# ORPHAN DISEASES IN HEPATOLOGY AND GASTROENTEROLOGY

November 2, 2023

Workshop

MADRID, SPAIN

7 CME CREDITS

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7 credit hours (CME) have been awarded for Workshop Madrid by the European Union of Medical Specialists (UEMS).

# PREFACE

Dear Colleagues,

on behalf of the scientific organisers from Spain and Germany, we would like to invite you to our interactive, practical workshop on “Orphan Diseases in Hepatology and Gastroenterology”.

Rare, orphan diseases are defined as having a prevalence of less than 1 out of 2000. Currently, between 600-800 diseases in GI and hepatology are thought to be “rare”. Some of them might be very familiar and weekly practice to you. In view of improved newborn screening strategies, the better diagnoses and advanced evidence-based treatment strategies (e.g. “orphan drugs”), the number of adult patients is rising from day to day.

We are very happy to welcome renowned specialists from all parts of the world to give an overview of the current State-of-the-Art in this field. The workshop is thought to reflect the current spectrum of diseases in this field - from liver to intestines, pancreas to visceral vessels and the huge area of metabolic diseases, e.g. “inborn errors of metabolism”, which as systemic diseases reliably manifest in the GI tract.

Apart from discussing the talks, we count on your engagement by using the voting systems and giving your thoughts about clinical decisions during the case presentations. A bias of this meeting is letting you experience the molecular frontier of the most advanced treatment strategies for your patients in the field.

In this sense, we would like to welcome you to Madrid, the Spanish capital with its outstanding tradition and to enjoy this stimulating background for your professional and personal benefit.

Yours very sincerely,

Agustin Albillos  Jose J.G. Marin  Stephan vom Dahl

# WORKSHOP - ORPHAN DISEASES IN HEPATOLOGY AND GASTROENTEROLOGY

## November 2, 2023

**Scientific Organization:**
Prof. Dr. Agustin Albillos, Madrid (Spain)
Prof. Dr. Stephan vom Dahl, Duesseldorf (Germany)
Prof. Dr. Jose J.G. Marin, Salamanca (Spain)

**Congress Venue:**
Hotel Meliá Castilla
Calle del Poeta Joan Maragall, 43
28020 Madrid
Spain

For admission to scientific events your name badge should be clearly visible.

Accompanying persons are not permitted during the conference at any time.

**Start of Registration:**
Wednesday, November 1, 2023
16:00 – 21:00 h
at the congress office

# Thursday, November 2, 2023

**08:30** Welcome and opening remarks
*Stephan vom Dahl, Duesseldorf*

## SESSION I

### Gastrointestinal manifestations of autoimmune and metabolic diseases

**Chairs:** *Stephan vom Dahl, Duesseldorf; Luca Fabris, Padova*

**08:45** Eosinophilic GI diseases
*Alain Schoepfer, Lausanne.*

**09:05** Refractory celiac disease
*Gerd Bouma, Amsterdam*

**09:25** Lysosomal storage diseases
*Carla Hollak, Amsterdam*

**09:45** Autoimmune pancreatitis
*Matthias Loehr, Stockholm*

**10:05** **Presentation of case studies and discussion**
*Gerd Bouma, Amsterdam; Carla Hollak, Amsterdam; Matthias Loehr, Stockholm*

**10:45** **Coffee break with poster session**

## SESSION II

### Orphan liver diseases

**Chairs:** *José C. Fernandez-Checa, Barcelona; José J.G. Marin, Salamanca*

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|---|---|
| **11:15** | Inborn errors in bile acid metabolism<br>*Maria J. Monte, Salamanca* |
| **11:35** | IgG4-related cholangitis<br>*Ulrich Beuers, Amsterdam* |
| **11:55** | Inborn errors in cholesterol metabolism<br>*Carmen Garcia-Ruiz, Barcelona* |
| **12:15** | Porto-sinusoidal vascular disorders<br>*Luis Téllez, Madrid* |
| **12:35** | **Presentation of case studies and discussion**<br>*Carmen Garcia-Ruiz, Barcelona; Maria J. Monte, Salamanca; Luis Téllez, Madrid* |
| **13:15** | **Lunch break** |
| **14:15** | **Poster Session**<br>Poster presentations and discussion in the Auditorium |

# Thursday, November 2, 2023

## SESSION III

### Advances in diagnosis and novel therapeutic approaches

**Chairs:** *Agustin Albillos, Madrid; Ali Canbay, Bochum*

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|---|---|
| **14:45** | Broad screening strategies for detection of rare inborn errors of metabolism<br>*David Kasper, Vienna* |
| **15:10** | New strategies in management of alpha1-antitrypsin deficiency<br>*Pavel Strnad, Aachen* |
| **15:35** | Inborn cholestatic disorders: Insights and new therapeutic options<br>*Verena Keitel-Anselmino, Magdeburg* |
| **16:00** | Refractory autoimmune hepatitis<br>*María Londoño, Barcelona* |
| **16:25** | Wilson disease<br>*Uta Merle, Heidelberg* |
| **16:50** | Concluding remarks<br>*Agustin Albillos, Madrid; Ali Canbay, Bochum* |
| **17:00** | **Networking with light refreshments** |
| **17:30** | **Presentation of Poster Awards**<br>*Agustin Albillos, Madrid; Stephan vom Dahl, Duesseldorf; José J.G. Marin, Salamanca* |
| **18:00** | **State-of-the-Art Lecture**<br>Molecular and gene-therapeutic approaches for rare genetic metabolic diseases<br>*Pramod Mistry, New Haven* |
| **18:30** | **Concluding remarks**<br>*Agustin Albillos, Madrid; Stephan vom Dahl, Duesseldorf; José J.G. Marin, Salamanca* |

# LIST OF SPEAKERS, MODERATORS AND SCIENTIFIC ORGANIZERS

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# REGISTRATION

You can register for the event via our homepage:
**www.falkfoundation.org**
**Registration is only possible online.**

# CONGRESS FEES

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|---|---|
| **Scientific Program of Workshop** | EUR 150 |
| **Students** (copy of student ID required) | EUR 75 |

**The congress fees include:**

– Pre-Opening and Welcome on Wednesday, November 1, 2023
– Refreshments during coffee break
– Lunch and networking with light refreshments
– A copy of the final program

# CONGRESS OFFICE AND REGISTRATION

**Opening Hours:**

| | |
|---|---|
| Wednesday, November 1 | 16:00 - 21:00 h |
| Thursday, November 2 | 08:00 - 20:00 h |

# ARRIVAL

**Hotel Meliá Castilla**
Calle del Poeta Joan Maragall, 43
28020 Madrid
Spain

**Travelling from the airport**

The Hotel Meliá Castilla is located 14 km from Madrid-Barajas Airport: http://www.aeropuertomadrid-barajas.com/eng/

**By taxi:**

Taking a taxi to the hotel will take about 15-20 min.

**By public transport:**

From Madrid Airport T1-T2-T3 take tram 8 towards Nuevos Ministerios. Change here to tram 10 towards Tres Olivos. Get off at Cuzco station.

Take the Paseo Castellana Impares exit. Go north on Paseo de la Castellana towards C. de Sor Ángela de la Cruz. Turn left. Turn right towards C. del Poeta Joan Maragall. Take the stairs. Turn left towards C. del Poeta Joan Maragall. Turn right onto C. del Poeta Joan Maragall.

# CONFLICTS OF INTEREST

Members of the scientific committee declare the following potential conflicts of interest:

Stephan vom Dahl: Genzyme-Sanofi, Takeda, BioMarin, Nutricia, Dr. Falk Pharma

Agustin Albillos: AbbVie, Boehringer, Gilead, Gore, Grifols, Janssen, Intercept, Pfizer

Jose J.G. Marin: no potential conflict of interest to report

# POSTER ABSTRACTS

1. Comparative assessment of tolerability in two therapeutic approaches in treatment of autoimmune hepatitis
   A. Genunche-Dumitrescu, C. Neagoe, C. Badea, M. Badea, A. Badea (Craiova, Bucharest, RO)
2. Wilson's disease: Descriptive study of series of cases
   H. Hassine, H. Dabbabi, S. Ben Azzouz, D. Cherif, H. Yacoub, H. Kchir, N. Maamouri (Tunis, TN)
3. Clinical and epidemiological features in 50 patients with microscopic colitis
   A. Jigaranu (Iasi, RO)
4. Mortality, morbidity, and incidence of metabolic derangement in adult patients with inborn errors of metabolism: Identification of "volatile diseases"
   J. Koehler, F. Weis, D. Schoeler, P. May, M. Michael, M. Bernhard, T. Luedde, S. Vom Dahl (Duesseldorf, DE)
5. Systemic manifestations of alkaptonuria (AKU) - An underdiagnosed treatable disease
   J. Koehler, S. Hummel, F. Weis, K. Von Gradowski, D. Schoeler, D. Schmitt, P. May, T. Luedde, S. Vom Dahl (Duesseldorf, DE)
6. Wilson disease – Case report
   A. Mehmedovic, A. Pilav, A. Puhalovic, N. Zubcevic, N. Custovic, A. Sinacevic (Sarajevo, BA)
7. New inflammatory markers in the diagnostics of autoimmune hepatitis and AIH-followed cirrhosis
   A. Michalak, W. Domerecka, A. Rycyk-Bojarzynska, B. Kasztelan-Szczerbinska, T. Malecka-Massalska, H. Cichoz-Lach (Lublin, PL)
8. Is eosinophilic esophagitis an important co-morbid condition of asthma?
   C. Neagoe, C. Bigea, A. Farmazon, R. Bala, L. Mustata, A. Genunche-Dumitrescu (Craiova, RO)
9. The influence of obesity on the prevalence of eosinophilic esophagitis in patients with GERD
   C. Neagoe, S. Cazacu, R. Bala, M. Mustata, C. Bigea, A. Genunche-Dumitrescu (Craiova, RO)
10. Rare case of liver Yolk sac tumor in 22-year-old man
    N. Nerma, A. Saray, A. Mehmedovic, N. Zubcevic, H. Kuric (Sarajevo, BA)
11. Rare cystic fibrosis transmembrane conductance regulator (CFTR) protein genetic variant p.Phe834Leu is related to chronic pancreatitis
    N. Oruc (Izmir, TR)
12. Safety profile of UDCA in patients with AIH, PBC during the treatment of non-hepatic malignancies
    M. Razov Radas (Zadar, HR)
13. Superior mesenteric artery syndrome: Clinical characteristics, diagnosis, and outcome in pediatric population – 11 years' experience
    M. Slae, L. Ohana-Sarna-Cahan, T. Orgad (Jerusalem, IL)
14. Transient elastography monitoring in infantile lysosomal acid lipase deficiency (Wolman disease)
    M. Slae, E. Shteyer (Jerusalem, IL)
15. Hemochromatosis/NAFLD
    Z. Trescec Svegovic (Koprivnica, HR)

16. A case of eosinophilic esophagitis with vomiting after novel coronavirus infection
K. Zheng (NanJing, CN)

17. Abdominal sonographic findings in rare inborn errors of metabolism: A single-center retrospective study in 131 adult GD, 38 GSD and 13 FAOD patients
J. Kueck, J. Koehler, P. May, D. Pullmann, D. Schoeler, T. Luedde, S. Vom Dahl, M. Kallenbach (Duesseldorf, DE)

# FULL CONTENT OF POSTER ABSTRACTS

**Poster Numbers 1 – 17**

## 1. Comparative assessment of tolerability in two therapeutic approaches in treatment of autoimmune hepatitis

**Amelia-Valentina Genunche-Dumitrescu** (Craiova, RO), Carmen Daniela Neagoe (Craiova, RO), Carmen Daniela Badea (Craiova, RO), Mihail Badea (Craiova, RO), Aurelian-Adrian Badea (Bucharest, RO)

**Introduction:** The aim of this comparative study was the retrospective assessment of the safety and tolerability of the budesonide-azathioprine combined therapy versus prednisone in association with azathioprine in patients with autoimmune hepatitis (AIH).

**Methods:** We studied 42 patients (28 females/14 males, mean ages 43.2 years) with AIH. A comparative study was performed on two groups of patients: A group composed of 25 patients who received a combined therapy with prednisone (40 mg/day and tapared to 10 mg/day) and azathioprine (1–2 mg/kg/day) and B group treated with Budenofalk® (3 mg, oral doses three times daily) in association with azathioprine (1–2 mg/kg/day). After the liver enzymes level was normalized, the dose of budesonide was reduced at 6 mg daily. The tolerability of therapies, the incidences and severity of adverse events was monitored for a 12-month period.

**Results:** At 6 months, complete biochemical remission occurred in 9 cases (36%) of the A group and in 11 cases (64.7%) in B group. In A group the side effects were: mild anemia (4 cases), osteoporosis (5 cases), severe leukopenia (2 cases), steroid diabetes (2 cases) and Cushing's syndrome (3 cases). Multiple side effects were observed in 6 patients (24%). Comparative, the rate of side effects in B group was significantly reduced (27.77%) and 15 patients (83.3%) did not develop steroid-specific side effects. After 6 months, disappearance of clinical symptoms, normal liver biochemistry and histological remission was observed in 18 cases: 7 patients in A group and 11 in B group. The incidences of the side-effects which appeared in a period between 6 and 12 months after debut of therapy were significantly reduced in B group: only one case with leukopenia due to azathioprine maintenance therapy and one case with thrombopenia. Comparatively, in group A were appeared most side effects: osteoporosis (2 cases), gastrointestinal bleeding (3 cases) diabetes (one case) and thrombocytopenia (one case). For whole 12 months period, the rate of the discontinuation of the therapy due to adverse events was: 36.0% in group A and 17.6% in B group.

**Discussion/Conclusion:** The combined therapy with budesonide and azathioprine assure a high efficacy in patients with AIH and determined low rate of steroid specific side effects. In association with azathioprine, budesonide is more tolerable than prednisone.

## 2. Wilson's disease: Descriptive study of series of cases

**Hajer Hassine** (Tunis, TN), Habiba Dabbabi (Tunis, TN), Sarra Ben Azzouz (Tunis, TN), Dhouha Cherif (Tunis, TN), Haithem Yacoub (Tunis, TN), Hela Kchir (Tunis, TN), Nadia Maamouri (Tunis, TN)

**Introduction:** Wilson's disease (WD) is a rare cupric toxicosis autosomal recessive, due to a default in the biliary excretion of copper that leads to its accumulation in the organism especially in the liver and in the brain. Its clinical presentation is heterogeneous dominated by the neuropsychiatric and hepatic presentations that determine the prognosis.

The goal of our study was to point out the clinical, diagnosis, therapeutic and evolving features of the WD.

**Methods:** We have proceeded by a retrospective study over a period of 10 years [January 2010–January 2020], collecting all of the cases of the WD followed on the Department of Gastroenterology B.

**Results:** Eight cases were collected. The average age at the diagnosis was 16 years old [4–39] with a female predominance (sex ratio H/F: 0.6). Four patients had family history of WD. The disease was first revealed by hepatic presentation in four patients (edema-ascetic decompensation inaugural in two cases, cholestatic jaundice in one case and elevated liver function tests in another case). Neurological presentation was observed in two patients and the WD was confirmed after family screening in two patients.

Six patients were cirrhotic. A neurological damage was present in seven patients: Parkinsonian syndrome (n = 3), mental retardation (n = 1), isolated dysarthia (n = 1), temporal epilepsy (n = 1) and isolated sensory deficit (n = 1). The ophthalmological examination with the slit lamp had objectified a ring of Kayser Fleischer in seven cases. All patients had high cupruria and collapsed ceruloplasmin levels.

Seven were treated by penicillamine with a good initial clinical and biological tolerance. Only one patient had lost sight. A patient developed within 5 years of treatment vasculitis that would be attributed to the penicillamine. During treatment follow up, there was no significant worsening on the stage of the disease.

**Discussion/Conclusion:** The WD is a rare and serious, even fatal condition in the lack of treatment. In our study, liver damage was often advanced to cirrhosis in three quarters of the cases, associated with neurological symptoms in the majority of cases. A systematic screening is therefore essential in families at risk for early diagnosis and treatment before the onset of complications.

## 3. Clinical and epidemiological features in 50 patients with microscopic colitis

**Anca Olivia Jigaranu** (Iasi, RO)

**Introduction:** Microscopic colitis (MC) is a chronic inflammatory disease of the colon than can cause watery non-bloody diarrhea more frequently in elderly patients. The associated symptoms are fecal incontinence, urgency, abdominal pain which lead to a poor quality of life.

**Methods:** This retrospective study included 50 patients with MC from whom we gathered clinical, epidemiological, biological and endoscopic data. Kaplan Meier curve was used to evaluate treatment response.

**Results:** The mean age was 60 years, 35 of the patients (70%) were women and 28 patients (56%) were smokers. Only 20% of the patients had an autoimmune disease associated and 70% of the patient were under PPI treatment. Regarding the histological subtypes 80% were lymphocytic colitis (LC) and 20% collagenous colitis (CC). Concerning the remission rate under Budesonide treatment there was no difference between LC and CC, with a 85% total remission rate and a cumulative relapse rate of 48% at two years of follow-up.

**Discussion/Conclusion:** In the study we conducted MC was more frequent in elderly women. Also, the use of PPI was the most highly incriminated risk factor. More than 80% of the patients achieved clinical remission even though almost half of them relapsed at the two years follow up.

## 4. Mortality, morbidity, and incidence of metabolic derange-ment in adult patients with inborn errors of metabolism: Identification of "volatile diseases"

**Jan Philipp Koehler** (Duesseldorf, DE), Frederic Weis (Duesseldorf, DE), David Schoeler (Duesseldorf, DE), Petra May (Duesseldorf, DE), Mark Michael (Duesseldorf, DE), Michael Bernhard (Duesseldorf, DE), Tom Luedde (Duesseldorf, DE), Stephan Vom Dahl (Duesseldorf, DE)

**Introduction:** Inborn errors of metabolism encompass many different disease entities. Most of the diseases are monogenetic and there is either a disease-related toxic accumulation of toxic degradation products or a deficiency of substrates important for metabolism. In the case of a metabolic derailment, which is often triggered by dietary errors or intercurrent diseases, it can lead to a life-threatening derailment in particularly volatile diseases. Data on incidence, mortality and morbidity in adult patients are scarce due to the small number of cases.

**Methods:** A retrospective analysis was performed of patient data from a total of 306 adult patients/543 inpatient cases with inborn errors of metabolism (♂/♀ = 130:176, Ø 37 years, range 18–76) who were treated as inpatients at Düsseldorf University Hospital between 2002 and 2022. Data recorded for each condition included reason for admission, length and course of treatment. Morbidity was equated with the term probability of hospitalization. This is calculated by dividing the mean number of IEM cases by the mean length of care in years.

**Results:** Regarding the ratio of IEM-associated admissions to all admissions during the observation period, the following top values were obtained: Urea cycle disorders (UCD, n = 118 cases) 55.9%; glycogen storage disease (GSD, n = 110) 48.2%, organic acidurias (OA, n = 108) 81.5%; Maple sirup urine disease (MSUD, n = 93) 97.8% and porphyrias (n = 95) 85.3%. In addition, the following annual probabilities of hospitalization for metabolic derailment were determined for the diseases: OA (n = 25 patients), 65.7%, MSUD (n = 19) 41.2%, UCD (n = 29) 29.1%, porphyrias (n = 76) 27.0%, GSD (n = 53) 13.2%, fatty acid oxidation disorders (FOAD, n = 15) 11.6%, and lysosomal storage disorders (LSD, n = 89) 0.01%. Among annual mortality rates, arginase deficiency stood out at 4%, propionic acid anemia at 2.5%, and Fabry disease at 2%. Further details of the analysis, such as the benefit to patients of early transfer to the ICU, will be presented at the workshop.

**Discussion/Conclusion:** This retrospective analysis is the first to report relevant data from a large German cohort of adult patients. Patients with MSUD, OA, and UCD have the highest likelihood of hospitalization and should therefore be especially informed about early symptoms of a derailment and its emergency treatment. Patients with hyperammonemic states benefit clinically from early transfer to the intensive care unit (ICU) for monitoring. Because of their high annual mortality rate, patients with arginase deficiency, propionic acidemia, and Fabry disease should be treated with utmost attention and transferred from the emergency department to an ICU as soon as possible. In contrast to the relatively "inert" LSD group, a small group of "volatile" inborn errors of metabolism can clearly be named.

## 5. Systemic manifestations of alkaptonuria (AKU) – An under-diagnosed treatable disease

**Jan Philipp Koehler** (Duesseldorf, DE), Sophie Hummel (Duesseldorf, DE), Frederic Weis (Duesseldorf, DE), Kathrin Von Gradowski (Duesseldorf, DE), David Schoeler (Duesseldorf, DE), Dominik Schmitt (Duesseldorf, DE), Petra May (Duesseldorf, DE), Tom Luedde (Duesseldorf, DE), Stephan Vom Dahl (Duesseldorf, DE)

**Introduction:** Alkaptonuria is an inborn error of metabolism with an incidence of 1:250.000–1:1.000.000. Due to a monogetic mutation of homogentisate 1,2-dioxygenase (HGD), the homogentisic acid (HGA) from tyrosine catabolism can no longer be degraded and its derivatives like benzoquinone acetic acid are visibly deposited as a brownish discoloration in the eyes, joints/spinal column, and internal organs ("ochronosis"). The disease is characterized by its osseous and internistic comorbidities. In Europe, oral nitisinone (NTBC), an inhibitor of 4-(OH)-phenylpyruvate dioxygenase, an enzyme upstream of HGD, has been approved for treatment since 2020. It significantly reduces urinary homogentisic acid excretion and clinically alters the course of the disease. The abstract analyses systemic manifestations, comorbidities and treatment status in a large German monocentric cohort.

**Methods:** In this retrospective work, a monocentric cohort of 25 patients (pts approximately one quarter of the total German AKU population; 13 w/12 m, median age 59 yrs, range 26–76 yrs) seen in our clinic from 2015–2023 were analyzed regarding to systemic manifestations, comorbidities and treatment status.

**Results:** About 84% (21/25) of the Düsseldorf cohort is now on therapy (Tx) with nitisinone, with an average dose varying between 2–10 mg/day. Tx was started at an average age of 52 3 3 yrs (mean 3 SEM). In all pts, HGA excretion was decreased from several g/day to < 300 mg/day, and no patient discontinued Tx. During the observation period of cumulative 64 treatment years, one patient died before the NTBC era, one patient refused treatment and 2 patients are currently awaiting NTBC treatment. These four pts were significantly older than patients already on treatment (52 vs. 68 yrs, p = 0.025). About 68% of the patients had bone pain and/or objective radiological/scintigraphic or MR-visible bone manifestations with typical signs of ochronosis, 48% showed echocardiographically altered heart valves or dilatation of the thoracic aorta. About 32% had a sonographic steatosis hepatis. No patient had evidence of chronic renal failure.

**Discussion/Conclusion:** If left untreated, alkaptonuria leads to many serious comorbidities such as height loss, severe bone pain, impaired movement due to spinal/joint pain and osteochondrosis, aortic valve stenosis, fatty liver disease and AKU-associated osteopenia/-porosis. Nitisinone has been available since 2020 and it should be installed as early as possible to prevent severe sequelae. Currently there is a tremendous lag between first symptoms and Dx, as well as between Dx and installation of Tx. Further studies, especially prospective observational studies analyzing the long-term benefit of nitisinone are urgently needed.

## 6. Wilson disease – Case report

**Amila Mehmedovic** (Sarajevo, BA), Aida Pilav (Sarajevo, BA), Amra Puhalovic (Sarajevo, BA), Nadza Zubcevic (Sarajevo, BA), Nerma Custovic (Sarajevo, BA), Adela Sinacevic (Sarajevo, BA)

**Introduction:** Wilson disease (WD) is an inherited autosomal recessive disorder that causes the body to retain excess copper. The liver of a person who has WD does not release copper into bile as it should, begins to damage the liver and causes degenerative changes in the brain, cirrhosis and Kayser-Fleischer rings. Copper is distributed to other tissues to which it is toxic. The gene concerned has been located on the chromosome region 13q14. Its presentation can be varied, neuropsychiatric changes become increasingly important. If not treated, WD can cause severe brain damage, liver failure and death.

**Methods:** A 21-year-old patient, male, was admitted at the Department of clinical hepatology, Clinical Centre University of Sarajevo with abdominal distension and encephalopathia. Previously, the patient was hospitalized at the Neurological Clinic due to tremors of the right hand.

Laboratory examination was performed of serum and urine. Radiological evaluation (abdominal, cardiac ultrasound, portosystemic Color Doppler ultrasound, RTG p/C, cranial, thorax, abdominal CT, cranial MRI), endoscopic evaluation (proximal endoscopy), liver biopsy and specialist examinations – ophthalmologist, endocrinologist, cardiologist, neurologist, hematologist.

**Results:** On laboratory investigation he had hemoglobin of 145 g/l with total and differential leucocyte counts within normal limits, thrombocytopenia (Tr 59 x 109 g/l). Results showed hyperammonemia (ammonia 70 umol/l), the total serum bilirubin was 21 umol/l, AST 44 IU/l, ALT 26 IU/l, alkaline phosphatase 4156 U/l, GGT 134 U/ml, albumin 30 g/l. Copper in serum was 9.82 mg/dl, ceruloplasmin 0.08 g/l (ref. 0.22–0.40). AFP H 11.50. Renal parameters were normal. MELD score 10.

Radiological exams verified splenomegaly, with elevated portal pressure, and during endoscopy esophageal varices of the first degree. After excluding chronic viral (Hepatitis B and C, TORCH) and autoimmune liver diseases, a liver biopsy is performed (liver steatosis, moderate interface hepatitis and lobular inflammation, presence of a connective tissue partition with cirrhosis. Hypothyroidism is proven, and therapy is included. Ophthalmological examination revealed bilateral KF rings. Cranial MRI- deep sulci on the convexity of the brain and a hazy shadow in the pons area were recorded. After the neurological examination, it was concluded that the changes could be in favor of WD.

D-penicillamine was started and patient showed marginal improvement in neurological status. Beta blocker, pantoprazole, L-ortinin L-aspartate is additionally included. There was no deterioration in the liver status, nor episodes of gastrointestinal hemorrhage.

Due to portal hypertension and pathohistologically verified cirrhosis, the patient was candidated for liver transplantation. So far, he has a stable MELD score, no transplantation was performed.

**Discussion/Conclusion:** WD should be considered in patients with unexplained liver or acute liver failure, in patients those with neurologic or psychiatric abnormalities and liver disease or in first-degree relatives of WD patients. Scoring system was developed at an international meeting in Leipzig that includes clinical and laboratory testing and yields three categories of patients; those in whom another diagnosis should be considered, those in whom further diagnostic testing is needed. This scoring system has recently been incorporated into the diagnostic algorithm for WD in the EASL guidelines. Corneal KF rings are present in over 95% of those with neurological or psychiatric features. WD patients may have jaundice, hepatomegaly, splenomegaly, ascites, esophageal or gastric varices or hepatic encephalopathy. Abnormal laboratory testing decreased serum ceruloplasmin levels (in 95% with chronic presentations), decreased serum copper levels, elevated 24-hour urine copper excretion. With advanced liver disease thrombocytopenia, coagulopathy, hypoalbuminemia and hyperbilirubinemia may be seen.

Liver biopsy is examined for histology to determine the stage of liver disease. Life-long medical therapy is required, treatment should be considered in two phases: removing or detoxifying the tissue copper that has accumulated and preventing its reaccumulation. Copper removal is achieved by the administration of potent chelators. The primary chelator that has been used is d-penicillamine. Trientine is a reasonable option for primary therapy because of its lower incidence of side effects. A newer chelating agent, tetrathiomolybdate, is still being evaluated.

Discontinuation of therapy can lead to the appearance of neurological or psychiatric symptoms or the development of ALF. Monitoring of therapy is critical to detect nonadherence or treatment failure.

The second phase of treatment, prevention of reaccumulation or maintenance therapy can be achieved with chelators or by use of zinc salts. Oral zinc acts by preventing intestinal copper absorption. The frequency of monitoring should be the greatest at the start of therapy for symptomatic patients and should be individualized based on symptoms and disease severity, examinations and testing should be performed twice a year to detect nonadherence or failure of treatment.

In appropriate patients, pharmacologic or interventional treatment of complications of portal hypertension and treatment of hepatic encephalopathy is needed.

LT is also indicated for patients with decompensated liver disease unresponsive to medical therapy. LT is curative for WD and patients do not require treatment for WD following transplantation. Whether LT is indicated in patients with predominantly neurologic manifestations is controversial. This is due to the unpredictability of resolution of neurologic manifestations posttransplantation in LT recipients [7, 8].

## 7. New inflammatory markers in the diagnostics of auto-immune hepatitis and AIH-followed cirrhosis

**Agata Michalak** (Lublin, PL), Weronika Domerecka (Lublin, PL), Anna Rycyk-Bojarzynska (Lublin, PL), Beata Kasztelan-Szczerbinska (Lublin, PL), Teresa Malecka-Massalska (Lublin, PL), Halina Cichoz-Lach (Lublin, PL)

**Introduction:** The aim of the study was to assess the usefulness of extended inflammatory parameters (EIP), such as activated neutrophils (NEUT-RI and NEUT-GI) and activated lymphocytes (RE-LYMP and AS-LYMP), in the course of autoimmune hepatitis (AIH) and to verify the existing correlations between them and selected common hematological indices.

**Methods:** Thirty AIH patients (20 without and 10 with already developed cirrhosis) and 30 healthy volunteers were recruited for the study. Parameters belonging to the EIP group and hematological markers [red blood cell distribution width (RDW) to platelet count (PLT) – RPR, RDW to lymphocyte (LYM) ratio – RLR, neutrophil to LYM ratio – NLR, mean PLT volume to PLT ratio – MPR], PLT to LYM ratio – PLR] were assessed in all participants.

**Results:** Patients with AIH showed significantly higher values of EIP (NEUT-RI, NEUT-GI and RE-LYMP) and hematological parameters (RPR, MPR and NLR) compared to controls ($p < 0.0001$). Among the examined EIP, the following were characterized by the highest diagnostic value in the course of AIH ($p < 0.0001$): NEUT-RI [area under the curve (AUC) = 0.860], NEUT-GI (AUC = 0.800) and RE-LYMP (AUC = 0.780). For basic hematological markers, these were: MPR (AUC = 0.750), PLR (AUC = 1.000) and RLR (AUC = 1.000). In addition, the following parameters: NEUT-GI (AUC = 0.890), MPR (AUC = 0.930), PLR (AUC = 0.860) and RPR (AUC = 0.910), have been found to play a significant role in the detection of already developed cirrhosis in the course of AIH ($p < 0.0001$).

**Discussion/Conclusion:** EIP and routinely obtained hematological markers may be useful in the diagnostics of AIH and in identifying features of liver fibrosis in its course. Our results appear to be a kind of novelty in hepatology.

## 8. Is eosinophilic esophagitis an important co-morbid condition of asthma?

**Carmen Daniela Neagoe** (Craiova, RO), Camelia Bigea (Craiova, RO), Anca Smaranda Farmazon (Craiova, RO), Raluca Bala (Craiova, RO), Lorena Maria Mustata (Craiova, RO), Amelia Valentina Genunche-Dumitrescu (Craiova, RO)

**Introduction:** Eosinophilic esophagitis (EoE) and asthma are frequently found as co-morbid conditions with similar T helper-2 responses driven pathophysiology and share common management strategies. Aim of our study was to evaluate the prevalence of EoE in patients with allergic asthma.

**Methods:** We included 54 consecutive, non-obese and non-smoking patients with allergic asthma, 20 males and 34 females, mean age 46 years 3 6.3. 23 patients (42.6%) were mild intermittent asthmatic and 4 patients (7.4%) were persistent asthmatics. All patients reported at least one symptom such as dysphagia, chest pain, heartburn, regurgitation in the previous week and at least 1 episod of food impactation in the last 12 months and no/slight response to treatment with PPI for 1 month. We practiced upper endoscopy in all patients and took 6 esophageal biopsies, from different levels, even if the mucosa appeared to be normal. A minimum of 15 eosinophils/ HPF in esophageal biopsies were required to consider the diagnose. We count eosinophils number from blood samples.

**Results:** All patients were diagnosed with asthma previous to EoE, average time frame between asthma and EoE diagnosis was near 5 years. 36 patients had endoscopic features such as: erosions, edema mild/moderate, furrows, white exudates, strictures and 18 patients had normal findings on endoscopy. No patient had concentric rings. 23 patients had erosions and edema, 5 patients associated erosions, edema and white exudates, 3 had edema and furrows, in 3 had edema, furrows and white exudates and 2 patients had strictures. Only in 6 (11.1%) male patients we found more than 15 eosinophils/ HPF and we considered the diagnose of EoE in these patients. There was no relation between the total eosinophil count in blood and the presence of EoE, and also there was no correlation between the severities of both conditions that can be attributable to the eosinophil count in the esophageal biopsy.

**Discussion/Conclusion:** In our study 11.1% of patients with asthma associated EoE. All of them were males, younger than the mean age (from 31 to 38 years), but we did not find any pathognomonic symptom or endoscopic lesion for EoE diagnosis, compared with the study group.

## 9. The influence of obesity on the prevalence of eosinophilic esophagitis in patients with GERD

**Carmen Daniela Neagoe** (Craiova, RO), Sergiu Marian Cazacu (Craiova, RO), Raluca Bala (Craiova, RO), Maria Lorena Mustata (Craiova, RO), Camelia Bigea (Craiova, RO), Amelia Valentina Genunche-Dumitrescu (Craiova, RO)

**Introduction:** Eosinophilic esophagitis (EoE) is a chronic immune-mediated disorder characterized clinically by esophageal dysfunction and at least 15 eosinophils/HPF in esophageal biopsies. Gastroesophageal reflux disease (GERD) represents a chronic disorder characterized by the regurgitation of gastric contents into the esophagus, associated frequently with esophageal eosinophilia and it is common in obese patients.

Aim of our study was to evaluate the prevalence of EoE in obese patients with GERD compared with normal weight patients with GERD.

**Methods:** Consecutive 263 patients obese or normal weight, without diabetes mellitus or obesity due to endocrine disease, non-smoking, with typical symptoms of GERD and/or symptoms of esophageal dysfunction, were included in the study. Patients were divided in 2 groups: 138 obese (40 males) – group A and 125 patients with normal weight (37 males) – group B, with similar mean age. Major symptoms in both groups were regurgitation, heartburn, dysphagia and chest pain. Blood samples were collected to determinate hs-CRP and leptin, and all of them underwent upper endoscopy with multiple biopsies.

**Results:** EoE was diagnosed in 8 patients (5.8%) in group A and in 7 patients in group B (5.6%) without significant statistical difference between two groups. Only 2 females had EoE, both from group A. All patients obese with EoE accused especially heartburn and regurgitation and less dysphagia (3 pts). The 7 patients from group B presented, mainly dysphagia and chest pain. Hs-CRP and leptin level were significantly higher in EoE in both groups, compared with GERD patients. At endoscopy, EoE patients from group A showed changes associated of GERD and EoE, but especially erosions and ulcers, while EoE patients from group B presented oedema, exudates furrows, strictures and less erosions.

**Discussion/Conclusion:** In our study, EoE wasn't so frequent associated with GERD in patients with or without obesity, but obesity influenced the symptomatology, accentuating reflux symptoms compared with symptoms of esofageal dysfunction in obese group with EoE. High level of leptin and hs-CRP correlated with EoE in both groups. Endoscopic findings were more typical for EoE in normal weight group compared with obese group with EoE.

## 10. Rare case of liver Yolk sac tumor in 22-year-old man

**Nerma Nerma** (Sarajevo, BA), Aida Saray (Sarajevo, BA), Amila Mehmedovic (Sarajevo, BA), Nadza Zubcevic (Sarajevo, BA), Haris Kuric (Sarajevo, BA)

**Introduction:** Extragonadal germ cell tumor (GCT) is extremely rare in adults. Less than 16 adult cases of primary Yolk sac tumor of the liver have been reported to date (1). Therefore, it is very important to obtain as much information as possible about the clinical presentation and course of the disease. We present a case of an unresectable primary yolk sac tumor of the liver in a 25-year-old man.

**Methods:** A 25-year-old man presented with a pain under the right rib. Ultrasound examination revealed large mass in the liver parenchyma. The patient was referred for an urgent CT scan and MRI of the abdomen which confirmed large mass in the right liver lobe, measuring approximately 13,5 x 12,5 x 15,5 cm and pathological lymphadenopathy in the porta hepatis with the largest diameter 38 x 26 mm. The described mass infiltrates and completely obliterates the right and middle hepatic vein and shows the compressive effect on the inferior vena cava with the consequent difficulty in flow. Laboratory examinations established high values of serum alpha-fetoprotein (AFP) 1440 ng/ml, carcinoembryonic antigen (CEA) 1280 ng/ml, as well as other tumor markers Ca19-9 4110 U/ml, CA 125 II 36.9 U/ml, CA 153 269 U/ml with beta HCG in normal range 2.40 mIU/ml, slightly elevated GGT 176 U/l and AP 165 U/l and reference values of total bilirubin 6.7 umol/l. The biopsy of the liver mass revealed it to be a nonseminomatous GCT, which is suggestive of a yolk sac tumor due to the positivity on CK 19 and focally on CDX2 and high values of AFP and CEA in the serum. Immunophenotypic, tumor cells were: SALL4+; CK-19+; CDX2+/-; CK7-, CK20-/+, CD56-; TTF-1-, p63-, HePar-; S-100P-, GATA3-, PAX-8-; CD30-; CD117-/+; AFP-. Ultrasound of the scrotum was normal. PET-CT showed secondary deposits in the retropancreatic lymph nodes and one micronode in the lung parenchyma. Ongologysts ndicated 4 cycles of systemic chemotherapy according to the protocol, followed by a revision and assessment of the possibility of surgery. The third cycle of chemotherapy was completed with a satisfactory response.

**Discussion/Conclusion:** Some reported cases of liver Yolk sac tumor were managed with surgery along with chemotherapy (2, 3). However, many other reported patients died of the disease despite the use of an aggressive therapeutic strategy (4, 5).

Although rare, primary yolk sac tumor of the liver should be considered as a differential diagnosis in young patients with large cystic tumors with necrosis and significantly elevated AFP.

## 11. Rare cystic fibrosis transmembrane conductance regulator (CFTR) protein genetic variant p.Phe834Leu is related to chronic pancreatitis

**Nevin Oruc** (Izmir, TR)

**Introduction:** Pathogenic variants in the cystic fibrosis transmembrane conductance regulator CFTR gene are causative of cystic fibrosis (CF), CF-related disorders and chronic pancreatitis. We reported a 31-year-old male chronic pancreatitis patient with rare CFTR genetic variant p.Phe834Leu.

**Methods:** Thirty-one years old male patient was admitted with repeated attacks of pancreatitis. Imaging studies and Endoscopic ultrasound confirmed chronic changes in the pancreas as well as fatty changes in pancreatic parancyma. Patient was not diabetic and had first acute pancreatitis attack at 26 years old. Risk factors for chronic pancreatitis development including, excessive alcohol drinking, hypertriglyceridemia, hypercalcemia, malformations of the pancreas, etc. were investigated. The exact cause of the disease was not specified by those investigations and patient diagnosed as "idiopathic chronic pancreatitis". Although there was no family history since patient was young conduction of a genetic examination was performed. Genetic testing was conducted using the next-generation sequencing (NGS) technology.

**Results:** CFTR gene sequencing showed rare c. 2502T > G(Phe834Leu) hetero-zygote variant. This variant is very rare and previously reported in two patients; one with chronic pancreatitis and one with CF disease. Although this mutation is reported as variants of unknown clinical significance in gene database, it was the one and only genetic variation detected in our CP patient. This variant is located in the 20th exon of the ENSG00000001626.14 transcript within the CFTR gene, with the accession number being rs200735475. The gene located in the region 117465784 - 117715971 on chromosome 7, has been modeled using the GTEx (https://gtexportal.org/home) web tool to determine the tissues where it is expressed. It has been observed to be expressed in a total of 14 tissues, with the highest level detected in pancreatic tissue.

**Discussion/Conclusion:** Rare CFTR genetic variant p.Phe834Leu is related to chronic pancreatitis. Fatty pancreatic changes with recurrent attacks in young patient is suspicious findings and genetic analysis confirmed CFTR protein genetic variant p.Phe834Leu as possible genetic background for clinical findings.

## 12. Safety profile of UDCA in patients with AIH, PBC during the treatment of non-hepatic malignancies

**Melanija Razov Radas** (Zadar, HR)

**Introduction:** Autoimmune hepatitis (AIH) is a non-contagious, chronic, inflammatory, autoimmune disease in which one's own immune system attacks healthy, normal liver cells. It can occur from early childhood up to old age, but is most frequent in young to middle adulthood. In Western Europe the incidence of AIH is 1.9 cases per 100,000 inhabitants per year. In our population incidence is the same – 1.87/100.000. Primary biliary cholangitis/cirrhosis (PBC) is a chronic autoimmune cholestatic liver disease with wide ranges of reported incidence and prevalence. In Western Europe annual incidence rate is 1.87 new cases per 100,000 inhabitants. In our population incidence is the same – 1.9/100.000. Among our patients, the youngest of whom is 15 years old and the oldest is 76 years old, malignant diseases were detected in two patients during the control interval. Zadar County has 170,000 patients. We registered 17 patients (16 women and 1 man) suffering from PBC and 9 patients (4 women, 5 men) from AIH. Two patients were treated for malignant disease – colon and thyroid gland. We monitored the safety profile of UDCA therapy during treatment for malignant diseases.

**Methods:** During regular check-ups, a patient examination, laboratory diagnostics, liver ultrasound imaging we recruited two patients with malignant diseases. Due to the ability of UDCA to breaks down into toxic lithocholic acid which can be toxic to liver cells and even cause liver failure, segmental bile duct injury, hepatocyte failure, and death, we carefully monitored patients during treatment for malignant diseases without interrupting therapy with UDCA.

**Results:** A 56-year-old woman, on UDCA and corticosteroid therapy for 36 years, and on levothyroxine therapy for hypothyroidism for 20 years. Total thyroidectomy was done in 2022 due to follicular variant of papillary carcinoma. Unhindered continued therapy with UDCA and corticosteroids during treatment for malignant disease. UDCA toxicity has not been reported.

A 66-year-old woman has been treated for PBC with UDCA since 2006. In 04/2022, radiation was performed, followed by surgery for rectal cancer. Chemotherapy was performed and intestinal continuity was established. During this process, she was on therapy with UDCA without consequences.

**Discussion/Conclusion:** In the long-term follow-up of PBC and AIH patients on therapy with UDCA +/- corticosteroids, no malignant liver disease was recorded, but two tumors unrelated to the underlying disease and therapeutic protocol. Without unwanted consequences, the therapy with UDCA was not interrupted during the entire treatment of the malignancy. This confirms the high safety profile of UDCA during the treatment of malignant tumors. A multicenter retrospective study is needed for a final conclusion.

## 13. Superior mesenteric artery syndrome: Clinical character-istics, diagnosis, and outcome in pediatric population – 11 years' experience

**Mordechai Slae** (Jerusalem, IL), Lea Ohana-Sarna-Cahan (Jerusalem, IL), Tamar Orgad (Jerusalem, IL)

**Introduction:** Superior mesenteric artery (SMA) syndrome is a rare gastrointestinal anatomical disorder, manifesting as proximal intestinal obstruction. There is scarce literature data regarding children suffering from SMA syndrome.

**Methods:** Retrospective data analysis of all pediatric patients aged 0 to 18 years old between the dates January 2010 to December 2020 with diagnosis of SMA syndrome in a tertiary medical center.

**Results:** Over the 11-year study period, 21 children < 18 years of age were diagnosed with SMA syndrome. The mean age was 13.5 years 3 4.15, eleven 52.3% were males. Nine children (42.8%) originated from multiple children's families (≥ 5 siblings), most of children (11, 52.3%) had a clear medical background. The most common symptom was abdominal pain (16, 76.2%), followed by vomiting 71.4%, nausea 47.6%, weight loss 38%, constipation 33.3%. The body weight percentile of 7 children (33.3%) was below the 3rd weight for age percentile. No electrolyte abnormalities were found.

Eleven children (52.3%) underwent abdominal US on admission of whom 81.1% had a normal exam. Upper GI series was done in 13 children (61.9%), 10 out of 13 were indicative of SMA syndrome. Sixteen children (76.1%) underwent gastroscopy, six children (37.5%) with no findings, 5 (31.5%) with signs of gastritis and 3 (18.7%) the diagnosis of SMA syndrome was achieved only on gastroscopy. Average time from beginning of symptoms to diagnosis was 5.7 3 4.7 months. The median length of hospitalization was 19.2 3 32.6 days. Four children (19%) were treated with TPN (total parenteral nutrition), of whom 2 had line associated complications (line sepsis and venous thrombosis).

**Discussion/Conclusion:** SMA syndrome is a rare condition in pediatric population. The diagnosis is challenging due to nonspecific presenting symptoms. Children commonly need psychiatric intervention. Complication, though potentially severe, are uncommon. Endoscopy might play a role in diagnosis.

## 14. Transient elastography monitoring in infantile lysosomal acid lipase deficiency (Wolman disease)

**Mordechai Slae** (Jerusalem, IL), Eyal Shteyer (Jerusalem, IL)

**Introduction:** Transient elastography is an emerging technique in the assessment of liver stiffness in patients with liver disease. Based on shear wave technology, this noninvasive imaging study produces indices of liver fibrosis, potentially replacing the more invasive follow-up test of liver biopsy or MRI-elastography, which in children commonly requires anesthesia.

In pediatric patients, it has been used to assess liver status in congenital and acquired liver disease. In addition, it has been reported and proposed as a tool for follow-up of liver storage diseases such as Wilson disease, since accumulated material in the liver can also cause liver stiffness. Follow-up of liver stiffness showed improvement with chelation therapy.

Infantile lysosomal acid lipase deficiency (LAL-D), or Wolman disease, is a rare genetic storage disease. Mutations in the LIPA gene cause dysfunction of the lysosomal acid lipase enzyme which metabolizes triglycerides and cholesterol esters, resulting in liver, intestinal and immune-cells storage, deficiency of HDL and excess of cholesterol and LDL. Without treatment, the disease is lethal. Other complications include failure to thrive, anemia, malnutrition and Hemophagocytic Lymphohistiocytosis (HLH), caused by cholesteryl ester-induced inflammasome activation in macrophages. There is a milder form of LAL-D in which the mutations cause milder disease in older children and adults.

Recently, enzyme replacement therapy (ERT) has been developed, and patients receiving this treatment become stable; however, adjustment of enzyme dose and dietary management are frequently required. All patients are instructed to keep a low-fat diet.

The need to assess liver status is very important in managing this liver disease. Given the invasive nature of liver biopsy, there is a risk that it will be avoided in assessment of disease course, leading to suboptimal management and decreased treatment success.

**Methods:** We report the use of transient elastography in monitoring of 4 cases of Wolman disease, and potential relation between severe score and a complication of the disease which affects the liver, namely HLH.

**Results:** Four children with Wolman disease have been followed up since the neonatal age (all were diagnosed at the age of 2 months old), until currently, the youngest being 2 years and 1 month old, the oldest 6 years and 10 months. All patients have been diagnosed by enzymatic activity testing and/or genetic confirmation of LIPA-gene known mutations. All four patients had adrenal calcifications. None had adrenal insufficiency. All patients have been treated by ERT with sebalipase-alpha. Two patients developed hypothyroidism after initiation of treatment. Three patients developed HLH – all at presentation, close to diagnosis, and one another time later, following an unadvised change to liberalized fat diet.

All patients underwent transient elastography by Fibroscan. Two patients had a fibrosis score of F1 (kPa = 5.3, 6.4, ages = 8 and 32 months respectively) and one a fibrosis score of F3 (kPa = 10.5, age = 64 months). The same patient underwent a liver biopsy with an Ishak score of F3. The fourth patient had a fibrosis score of F4 (kPa = 16.1, age = 20 months). This patient had presented with recurrent fever and hepatic deterioration prior to that. Infectious workup

was negative. The patient has eventually met the criteria for HLH, including fever, splenomegaly, hypertriglyceridemia, pancytopenia, elevated ferritin, increased levels of CD25. The patient was treated with systemic steroids and improved. Follow up Fibroscan demonstrated an improved fibrosis score – F3 (kPa = 10.2, age = 32 months). CD25 levels decreased from peak levels of 6371 to 2709 U/ml. In the cohort, there was no correlation between Fibroscan fibrosis scores and ALT, triglycerides, cholesterol or CD25 levels, however, in the fourth patient, decrease in CD25 levels paralleled improvement in liver Fibroscan fibrosis scores.

**Discussion/Conclusion:** Transient elastography may be used to assess liver status in Wolman disease and monitor for complications. Similar to other liver diseases, there is no clear relationship between the transient elastography fibrosis score and liver enzymes or disease-specific metabolites. Larger prospective studies are needed to confirm the role of transient elastography in monitoring the liver status of LAL-D.

## 15. Hemochromatosis/NAFLD

**Zdenka Trescec Svegovic** (Koprivnica, HR)

**Introduction:** Hemochromatosis is HFE- mediated genetic iron overload. C282Y is the major mutation and H63D the minor mutation of the HFE gene. Individuals with 2 copies of C282Y or 1 copy of both mutations (compound heterozygote) are at risk for iron overload.

Advanced hemochromatosis typically involves the liver and may also involve pancreas, heart, pituitary gland and other organs. Most patients are asymptomatic at diagnosis. Symptoms are fatigue, arthralgias and abdominal pain. Screening studies include serum iron/total iron binding capacity (abnormal if > 45%) and serum ferritin > 200 ug/l in women, > 250 ug/l in men.

**Methods:** A case report which shows how to cure both hemochromatosis and NAFLD.

**Results:** A 54-year-old woman was hospitalized in Department of Gastroenterology in April 2020 because of acute focal exudative pancreatitis of the body and tail of pancreas CTSI 4. Gastroscopy showed GERB LA gr A, gastroduodenitis chr. We cured her with antibiotics coamoxiclav, ciprofloxacin and metronidazole and supportive measures. Her inflammatory factors were high, CA19-9 and CEA normal, Fe 4.7 umol/l, ferritin 1689 ug/l, total bil 28 umol/l, AST 21, ALT 24, ALP 62, GGT 181 and LDH 131, albumins 31.5 g/l, glucose, creatinine, potassium and coagulation normal, cholesterol 10.1 mmol/l, HDL 1.4, LDL 7 and triglycerides 3.4 mmol/l. At home she continued to take ciprofloxacin and metronidazole, IPP, Cholib 145/40 mg (fenofibrate/simvastatin). Hepatitis markers are negative. DNA analysis (made in Clinical Hospital Zagreb, Rebro) showed heterozygous mutation for H63D and interaction of HFE protein with receptor for transferrin (hemochromatosis/NAFLD). MSCT and MRI of abdomen and liver were normal, she has no pathological accumulation of iron. We started phlebothomy once monthly and liver enzymes were normal and ferritin around 600 after one year of therapy.

Fibroscan showed no fibrosis F0/4, steatosis of liver CAP 320 dB/m. Vitamin D was low so we started supplementation with 4000 IU/daily and Silybum marianum for liver lesion. Endocrinologist in Clinical Hospital Centre Zagreb treated hyperlipidemia with rosuvastatin (Rosix®) 20 mg and Tricor (Fenolip®)160 mg and after 6 months cholesterol was 4.9, HDL 2.1, LDL 2.9, triglycerides 1.0. Molecular-genetic analysis for lipoprotein lipase LPL showed genotype LPL-PVU II: +/+ (homozygote +/+). PvuII is one of polymorphism in 6. intron of gene LPL where is supstitution of nucleotides C > T. Genotype LPL-PVUII +/+ means risk for development of hypertriglyceridemia, atherosclerosis, disease of cardiovascular system and pancreatitis. In February 2023 control showed normal ultrasound of abdomen and Fibroscan (SCD 1.9 cm, M probe 10/10 measurement, 6 kPa, IQR 8%, CAP 133 dB/m). She is asymptomatic patient. Ferritin is 500 ug/l, red blood count and biochemistry are normal. She in on diet and lost 10 kilograms.

**Discussion/Conclusion:** my patient has hemochromatosis and NAFLD under good control. Now she has phlebotomy every month. Early diagnosis (precirrhotic stage) and treatment leads to normal life expectancy.

## 16. A case of eosinophilic esophagitis with vomiting after novel coronavirus infection

**Kai Zheng** (NanJing, CN)

**Introduction:** The patient, female, 77-year-old, was admitted to the hospital on March 12, 2023 due to vomiting and poor appetite after a novel coronavirus infection 2 months ago. Cranial and whole abdomen CT: bilateral basal ganglia area, left frontal lobe infarction softening foci possible, suggest MRI further examination; left lateral fissure pool widening, consider arachnoid cysts possible, suggest MRI further examination; CT plain scan of the gastrointestinal tract did not show any obvious abnormality, endoscopy is recommended for further examination. Blood EBV DNA < 5.0E+02 copies/ml; cytomegalovirus DNA < 5.0E+02 copies/ml. Initial treatment was based on antinausea, nutritional support, acid suppression and gastric protection, symptoms did not improve. Endoscopy: the esophagus was patent, and there were multiple ulcerative erosions of different sizes near the cardia with pus covering the surface, and biopsy was taken. Pathology report suggested chronic inflammation of mucosa with squamous epithelial hyperplasia, localized inflammatory exudation and necrosis, and localized eosinophilic infiltration (20–50/HPF), and the patient had no history of drug or food allergy. Based on the pathological findings, eosinophilic esophagitis was diagnosed.

**Methods:** Oral inhaled budesonide (2 mg qd) was administered. The patient's vomiting was not present and appetite was significantly improved after 4 days administration. The patient was discharged with improvement in symptoms after being given budesonide. Patient continued oral budesonide therapy after discharge.

**Results:** On May 25, 2023, endoscopy was repeated, the esophageal mucosa was normal, local manifestations disappeared, and the number of local eosinophilic infiltration was reduced.

**Discussion/Conclusion:** Eosinophilic esophagitis is a chronic, allergen-triggered, Th2 cell-mediated esophageal disease characterized by inflammation with predominantly eosinophilic infiltration of the esophagus (at least 15–20 eosinophils in each high magnification field of view), which in turn triggers clinical symptoms, mainly esophageal dysfunction. Budesonide, as a topical steroid, is the first line of treatment for eosinophilic esophagitis and has a better safety profile compared to systemic corticosteroids. In our case, the patient was negative for food intolerance and started vomiting from a novel coronavirus infection, which eventually led to the diagnosis of eosinophilic esophagitis, and the novel coronavirus may be one of the causative factors in the development of eosinophilic esophagitis.

## 17. Abdominal sonographic findings in rare inborn errors of metabolism: A single-center retrospective study in 131 adult GD, 38 GSD and 13 FAOD patients

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**Introduction:** Glycogen storage diseases (GSD), Gaucher disease (GD) and fatty acid oxidation disorders (FAOD) are monogenetic enzyme deficiencies with a frequent gastrointesti-

nal/hepatic phenotype. Whereas GSD reside on dysregulated metabolism of glycogen, GD is a storage disease (LSD) caused by impaired lysosomal degradation of glucocerebroside with subsequent storage of glycolipids in macrophage-monocytic cells. FAODs lead to impairment of mitochondrial β-oxidation during stress. The specific nature of abdominal ultrasound findings in these patients is unknown but all diseases have a potential for cirrhotic or malignant transformation.

**Methods:** This study focuses on abdominal sonographic findings in GSD, GD type I and FAOD. Data were used from a single-center retrospective study: here, 38 adult GSD type Ia/b patients, 131 adult GD type 1 patients and 13 adult patients with FAODs (VLCAD, MCAD) were examined with standard abdominal B-mode ultrasound. If focal liver lesions were found, an advanced standard workup using elastography and contrast-enhanced ultrasound (CEUS) was performed in a fraction of patients. The study was approved by local nameable IRB votes.

**Results:** All three entities regularly display signs of hepatosplenomegaly and/or hepatic steatosis. Out of 38 screened patients with GSD type Ia or Ib, 10 patients with hepatic adenomatosis were identified, one leading to hepatic surgery. No HCC was found. In 131 screened patients with GD I, 15 patients with focal liver or splenic lesions were found. Three of these patients finally developed HCC, published earlier. In 13 screened patients with FAOD, 7 had hepatomegaly, splenomegaly and/or steatosis hepatis. Focal lesions were absent.

**Discussion/Conclusion:** Particular IEM are associated with specific abdominal ultrasound findings. Simple B-mode ultrasound and CEUS can help detect early potential disease-associated complications such as fibrosis, cirrhosis and transformation of hepatic/extrahepatic benign into malignant lesions. GI sonologists should aim at getting knowledge about IEM-specific ultrasound findings.

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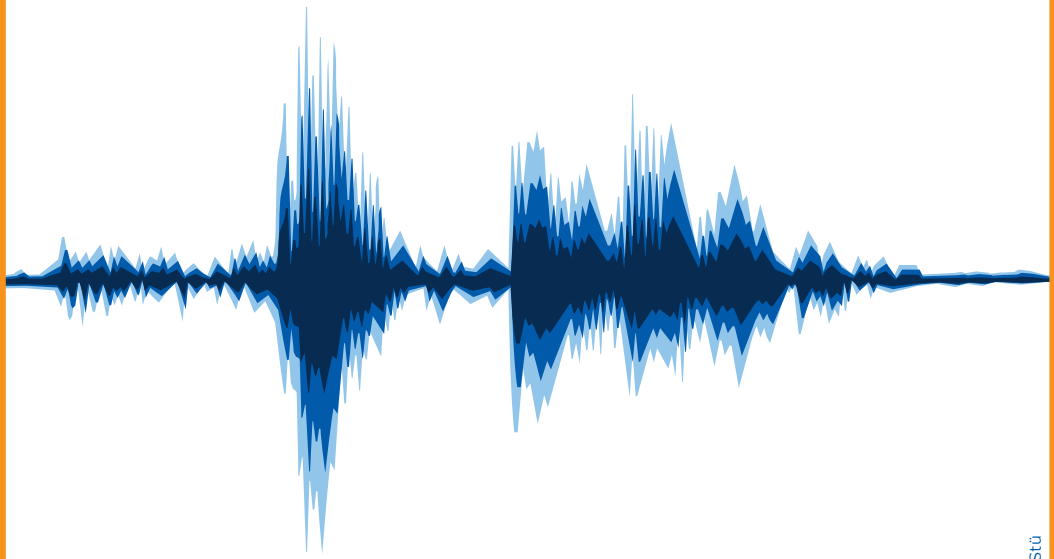

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