Liver Digest

A weekly update of PLRC happenings

August 1, 2019

PITTSBURGH LIVER RESEARCH CENTER

A partnership of University of Pittsburgh & UPMC

www.livercenter.pitt.edu

Featured Faculty - Dr. Michael Oertel

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- Funding Opportunity

Next Week's Seminar

PLRC Seminar Series

Thursday, August 8, 2019

Noon - 1:00 p.m.

S120 BST

Kenichi Ikejima, MD, PhD

Professor of Medicine, Department of Gastroenterology

Juntendo University Graduate School of Medicine, Japan

"Pathophysiological basis of steatohepatitis and therapeutic approaches"

Pizza will be provided.

PLRC Meet & Greet - September 12

Please save the date for the **PLRC's Meet and Greet!**

September 12, 2019

4:30-7:30 p.m.

Ballroom A - University Club

123 University Place

Pittsburgh, PA 15260

Invitations containing program details and requesting RSVPs will be forthcoming.

Faculty Collaboration Highlights

Special Article:

Carey EJ, Lai JC, Sonnenday C, Tapper EB, Tandon P, **Duarte-Rojo A, Dunn MA**, Tsien C, Kallwitz ER, Ng V, Dasarathy S, Kappus M, Bashir MR, Montano-Loza AJ. A North American Expert Opinion Statement on Sarcopenia in Liver Transplantation. Hepatology. 2019 Jun 20. doi: 10.1002/hep.30828. [Epub ahead of print] PubMed PMID: 31220351.

ABSTRACT

Loss of muscle mass and function, or sarcopenia, is a common feature of cirrhosis and contributes significantly to morbidity and mortality in this population. Sarcopenia is a main indicator of adverse outcomes in this population, including poor quality of life, hepatic decompensation, mortality in patients with cirrhosis evaluated for LT, longer hospital and intensive care unit stay, higher incidence of infection following LT, and higher overall health care cost. While it is clear that muscle mass is an important predictor of LT outcomes, many questions remain, including the best modality for assessing muscle mass, the optimal cut-off values for sarcopenia, the ideal timing and frequency of muscle mass assessment, and how to best incorporate the concept of sarcopenia into clinical decision making. For that reason, we assembled a group of experts to form the North American Working Group on Sarcopenia in Liver Transplantation to use evidence from the medical literature to address these outstanding questions regarding sarcopenia in LT. We believe sarcopenia assessment should be considered in all patients with cirrhosis evaluated for liver transplantation. Skeletal muscle index (SMI) assessed by computed tomography constitutes the best studied technique for assessing sarcopenia in patients with cirrhosis. Cut-off values for sarcopenia, defined as SMI <50 cm2 /m2 in male and <39 cm2 /m2 in female patients constitute the validated definition for sarcopenia in patients with cirrhosis. The management of sarcopenia requires a multi-pronged approach including nutrition, exercise and additional pharmacological therapy as deemed necessary. Future studies should evaluate whether recovery of sarcopenia with nutritional management in combination with an exercise program is sustainable, and how improvement in muscle mass might be associated with improvement in clinical outcomes.

For full text, please **click here**.

Case Report:

Del Brío Castillo R, **Squires JE, McKiernan PJ**. A novel mutation in VPS33B gene causing a milder ARC syndrome phenotype with prolonged survival. JIMD Rep. 2019 Mar 22;47(1):4-8. doi: 10.1002/jmd2.12027. eCollection 2019 May. PubMed PMID: 31240160; PubMed Central PMCID: PMC6498830.

ABSTRACT

INTRODUCTION: ARC (arthrogryposis, renal dysfunction, and cholestasis) syndrome is an uncommon multisystem disorder that entails a very poor prognosis. It is caused by mutations in either VPS33B or VIPAS39 gene, both playing a key role in intracellular trafficking. We report two siblings born to first cousin parents with a novel mutation in VPS33B who have both shown prolonged survival.

CASES PRESENTATION: The index patient presented with bilateral hip dysplasia and arthrogryposis, failure to thrive, undernourishment, developmental delay, and low gamma-glutamyl transferase cholestasis. She at age 2 years underwent external biliary diversion with improvement in pruritus but liver disease continued to progress. She developed stomal bleeding at 7 years of age and liver biopsy displayed cirrhosis. Her 3-year-old sibling showed a similar trajectory as well as he had ichthyotic skin with excoriations. Their renal involvement was mild and stable. Genetic analysis in both patients revealed a novel homozygous mutation in NM_018668.4 (VPS33B):c.1157A>C (p.His386Pro).

CONCLUSIONS: ARC syndrome is a severe disorder with few patients reported to survive beyond 12 months of age. This report discloses a novel mutation in the VPS33B gene and describes a phenotype with prolonged survival, mild renal involvement, and progressive liver disease.

For full text, please **click here**.

Clinical Observations Article:

Ioannis A. Ziogas, Dirk J. van der Windt, Gregory C. Wilson, **Alessandro Furlan, Michael A. Nalesnik**, Samer Tohme, **David A. Geller**. Surgical Management of Ciliated Hepatic Foregut Cyst. Hepatology. 2019 Jul 25. doi: 10.1002/hep.30877. [Epub ahead of print]

ABSTRACT

The increased use of high-sensitivity abdominal imaging has resulted in a higher rate of incidentally found liver lesions [1]. Ciliated hepatic foregut cyst (CHFC) is a rare, benign, cystic lesion of the liver with unique pathogenesis: It develops secondary to embryonic foregut cell migration from the dorsal bud, which becomes the esophagus and trachea, into the ventral bud that develops into the liver. The inner epithelial layer produces a thick mucoid content resulting in an increased density on radiologic imaging, which makes differentiation from solid liver tumors challenging. It is important for

hepatologists and gastroenterologists to consider CHFC in the differential diagnosis of atypical liver lesions, as CHFC carries a risk of transformation into squamous cell carcinoma. A suspicion of CHFC is therefore an indication for surgical resection. We investigated the management of CHFC in a large volume tertiary hepatobiliary center.

For full text, please **click here.**

Original Article:
Henkel SA, Squires JH, Ayers M, Ganoza A, **McKiernan P, Squires JE**. Expanding etiology of progressive familial intrahepatic cholestasis. World J Hepatol. 2019 May 27;11(5):450-463. doi: 10.4254/wjh.v11.i5.450. PubMed PMID: 31183005; PubMed Central PMCID: PMC6547292.

ABSTRACT

BACKGROUND: Progressive familial intrahepatic cholestasis (PFIC) refers to a disparate group of autosomal recessive disorders that are linked by the inability to appropriately form and excrete bile from hepatocytes, resulting in a hepatocellular form of cholestasis. While the diagnosis of such disorders had historically been based on pattern recognition of unremitting cholestasis without other identified molecular or anatomic cause, recent scientific advancements have uncovered multiple specific responsible proteins. The variety of identified defects has resulted in an ever-broadening phenotypic spectrum, ranging from traditional benign recurrent jaundice to progressive cholestasis and end-stage liver disease.

AIM: To review current data on defects in bile acid homeostasis, explore the expanding knowledge base of genetic based diseases in this field, and report disease characteristics and management.

METHODS: We conducted a systemic review according to PRISMA guidelines. We performed a Medline/PubMed search in February-March 2019 for relevant articles relating to the understanding, diagnosis, and management of bile acid homeostasis with a focus on the family of diseases collectively known as PFIC. English only articles were accessed in full. The manual search included references of retrieved articles. We extracted data on disease characteristics, associations with other diseases, and treatment. Data was summarized and presented in text, figure, and table format.

RESULTS: Genetic-based liver disease resulting in the inability to properly form and secrete bile constitute an important cause of morbidity and mortality in children and increasingly in adults. A growing number of PFIC have been described based on an expanded understanding of biliary transport mechanism defects and the development of a common phenotype.

CONCLUSION: We present a summary of current advances made in a number of areas relevant to both the classically described FIC1 (ATP8B1), BSEP (ABCB11), and MDR3 (ABCB4) transporter deficiencies, as well as more recently described gene mutations -- TJP2 (TJP2), FXR (NR1H4), MYO5B (MYO5B), and others which expand the etiology and understanding of PFIC-related cholestatic diseases and bile transport.

For full text, please **click here**.

Funding Opportunity

Advanced Fellowship Training in Pediatric Nutrition

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)

Our mailing address is:
Pittsburgh Liver Research Center
200 Lothrop St. | Pittsburgh, PA 15261