SCIENTIFIC PAPERS

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Clinical abstract- From womb to recovery: navigating the journey of complete d-TGA

Student
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From womb to recovery: navigating the journey of complete d-TGA

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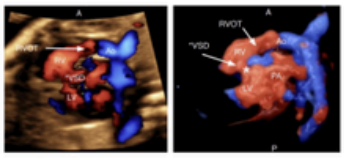
Case history

Part 1: Prenatal appointment
A pregnant 29-year-old patient at 22 + 6 days of gestation.Her obstetric history included an early pregnancy complication at 6+2 weeks when she was admitted for vaginal bleeding and diagnosed with a **3 cm subchorionic hematoma. Second-trimester ultrasound** that raised suspicion of a congenital heart defect:
→ absence of the normal crossover of the great arteries
→ aorta arising from the right ventricle and the pulmonary artery from the left ventricle
→ abnormal **three-vessel view and trachea (3VT) view**
→ abnormal blood flow patterns – visible on color Doppler imaging

Part 2: Prenatal Cardiology Clinic
Results from fetal echocardiogram:
- confirmed diagnosis of complete d-TGA
- ventricular septal defect (VSD)
- outflow congenital heart disease (CHD)
- good atrial communication (FO index = 33%)
- preserved pulmonary circulation.



Prenatal monitoring evaluations at **25, 28, 30, and 34 weeks of gestation.** → Stable fetal **hemodynamics and expected growth.**

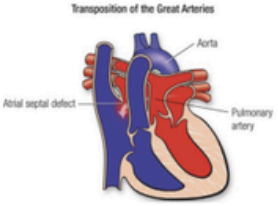
Part 3: Delivery

Fetal heart had good atrial communication (FO index=27%)

Delivery was performed via cesarean section. Neonate was born with a birth weight of 3700 g with Apgar scores of **5/7/7/7**.

It was concluded that there was no immediate need for a Rashkind procedure (a balloon septostomy) postnatally.

Introduction



d-TGA is a congenital heart disease. It accounts for approximately **8–10%** of all congenital heart defects. Leads to life-threatening hypoxemia if untreated.

For the survival of a newborn with a defect, **a connection between the systemic and pulmonary circulation is essential**:
→ patent foramen ovale
→ persistent ductus arteriosus
→ ventricular septal defect
→ atrial septal defect

Discussion

Early prenatal diagnosis of congenital heart defects, such as complete d-TGA, is crucial for optimizing outcomes.
→ advancements in prenatal ultrasound screening have significantly improved its detection up to 77%
→ early pregnancy detection remains challenging due to the normal appearance of the four-chamber heart view and technical limitations in visualizing the great arteries.

The **connections between the systemic and pulmonary blood circulations** in atrial septal defect, patent ductus arteriosus, or ventricular septal defect allow the neonate with TGA to survive until the arterial switch surgery.

d-TGA can present as either a planned or emergent condition:
→ planned cases: **prostaglandin E1 (PGE1)** is administered to maintain ductal patency until surgery
→ emergent cases: **immediate postnatal intervention** (balloon atrial septostomy

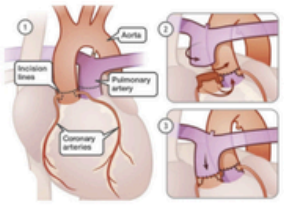
Conclusion

- **Prenatal screening is essential** for the early detection and potential treatment planning of fetal heart defects.
- Although prenatal detection of d-TGA may not change monitoring during pregnancy, it is **essential for timely postnatal intervention** and improves neonatal outcomes.
- The **connections between the systemic and pulmonary** blood circulations allow the neonate with TGA to survive until the arterial switch surgery.

Part 4: Corrective surgery

2 weeks of age: neonate underwent **planned corrective cardiac surgery**

The treatment of choice in surgical management is currently the Jatene procedure—anatomical correction, which restores the normal anatomy of the heart.
- is performed in newborns **up to the 3rd week of life**
- is carried out using cardiopulmonary bypass and deep hypothermia.



Part 5: Postnatal course

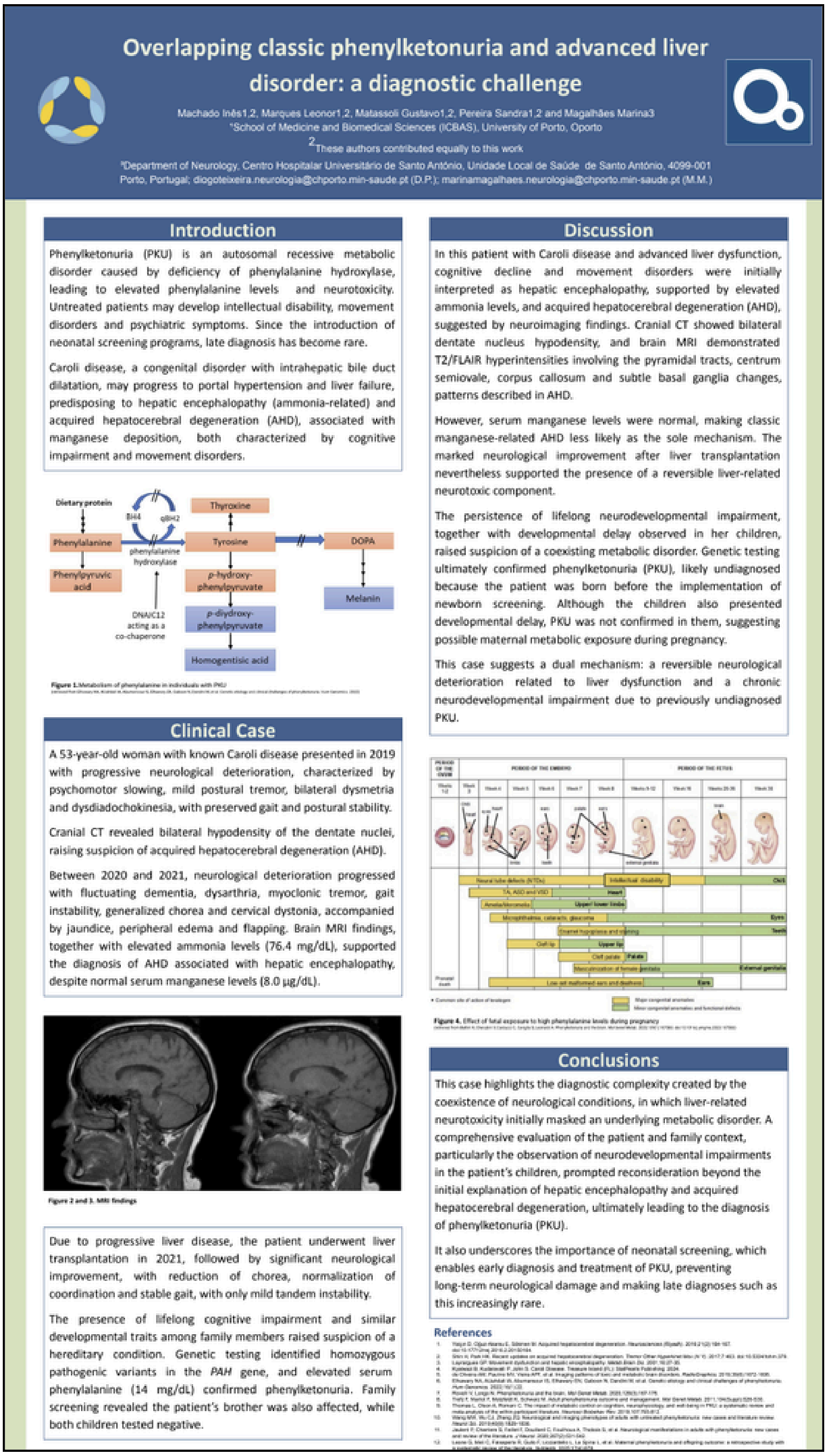
- **intensive care** with mechanical ventilation
- **catecholamine** infusion
- teicoplanin and ceftazidime (wound infection)

Follow-up echocardiography confirmed good myocardial contractility and no pericardial effusion.

[1] [2] Guo J, Ling W, Dang T, Guo S, Ma H, Huang Q, Zeng L, Weng Z, Wu Q. Prenatal transposition of great arteries diagnosis and management: a Chinese single-center study. Front Cardiovasc Med. 2024 Mar 6;11:1341005. doi: 10.3389/fcvm.2024.1341005. PMID: 38510199; PMCID: PMC10951393.
[3]Hu Q, Deng C, Zhu Q, Yang K, Liu H, Liao H, Wang X, Yu H. Dextro-transposition of the great arteries in one twin: case reports and literature review. Transl Pediatr. 2022 Apr;11(4):601-609. doi: 10.21037/tp-21-569. PMID: 35558075; PMCID: PMC9085850.
[4]Karmegaraj B. Four-Dimensional Ultrasound Imaging of Spatial Relationship of Great Arteries in Fetuses With Transposition of Great Arteries. J Ultrasound Med. 2024 Sep;43(9):1763-1767. doi: 10.1002/jum.16482. Epub 2024 May 16. PMID: 38752383.
[5] Anderson BR, Ciarlegio AJ, Hayes DA, Quiegebeur JM, Vincent JA, Bacha EA. Earlier arterial switch operation improves outcomes and reduces costs for neonates with transposition of the great arteries. J Am Coll Cardiol. (2014) 63(5):480–7. 10.1016/j.jacc.2013.08.1645
[6] Rutledge JM, Nihill MR, Fraser CD, Smith OE, McMahon CJ, Bezold LI. Outcome of 121 patients with congenitally corrected transposition of the great arteries. Pediatr Cardiol. (2002) 23(2):137–45. 10.1007/s00246-001-0037-8

Clinical abstract- Overlapping classic phenylketonuria and advanced liver disorder: a diagnostic challenge

Student
Gustavo Matassoli



Overlapping classic phenylketonuria and advanced liver disorder: a diagnostic challenge

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Introduction

Phenylketonuria (PKU) is an autosomal recessive metabolic disorder caused by deficiency of phenylalanine hydroxylase, leading to elevated phenylalanine levels and neurotoxicity. Untreated patients may develop intellectual disability, movement disorders and psychiatric symptoms. Since the introduction of neonatal screening programs, late diagnosis has become rare.

Caroli disease, a congenital disorder with intrahepatic bile duct dilatation, may progress to portal hypertension and liver failure, predisposing to hepatic encephalopathy (ammonia-related) and acquired hepatocerebral degeneration (AHD), associated with manganese deposition, both characterized by cognitive impairment and movement disorders.

Figure 1. Metabolism of phenylalanine in individuals with PKU

Clinical Case

A 53-year-old woman with known Caroli disease presented in 2019 with progressive neurological deterioration, characterized by psychomotor slowing, mild postural tremor, bilateral dysmetria and dysdiadochokinesia, with preserved gait and postural stability.

Cranial CT revealed bilateral hypodensity of the dentate nuclei, raising suspicion of acquired hepatocerebral degeneration (AHD).

Between 2020 and 2021, neurological deterioration progressed with fluctuating dementia, dysarthria, myoclonic tremor, gait instability, generalized chorea and cervical dystonia, accompanied by jaundice, peripheral edema and flapping. Brain MRI findings, together with elevated ammonia levels (76.4 mg/dL), supported the diagnosis of AHD associated with hepatic encephalopathy, despite normal serum manganese levels (8.0 µg/dL).

Figure 2 and 3. MRI findings

Due to progressive liver disease, the patient underwent liver transplantation in 2021, followed by significant neurological improvement, with reduction of chorea, normalization of coordination and stable gait, with only mild tandem instability.

The presence of lifelong cognitive impairment and similar developmental traits among family members raised suspicion of a hereditary condition. Genetic testing identified homozygous pathogenic variants in the *PAH* gene, and elevated serum phenylalanine (14 mg/dL) confirmed phenylketonuria. Family screening revealed the patient's brother was also affected, while both children tested negative.

Discussion

In this patient with Caroli disease and advanced liver dysfunction, cognitive decline and movement disorders were initially interpreted as hepatic encephalopathy, supported by elevated ammonia levels, and acquired hepatocerebral degeneration (AHD), suggested by neuroimaging findings. Cranial CT showed bilateral dentate nucleus hypodensity, and brain MRI demonstrated T2/FLAIR hyperintensities involving the pyramidal tracts, centrum semiovale, corpus callosum and subtle basal ganglia changes, patterns described in AHD.

However, serum manganese levels were normal, making classic manganese-related AHD less likely as the sole mechanism. The marked neurological improvement after liver transplantation nevertheless supported the presence of a reversible liver-related neurotoxic component.

The persistence of lifelong neurodevelopmental impairment, together with developmental delay observed in her children, raised suspicion of a coexisting metabolic disorder. Genetic testing ultimately confirmed phenylketonuria (PKU), likely undiagnosed because the patient was born before the implementation of newborn screening. Although the children also presented developmental delay, PKU was not confirmed in them, suggesting possible maternal metabolic exposure during pregnancy.

This case suggests a dual mechanism: a reversible neurological deterioration related to liver dysfunction and a chronic neurodevelopmental impairment due to previously undiagnosed PKU.

Figure 4. Effect of fetal exposure to high phenylalanine levels during pregnancy

Conclusions

This case highlights the diagnostic complexity created by the coexistence of neurological conditions, in which liver-related neurotoxicity initially masked an underlying metabolic disorder. A comprehensive evaluation of the patient and family context, particularly the observation of neurodevelopmental impairments in the patient's children, prompted reconsideration beyond the initial explanation of hepatic encephalopathy and acquired hepatocerebral degeneration, ultimately leading to the diagnosis of phenylketonuria (PKU).

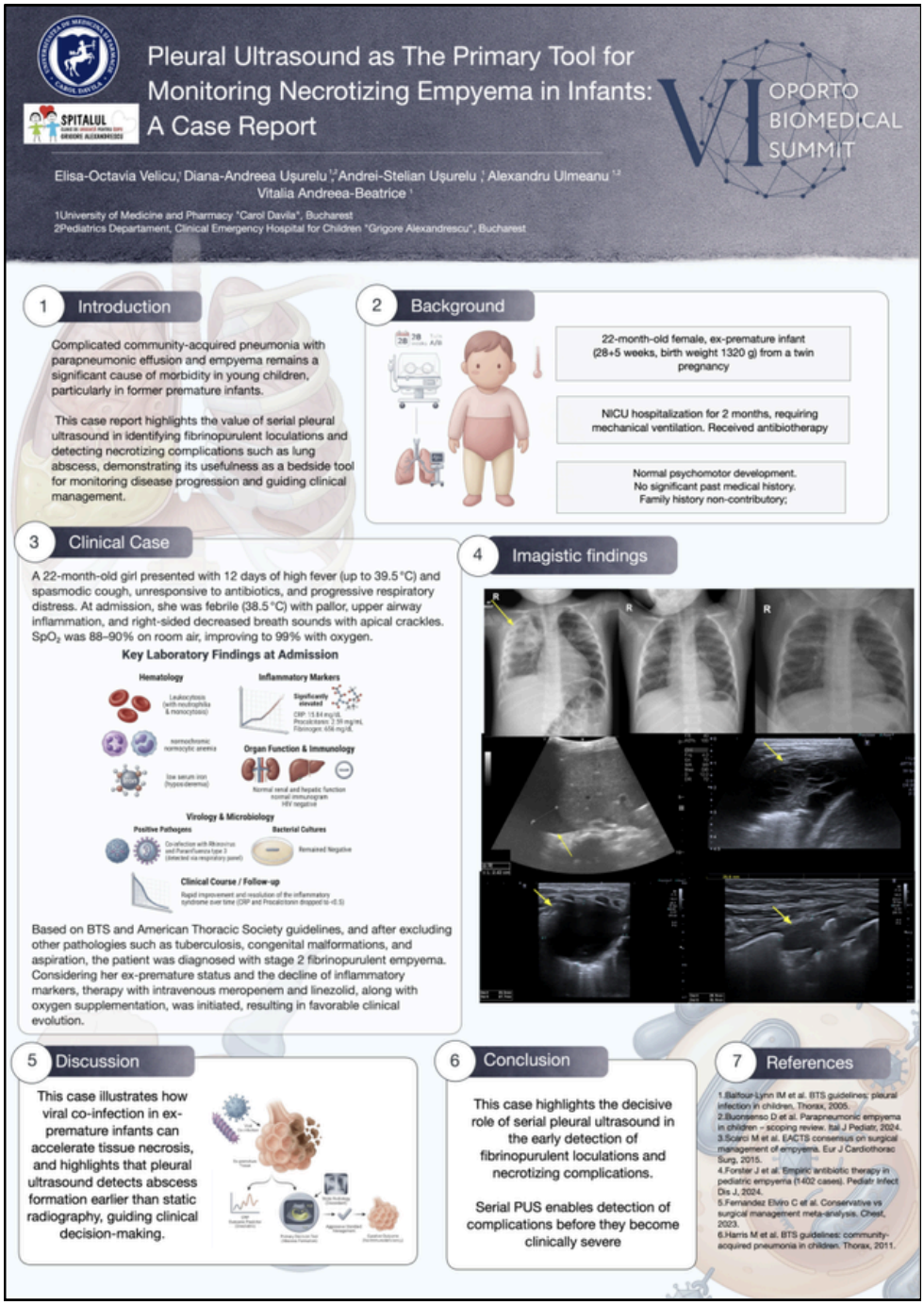
It also underscores the importance of neonatal screening, which enables early diagnosis and treatment of PKU, preventing long-term neurological damage and making late diagnoses such as this increasingly rare.

References

Clinical abstract- Pleural Ultrasound as The Primary Tool for Monitoring Necrotizing Empyema in Infants: A Case Report

Student

Elisa-Octavia Velicu



Clinical abstract- Robotic Management of Stage 4 Endometriosis: A Case of Diagnostic Discrepancy

Student

Fericel George Iulian

Robotic Management of Stage 4 Endometriosis: A Case of Diagnostic Discrepancy

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[3]- Institut Franco-Européen Multidisciplinaire d'Endométriose

Introduction

- Endometriosis is a chronic inflammatory disease affecting approximately 10% of reproductive-age women.
- Stage 4 features deep infiltrating lesions impacting the gastrointestinal tract, extra-pelvic structures, and fertility.
- Multidisciplinary, robotic-assisted surgical approach is essential for managing multi-organ infiltration.

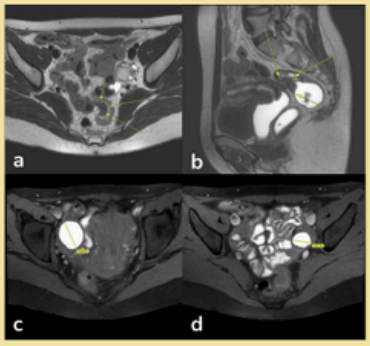


Fig. 1: Endometriosis lesions on MRI.
a - Ax T2, b - Sag T2 - rectal lesion
c, d - Ax T1 FS SFOV - ovarian endometrioma

Discussion

- Key feature: the significant discrepancy between imaging and surgical findings.
- MRI missed a 3cm ileal nodule and diaphragmatic lesions.
- Robotic assistance was vital for precise nerve-sparing and complex suturing.
- The NOSE technique - minimally invasive extraction, reducing incisional endometriosis risk and enhancing recovery.

Conclusion

- Endometriosis is a systemic condition that is frequently more extensive than imaging reveals.
- Accurate diagnosis still relies on high clinical suspicion and careful surgical inspection.
- Comprehensive multidisciplinary approach is crucial to reduce the risk of missed lesions.

Case Report

- 34-year-old female presenting with dysmenorrhea, daily chronic pelvic pain, positional dyspareunia, and painful defecation, also a 2-year history of primary infertility.
- MRI and transvaginal ultrasound suggested deep infiltrating endometriosis.
- Hysterosalpingography - negative Cotte test on the left side.
- Course of treatment: a three-hour robot-assisted laparoscopy was successfully performed.
- Bilateral ovarian cystectomy - without parenchymal coagulation to preserve ovarian reserve.
- A 9-cm colorectal segment resection using the NOSE technique, extracting the specimen transvaginally.
- A 3-cm white, fibrotic endometriotic lesion on the ileum, causing stenosis and missed on MRI, was resected alongside diaphragmatic lesions.
- Final rASRM score of 78.
- Immediate outcome: restored pelvic anatomy and optimized fertility potential.
- Postoperative continuous dienogest therapy was continued.
- 2-month follow-up: complete resolution of severe symptoms and normal healing of the vaginal vault.

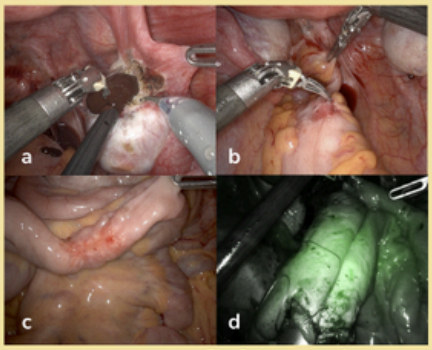


Fig. 2: Intraoperative aspects.
a - ovarian endometrioma
b - rectal and Douglas pouch lesions
c - ileal lesion
d - side-to-side ileal anastomosis with 60 mm endoGIA stapler and ICG testing

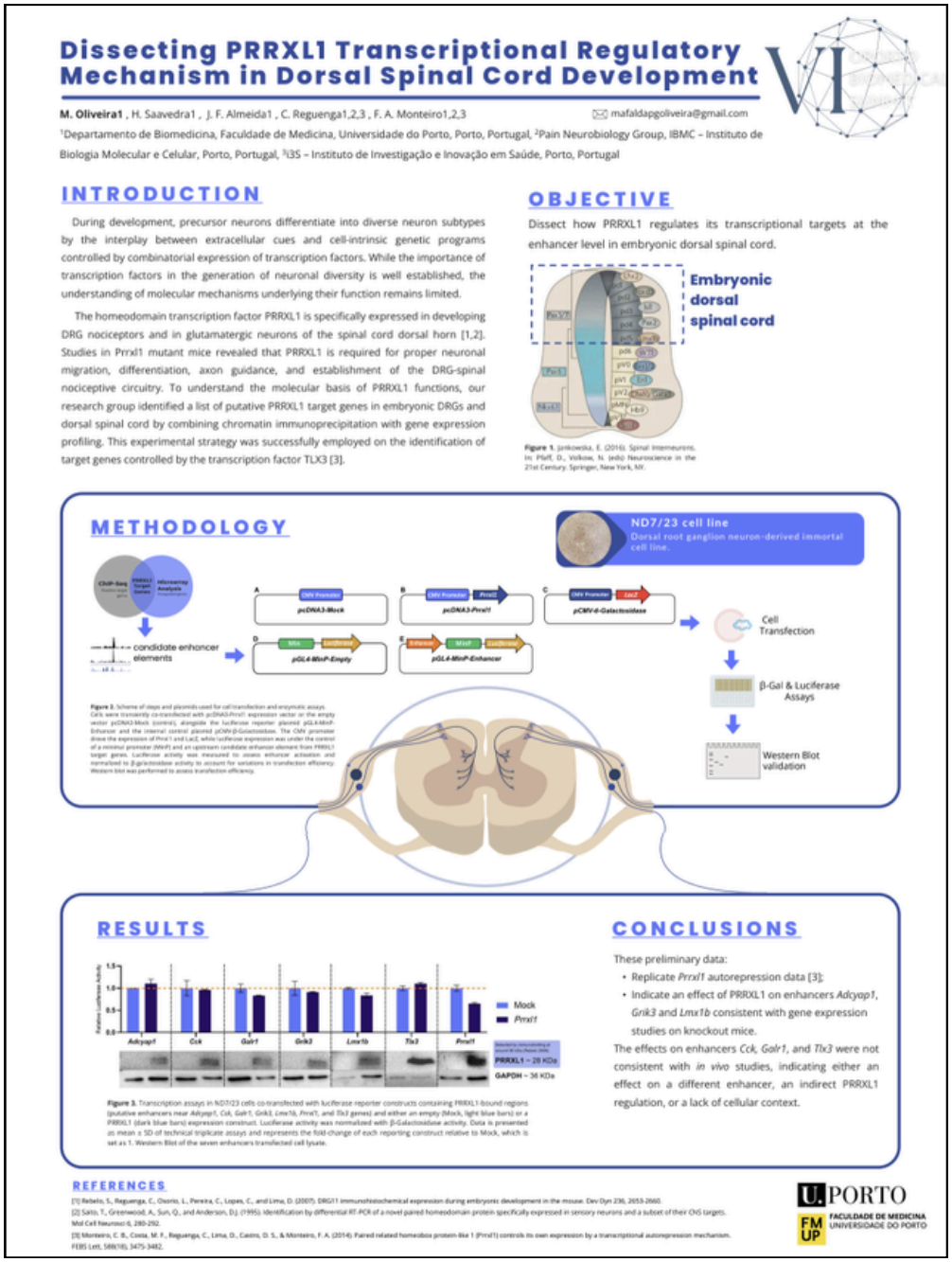
Fig. 3: Resection specimens

References

Research abstract- Dissecting PRRXL1 Transcriptional Regulatory Mechanism in Dorsal Spinal Cord Development

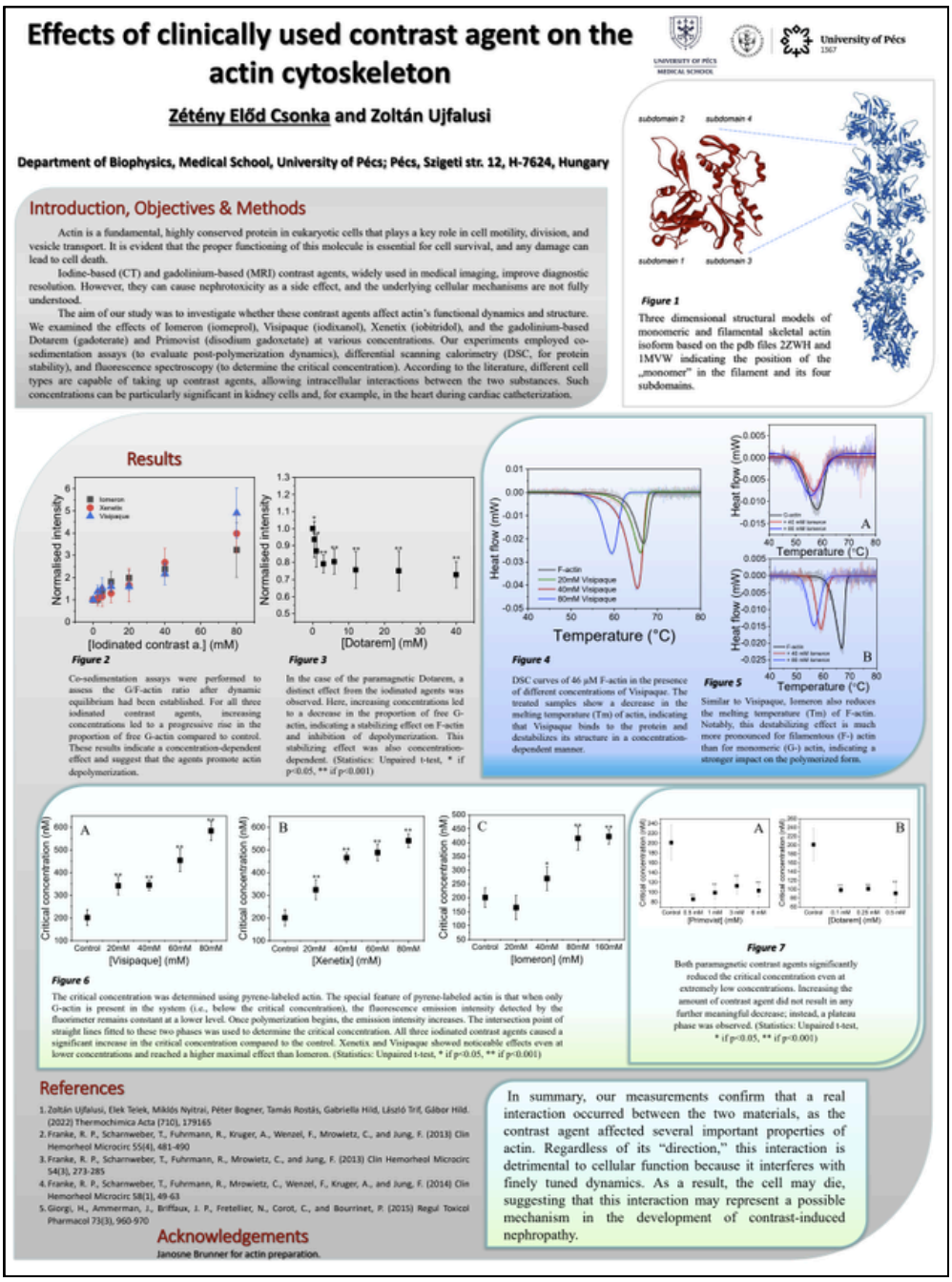
Student

Mafalda Pinto Gomes de Oliveira



Research abstract- Effects of Clinically Used Contrast Agents on the Actin Cytoskeleton

Student
Zétény Előd Csonka



Effects of clinically used contrast agent on the actin cytoskeleton

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Introduction, Objectives & Methods

Actin is a fundamental, highly conserved protein in eukaryotic cells that plays a key role in cell motility, division, and vesicle transport. It is evident that the proper functioning of this molecule is essential for cell survival, and any damage can lead to cell death.

Iodine-based (CT) and gadolinium-based (MRI) contrast agents, widely used in medical imaging, improve diagnostic resolution. However, they can cause nephrotoxicity as a side effect, and the underlying cellular mechanisms are not fully understood.

The aim of our study was to investigate whether these contrast agents affect actin's functional dynamics and structure. We examined the effects of Iomeron (iomeprol), Visipaque (iodixanol), Xenetix (iobitridol), and the gadolinium-based Dotarem (gadoterate) and Primovist (disodium gadoxetate) at various concentrations. Our experiments employed co-sedimentation assays (to evaluate post-polymerization dynamics), differential scanning calorimetry (DSC, for protein stability), and fluorescence spectroscopy (to determine the critical concentration). According to the literature, different cell types are capable of taking up contrast agents, allowing intracellular interactions between the two substances. Such concentrations can be particularly significant in kidney cells and, for example, in the heart during cardiac catheterization.

Figure 1
Three dimensional structural models of monomeric and filamental skeletal actin isoform based on the pdb files 2ZWH and 1MVW indicating the position of the „monomer" in the filament and its four subdomains.

Results

Figure 2
Co-sedimentation assays were performed to assess the G/F-actin ratio after dynamic equilibrium had been established. For all three iodinated contrast agents, increasing concentrations led to a progressive rise in the proportion of free G-actin compared to control. These results indicate a concentration-dependent effect and suggest that the agents promote actin depolymerization.

Figure 3
In the case of the paramagnetic Dotarem, a distinct effect from the iodinated agents was observed. Here, increasing concentrations led to a decrease in the proportion of free G-actin, indicating a stabilizing effect on F-actin and inhibition of depolymerization. This stabilizing effect was also concentration-dependent. (Statistics: Unpaired t-test, * if $p<0.05$, ** if $p<0.001$)

Figure 4
DSC curves of 46 μM F-actin in the presence of different concentrations of Visipaque. The treated samples show a decrease in the melting temperature (Tm) of actin, indicating that Visipaque binds to the protein and destabilizes its structure in a concentration-dependent manner.

Figure 5
Similar to Visipaque, Iomeron also reduces the melting temperature (Tm) of F-actin. Notably, this destabilizing effect is much more pronounced for filamentous (F-) actin than for monomeric (G-) actin, indicating a stronger impact on the polymerized form.

Figure 6
The critical concentration was determined using pyrene-labeled actin. The special feature of pyrene-labeled actin is that when only G-actin is present in the system (i.e., below the critical concentration), the fluorescence emission intensity detected by the fluorimeter remains constant at a lower level. Once polymerization begins, the emission intensity increases. The intersection point of straight lines fitted to these two phases was used to determine the critical concentration. All three iodinated contrast agents caused a significant increase in the critical concentration compared to the control. Xenetix and Visipaque showed noticeable effects even at lower concentrations and reached a higher maximal effect than Iomeron. (Statistics: Unpaired t-test, * if $p<0.05$, ** if $p<0.001$)

Figure 7
Both paramagnetic contrast agents significantly reduced the critical concentration even at extremely low concentrations. Increasing the amount of contrast agent did not result in any further meaningful decrease; instead, a plateau phase was observed. (Statistics: Unpaired t-test, * if $p<0.05$, ** if $p<0.001$)

References

1. Zoltán Ujfalusi, Elek Telek, Miklós Nyitrai, Péter Bogner, Tamás Rostás, Gabriella Hild, László Trif, Gábor Hild. (2022) Thermochimica Acta (710), 179165
2. Franke, R. P., Scharnweber, T., Fuhrmann, R., Kruger, A., Wenzel, F., Mrowietz, C., and Jung, F. (2013) Clin Hemorheol Microcirc 55(4), 481-490
3. Franke, R. P., Scharnweber, T., Fuhrmann, R., Mrowietz, C., and Jung, F. (2013) Clin Hemorheol Microcirc 54(3), 273-285
4. Franke, R. P., Scharnweber, T., Fuhrmann, R., Mrowietz, C., Wenzel, F., Kruger, A., and Jung, F. (2014) Clin Hemorheol Microcirc 58(1), 49-63
5. Giorgi, H., Ammerman, J., Briffaux, J. P., Fretellier, N., Corot, C., and Bourrinet, P. (2015) Regul Toxicol Pharmacol 73(3), 960-970

Acknowledgements

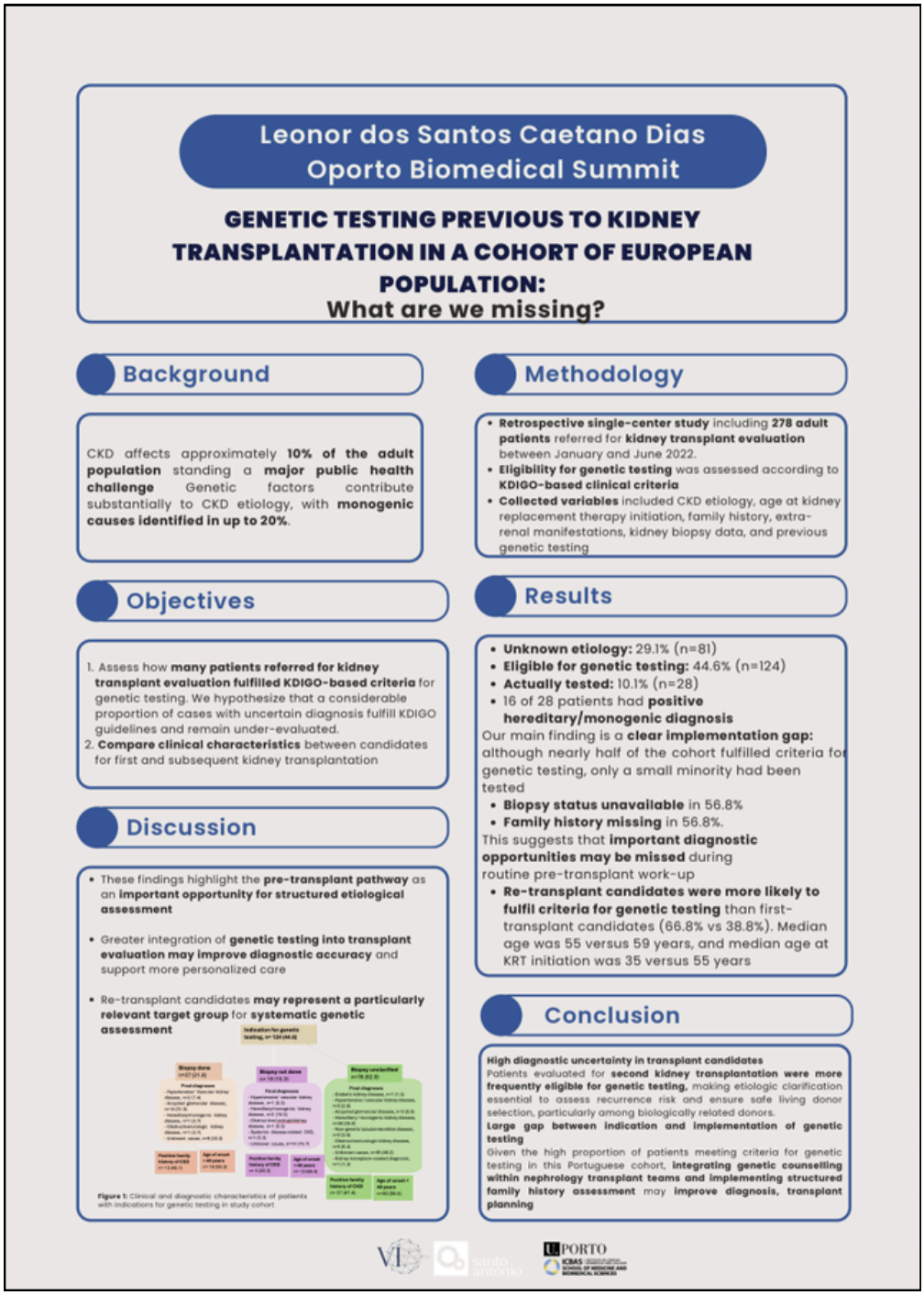
Janosne Brunner for actin preparation.

In summary, our measurements confirm that a real interaction occurred between the two materials, as the contrast agent affected several important properties of actin. Regardless of its "direction," this interaction is detrimental to cellular function because it interferes with finely tuned dynamics. As a result, the cell may die, suggesting that this interaction may represent a possible mechanism in the development of contrast-induced nephropathy.

Research abstract- Genetic testing previous to kidney transplantation in a cohort of European population: what are we missing?

Student

Leonor dos Santos Caetano Dias



Leonor dos Santos Caetano Dias
Oporto Biomedical Summit

GENETIC TESTING PREVIOUS TO KIDNEY TRANSPLANTATION IN A COHORT OF EUROPEAN POPULATION:
What are we missing?

Background

CKD affects approximately **10% of the adult population** standing a **major public health challenge** Genetic factors contribute substantially to CKD etiology, with **monogenic causes identified in up to 20%**.

Methodology

- **Retrospective single-center study** including **278 adult patients** referred for **kidney transplant evaluation** between January and June 2022.
- **Eligibility for genetic testing** was assessed according to **KDIGO-based clinical criteria**
- **Collected variables** included CKD etiology, age at kidney replacement therapy initiation, family history, extra-renal manifestations, kidney biopsy data, and previous genetic testing

Objectives

1. Assess how **many patients referred for kidney transplant evaluation fulfilled KDIGO-based criteria** for genetic testing. We hypothesize that a considerable proportion of cases with uncertain diagnosis fulfill KDIGO guidelines and remain under-evaluated.
2. **Compare clinical characteristics** between candidates for first and subsequent kidney transplantation

Results

- **Unknown etiology:** 29.1% (n=81)
- **Eligible for genetic testing:** 44.6% (n=124)
- **Actually tested:** 10.1% (n=28)
- 16 of 28 patients had **positive hereditary/monogenic diagnosis**

Our main finding is a **clear implementation gap:** although nearly half of the cohort fulfilled criteria for genetic testing, only a small minority had been tested

- **Biopsy status unavailable** in 56.8%
- **Family history missing** in 56.8%.

This suggests that **important diagnostic opportunities may be missed** during routine pre-transplant work-up

- **Re-transplant candidates were more likely to fulfil criteria for genetic testing** than first-transplant candidates (66.8% vs 38.8%). Median age was 55 versus 59 years, and median age at KRT initiation was 35 versus 55 years

Discussion

- These findings highlight the **pre-transplant pathway** as an **important opportunity for structured etiological assessment**
- Greater integration of **genetic testing into transplant evaluation may improve diagnostic accuracy** and support more personalized care
- Re-transplant candidates **may represent a particularly relevant target group** for **systematic genetic assessment**

Conclusion

High diagnostic uncertainty in transplant candidates
Patients evaluated for **second kidney transplantation were more frequently eligible for genetic testing,** making etiologic clarification essential to assess recurrence risk and ensure safe living donor selection, particularly among biologically related donors.
Large gap between indication and implementation of genetic testing
Given the high proportion of patients meeting criteria for genetic testing in this Portuguese cohort, **integrating genetic counselling within nephrology transplant teams and implementing structured family history assessment** may **improve diagnosis, transplant planning**

Research abstract- Three Vascular Phenotypes in the Spleen Controlled by the Dosage of a Single Transcription Factor

Student
Kata Váradi