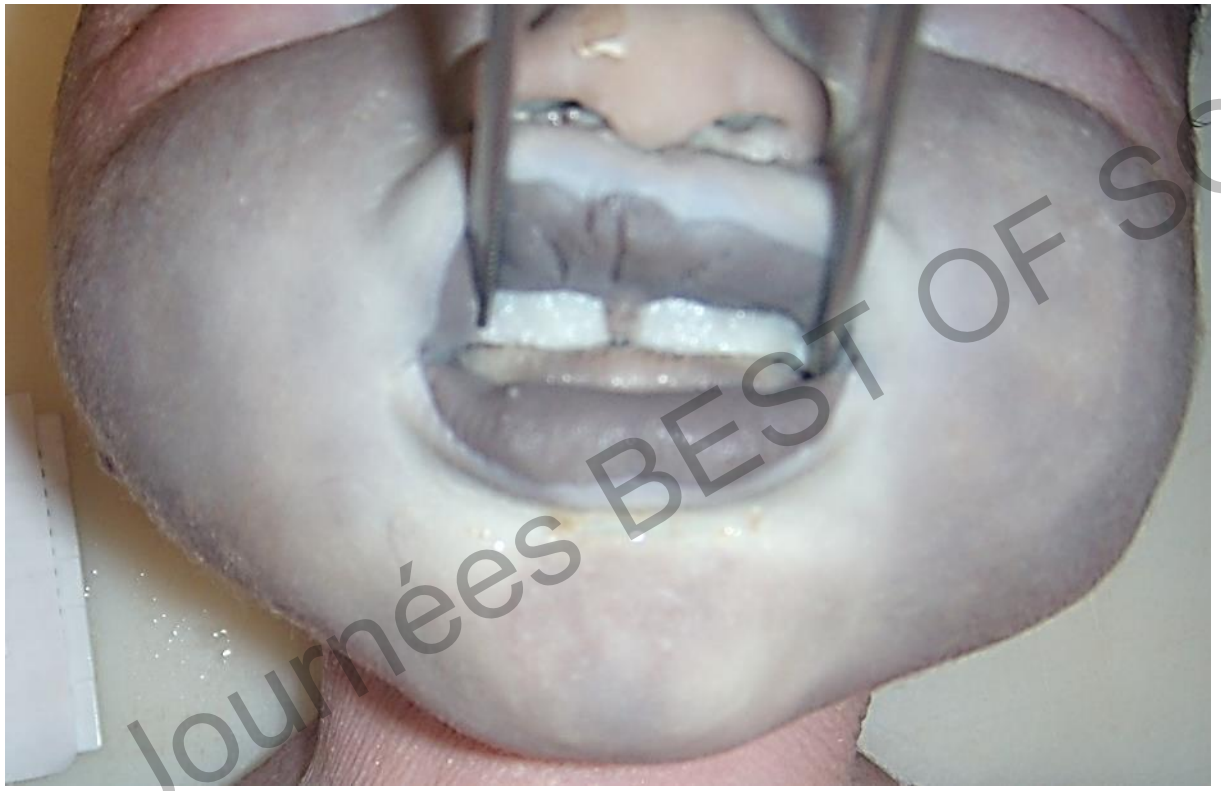
FETAL AUTOPSY – GROSS EXAMINATION





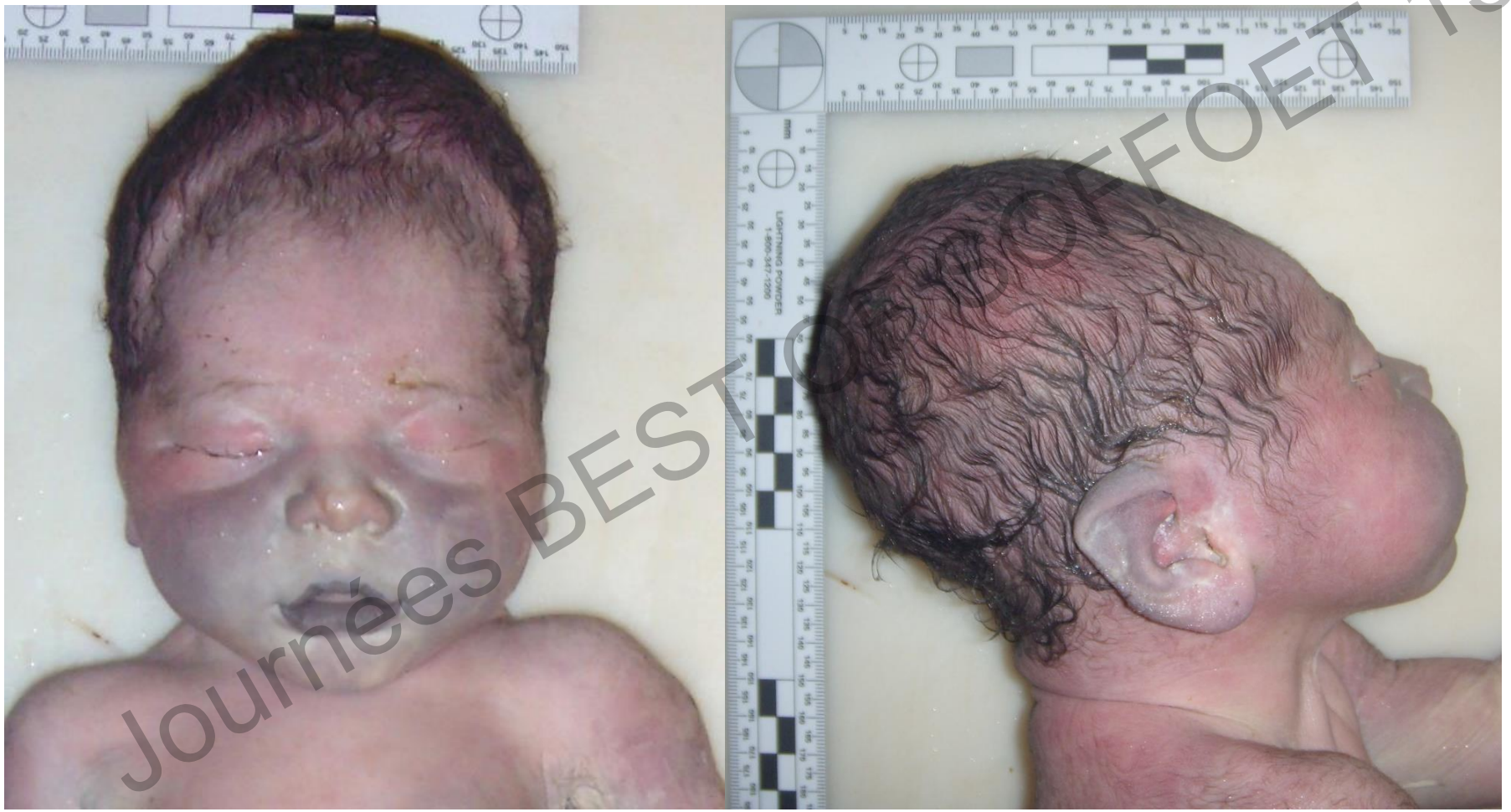
- Elongated head, parieto-occipital prominence with sloping forehead
- Large ears (>P95), with vertically deformed helix, (vertical compression type)
- Hypertelorism
- Chubby cheeks
- Thin upper lip and thick lower lip, upturned corners

FETAL AUTOPSY – GROSS EXAMINATION



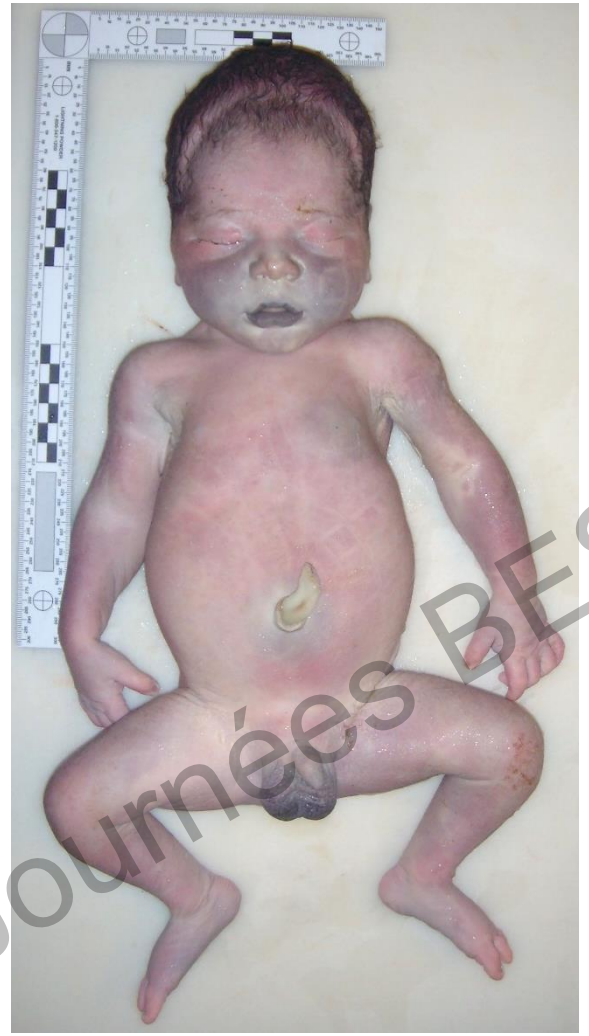
- Lower maxillary labial frenum attachment (alveolar ridge)

FETAL AUTOPSY – GROSS EXAMINATION

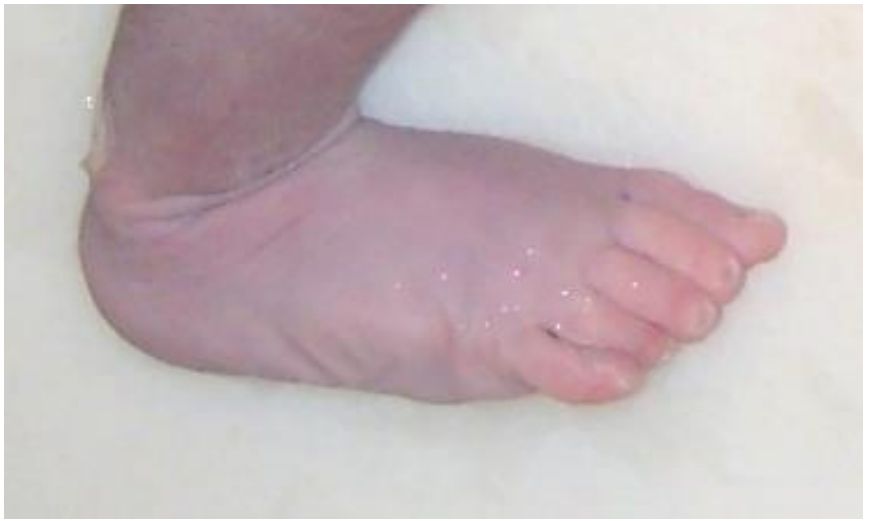


- Short and large neck

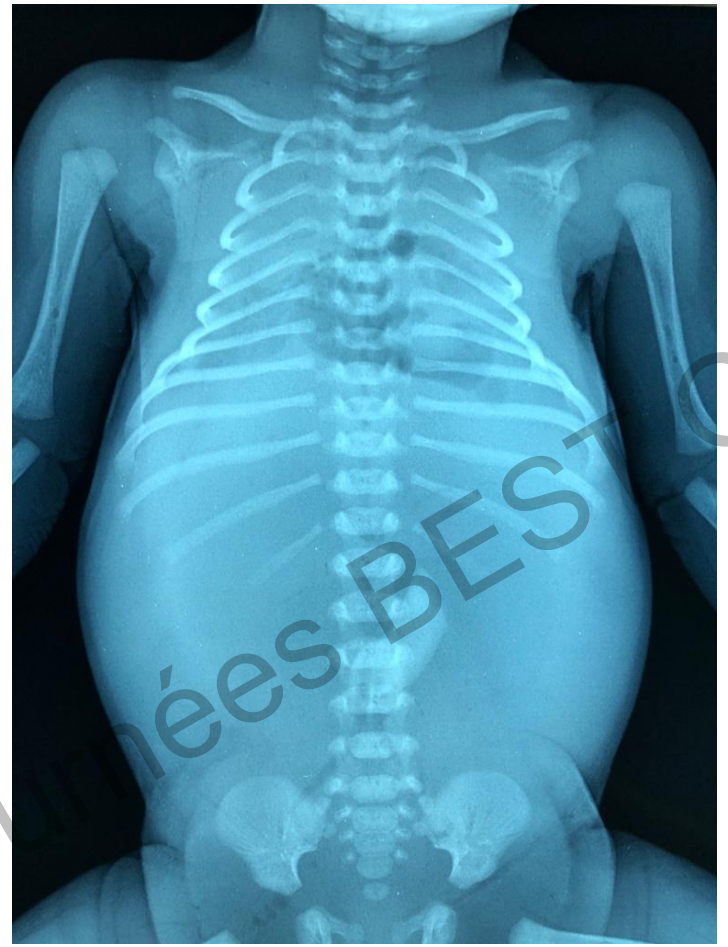
FETAL AUTOPSY – GROSS EXAMINATION



- Wrist swelling
- Genu valgum, pes planus and clinodactyly of the 5th right toe
- Joint hypermobility



X-RAY



- Horizontal (flat) conformation of the ribs: 7th to the 12th.
- No other skeletal malformations.

FETAL AUTOPSY – GROSS EXAMINATION

- Fetal eyes were fixed in 10% neutral buffered formalin.
- Eyes were inspected macroscopically and with the dissecting microscope, including transillumination, for further abnormalities, with particular emphasis on the lens.
- The horizontal plane was identified and the specimen was bisected horizontally next to the optic nerve.
- **Confirmed the presence of lens opacity suggesting cataracts in both eyes.**

FETAL AUTOPSY - HISTOLOGY

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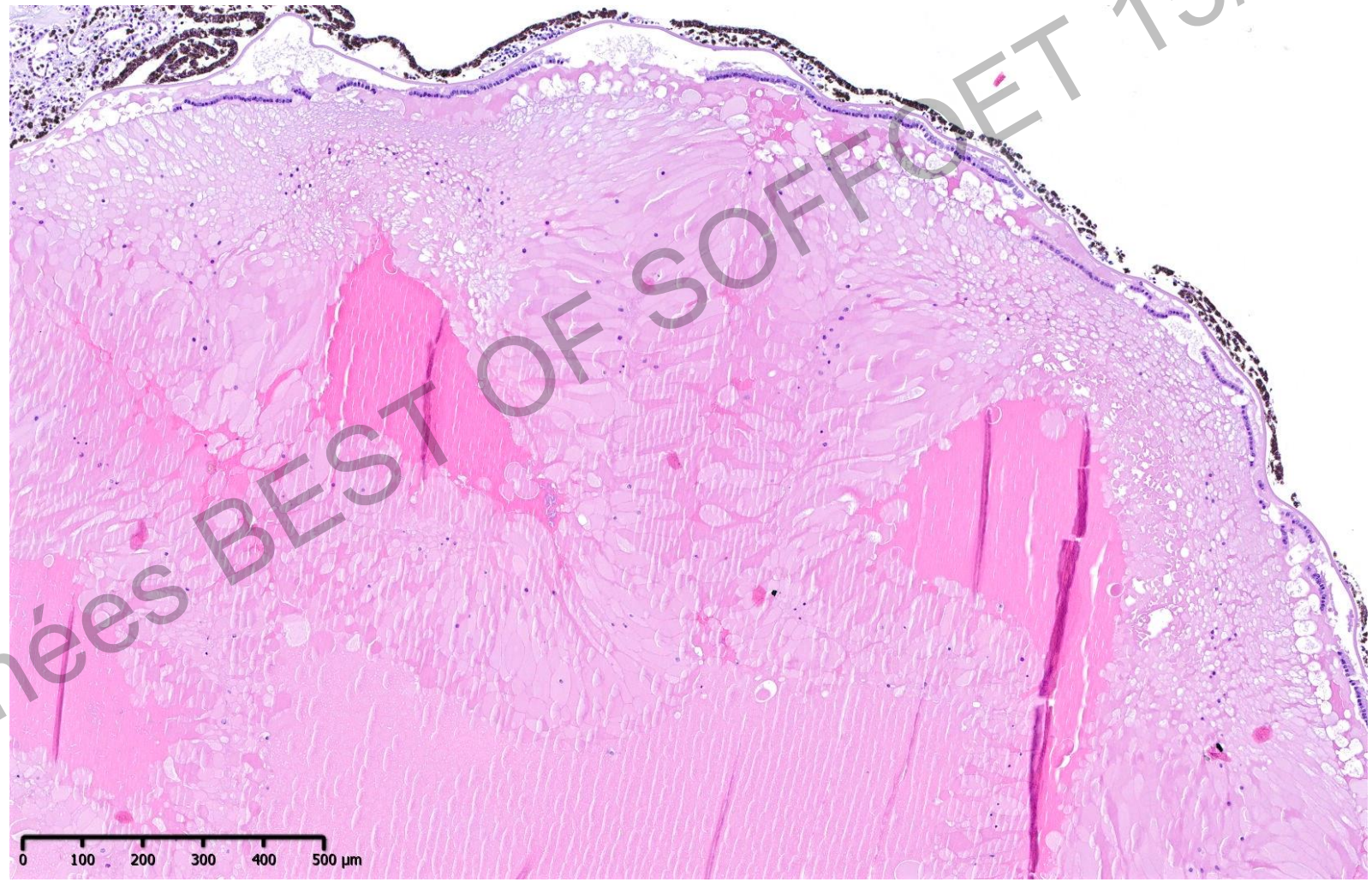

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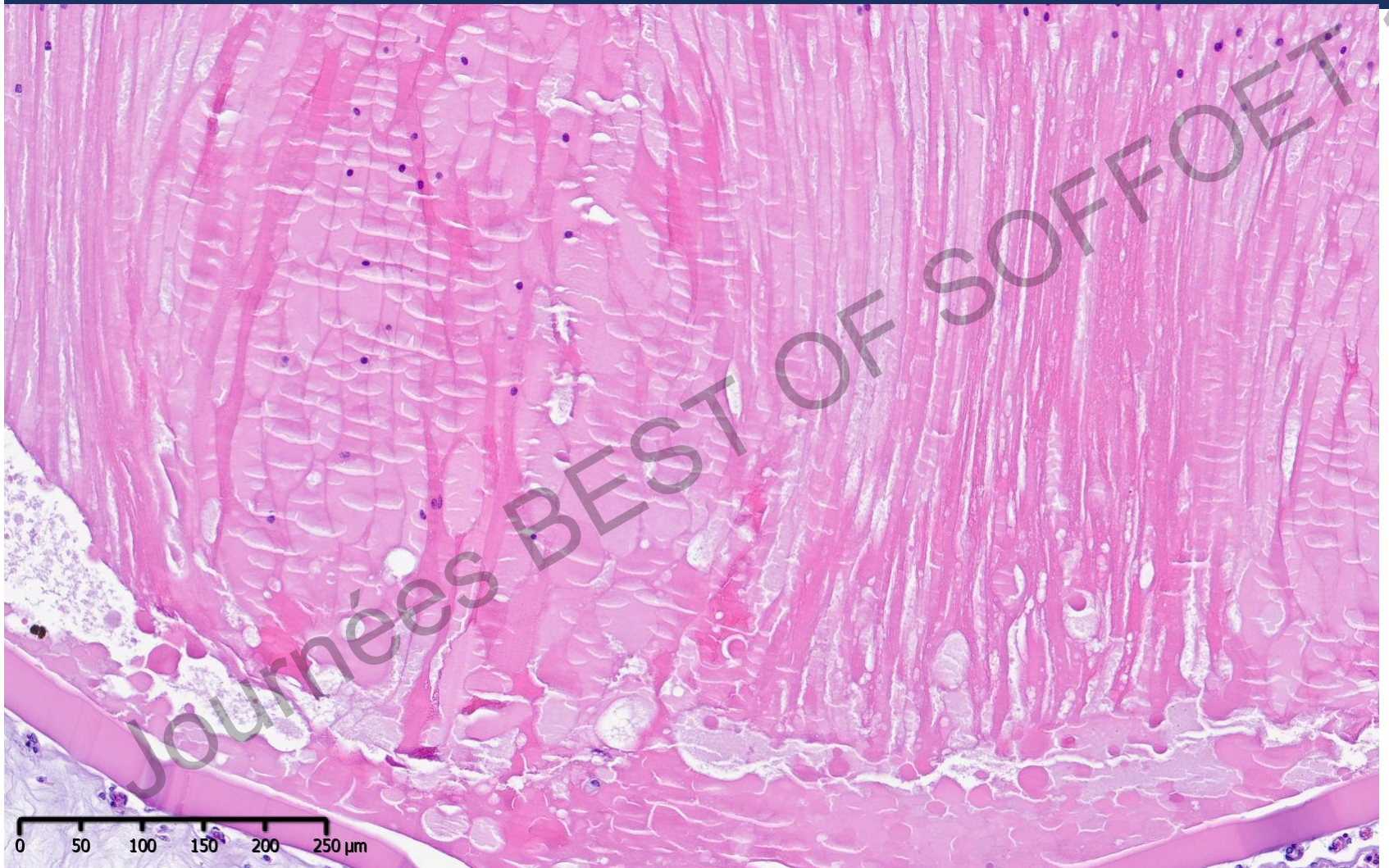

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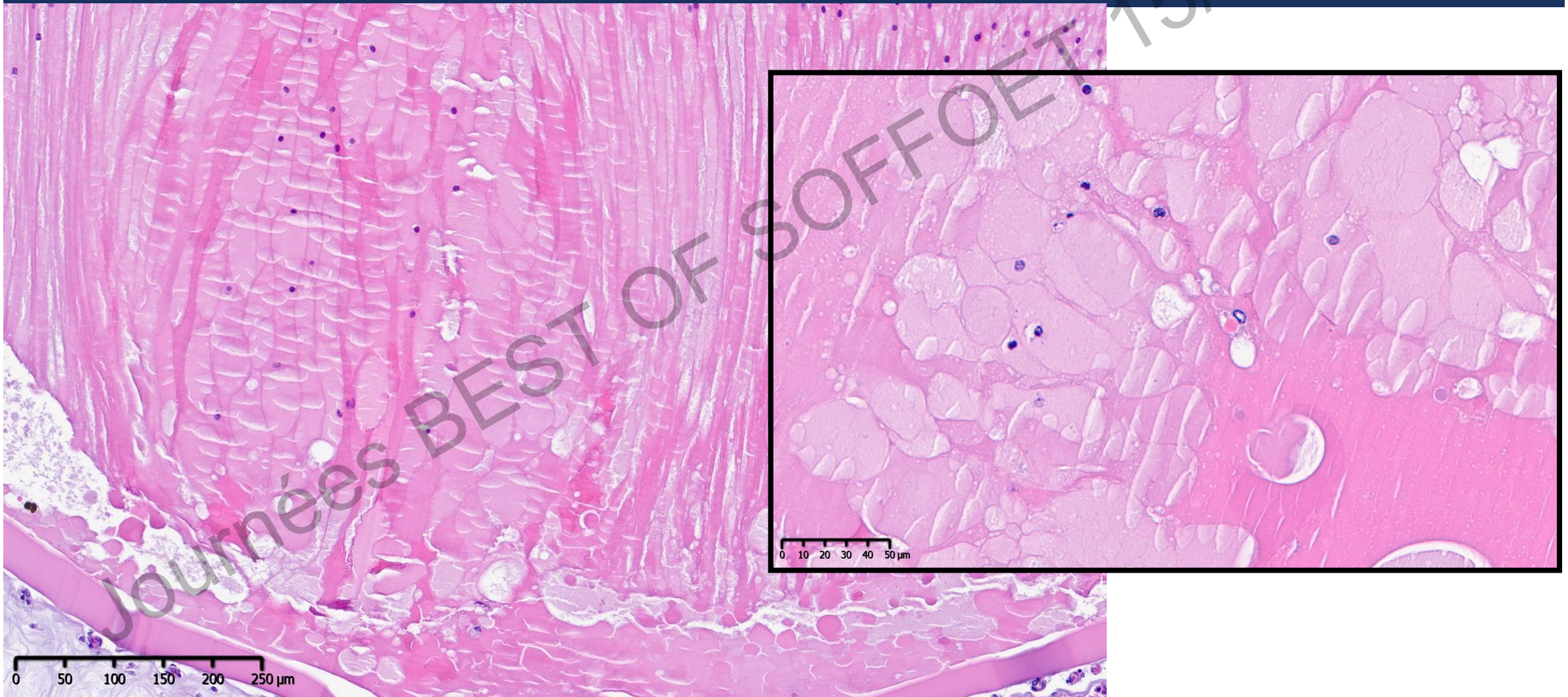

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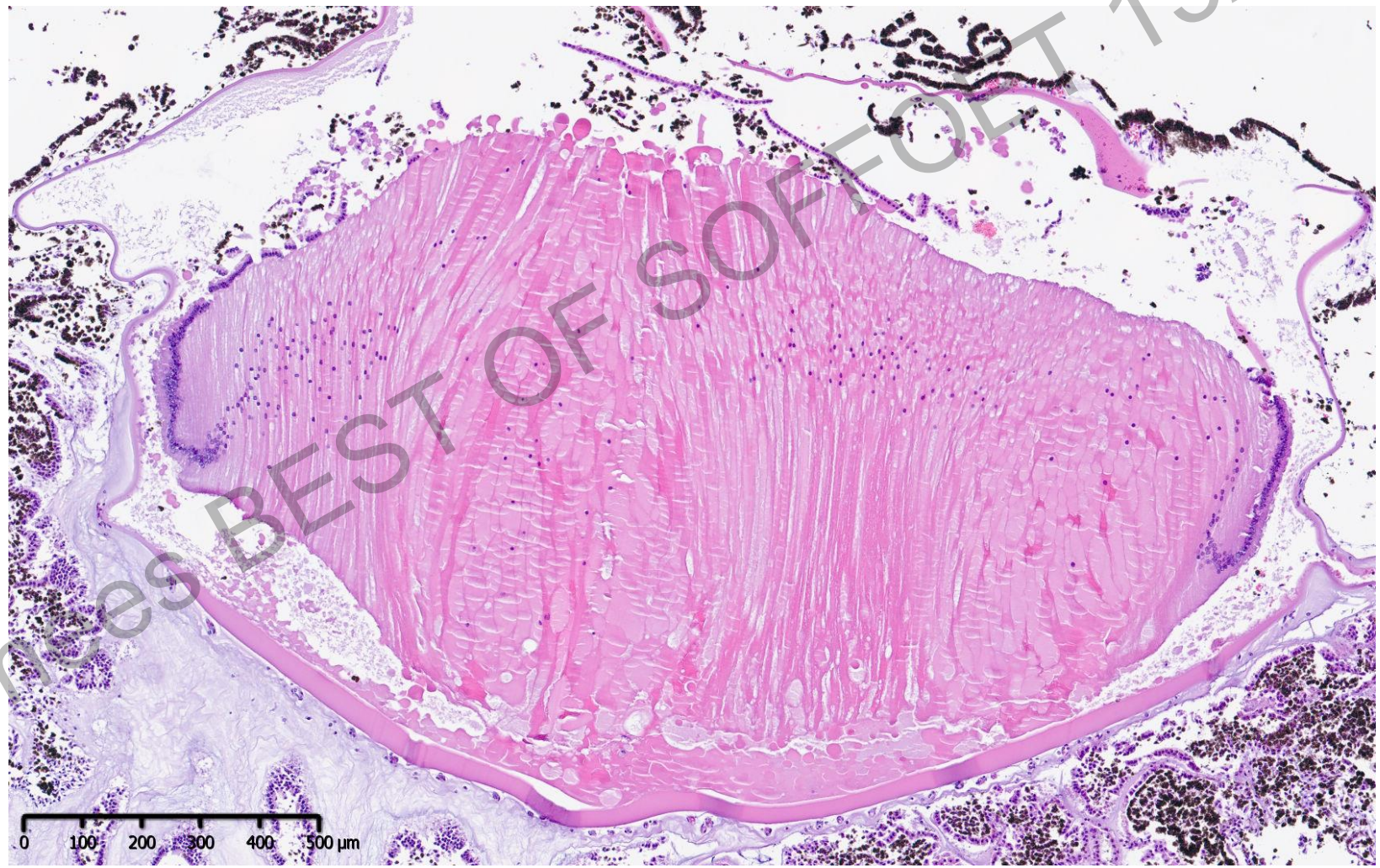

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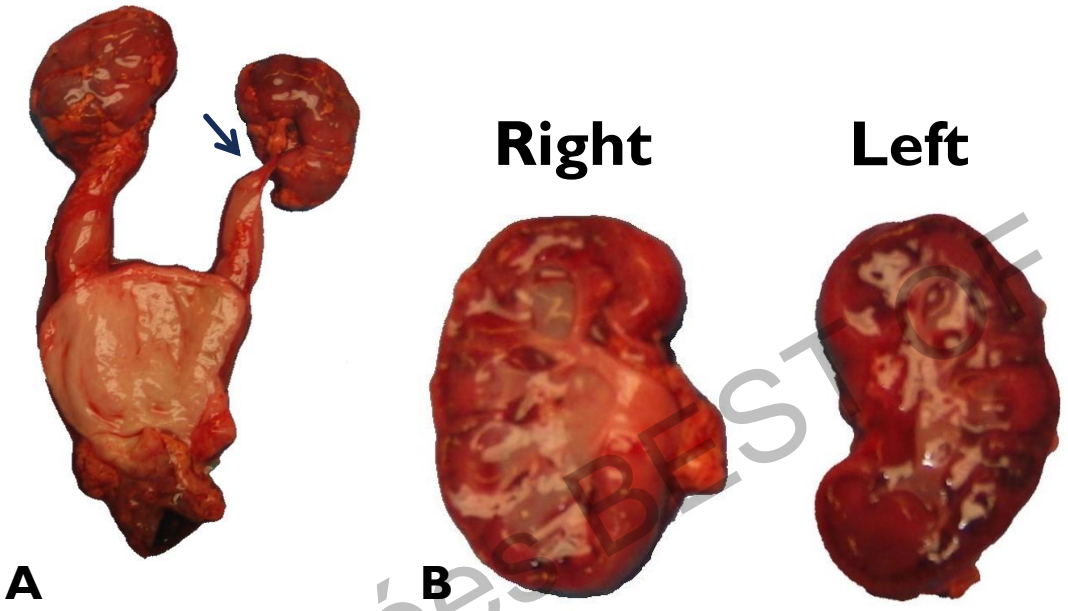
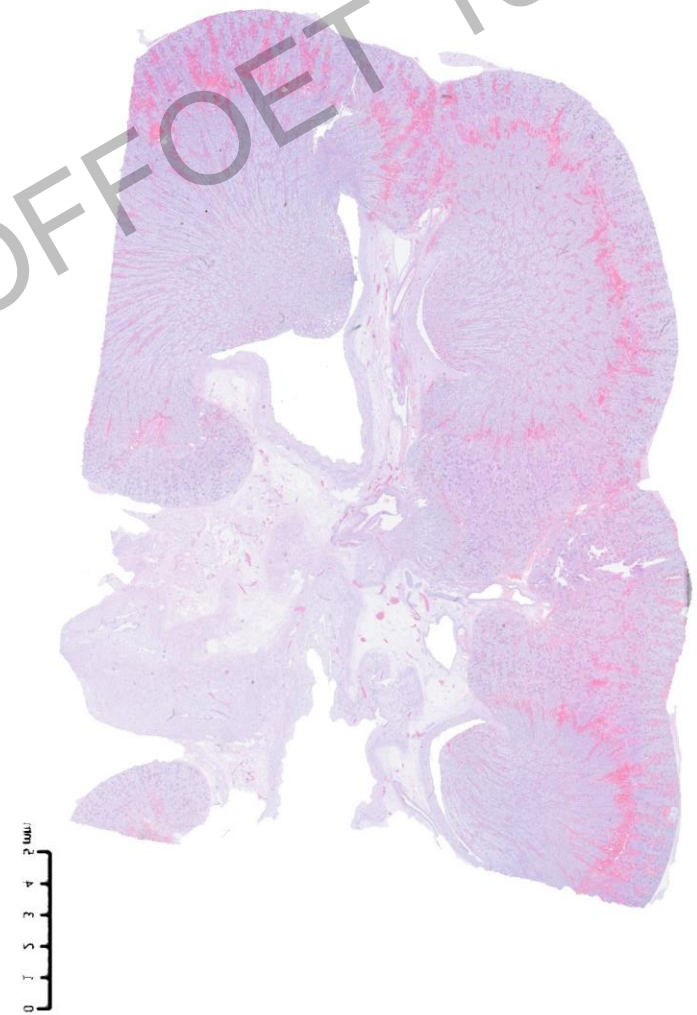


Maximum ureteric Ø
Right: 14 mm
Left: 12 mm

- Increased weight of the kidneys (due to hydronephosis, P98th).
- Bilateral hydronephrosis (more exuberant at the right kidney), ureteral and bladder dilatation with thickened wall, associated with urethral stenosis (bulbar and membranous).
- Left pieloureteral junction stenosis (arrow).
- Placenta: unremarkable findings.

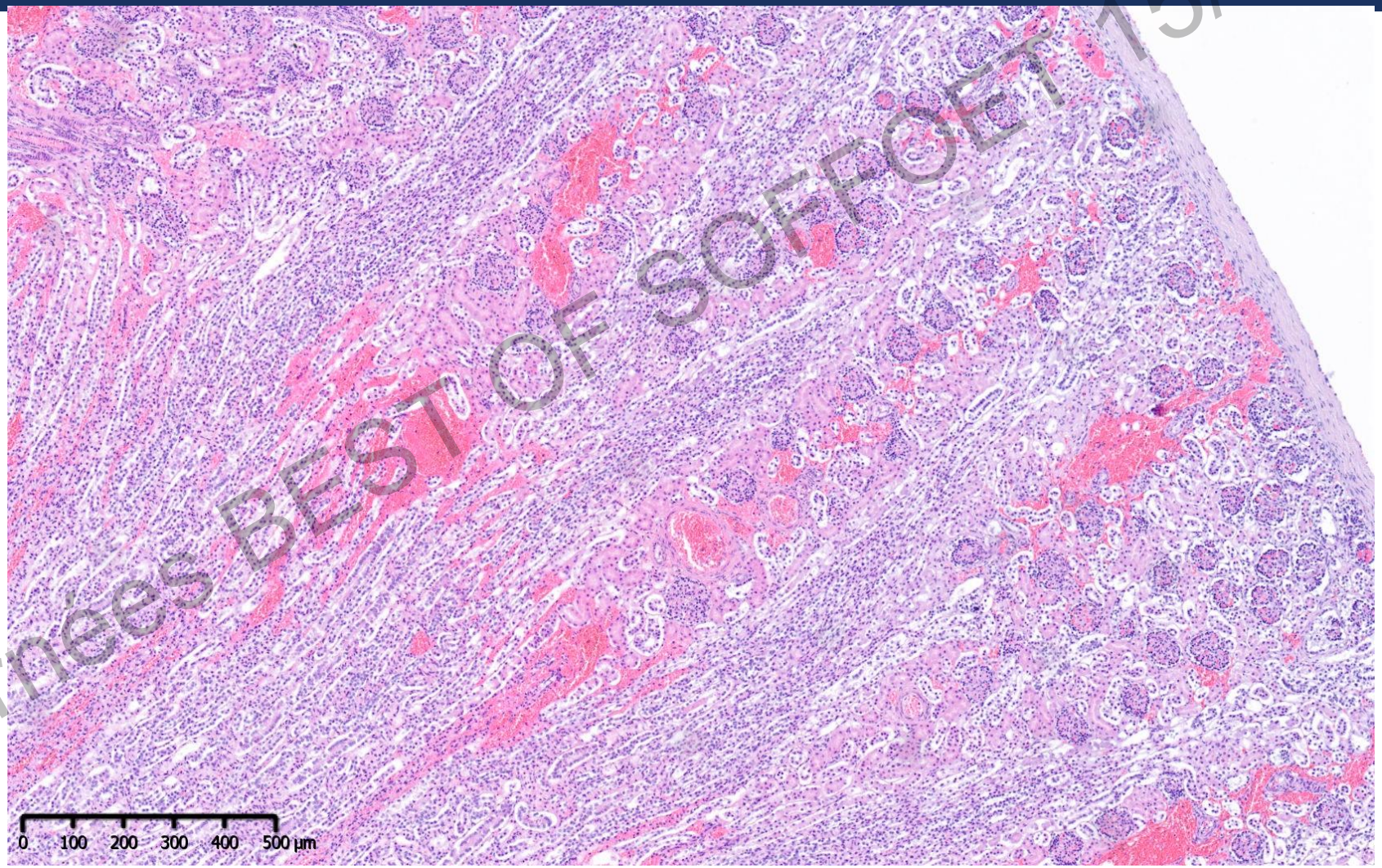
FETAL AUTOPSY - HISTOLOGY

Right



Left

FETAL AUTOPSY - HISTOLOGY



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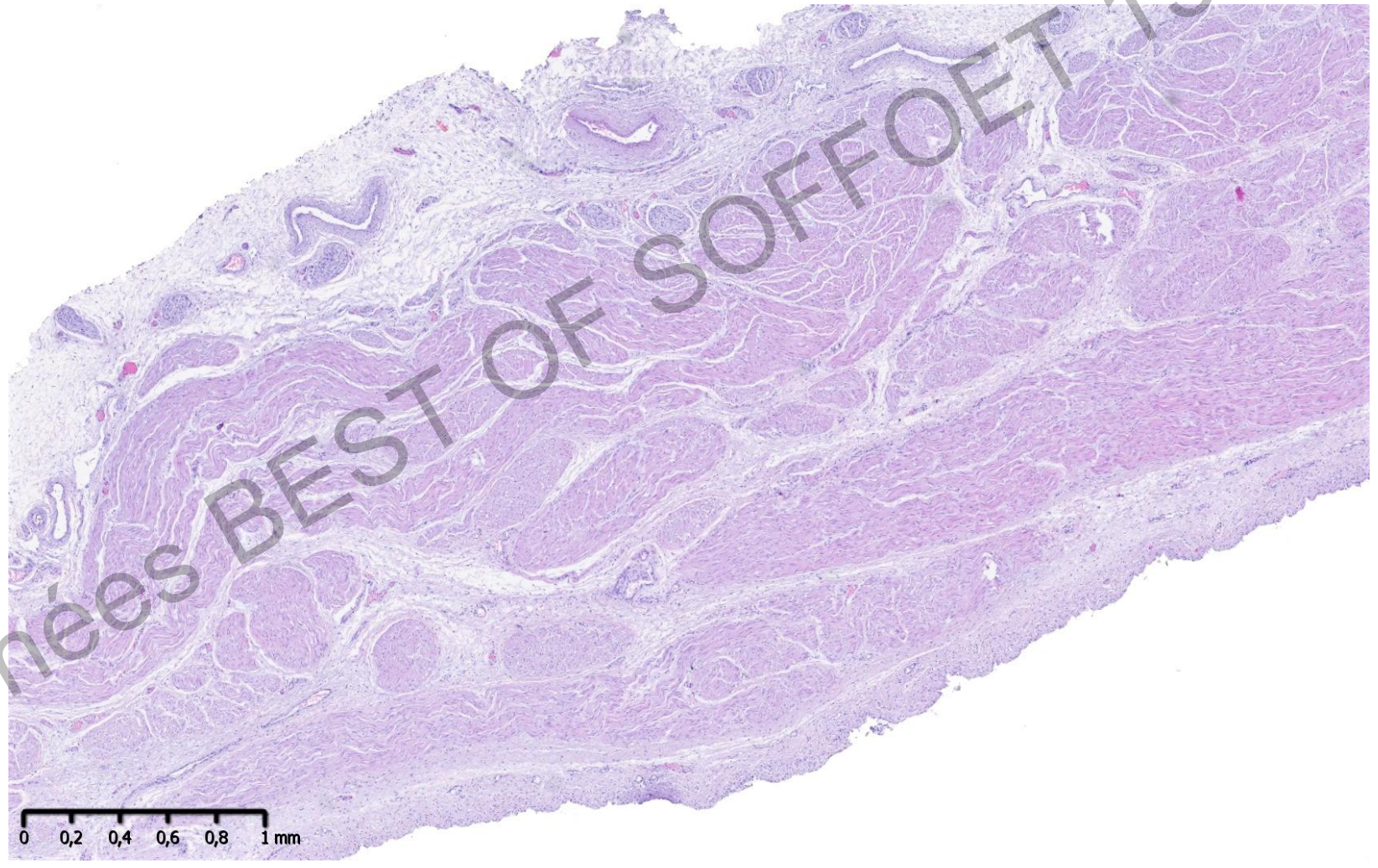

LOWE SYNDROME

- Segregation study confirmed that the identified *OCRL* gene variant was maternally inherited.

- Since heterozygous females may present ophthalmologic alterations associated with the Syndrome, ophthalmological evaluation was requested.

CONCLUSION

This clinical case reports a new presentation of Lowe Syndrome, expanding its molecular and phenotypic spectrum (craniofacial dysmorphism and CAKUT).

It also highlights the importance of a specific prenatal diagnosis in an ongoing pregnancy, with implications for the current pregnancy as well as for genetic counseling to the couple, allowing informed reproductive options.