yong.xie@outlook.com

From: Cella, Ellen <Ellen.Cella@seattlechildrens.org>
Sent: Friday, May 10, 2013 4:59 PM
To: 'yong.xie@outlook.com'
Cc: Kuiper, Victoria
Subject: FW: J. Xie

Dr. Horslen is the Medical Director of Solid Organ Transplantation of SCH.

Yong,

I forwarded your email to Dr. Horslen. He separated out your concerns and put his responses in red. I hope this helps to answer your questions.

Ellen Cella RN, BSN
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Our biggest concern is the reason of his liver damage. The biopsy shows severe fibrotic changes and tells us that this is not a liver that will recover. The pattern is of a developmental nature with the liver and the injury probably started before Jianhua was born. The genes that determine liver development in utero are only gradually being discovered and the mechanisms of fetal liver injury are not well understood yet. But we can say that the pattern of injury is not what one sees with infection, autoimmune injury, vascular insufficiency, toxic effect or metabolic disease.

Without the reason, the damage in his body may not be limited to his liver only (spleen is still big while liver data are improving), and there might be other things happening while he is waiting. There is no evidence of any other organ system in his body being primarily affected, this does not mean that if his liver function worsens again that other organs may not be secondarily affected. Kidneys, heart and lungs function can all be compromised by advanced liver disease of any cause. This is why he needs a liver transplant, but presently there is no evidence of other organ involvement.

"Fat in Stool" is still observed everyday at home, could this be a serious problem? All patients with advanced liver disease have fat in their stool, because bile is required for fat digestion in the intestine and will chronic liver disease bile flow is compromised. This is also the reason that we are supplementing fat soluble vitamins - source CF (contains vitamins A, D, E & K) and extra vitamin D (cholecalciferol) and vitamin E. The fat in the stool is not harmful in itself it just means that he his not absorbing it from his formula.

His blood test is continuously improving slowly while taking his medicine and Pregestimil, which is given to babies with metabolic diseases. The formula (Pregestimil) and medicines are not given to children with metabolic diseases unless they have problems with bile flow or fat malabsorption. There are no metabolic diseases that are improved with what he is taking.

We didn't see many metabolic testings in the lab list, how can we be certain that it's not related to metabolic things?

- Blood gases show no acidosis
- Ammonia levels not progressively increasing and without protein restriction this rules out a defect of the urea cycle
- Normal electrolytes rules out defect of steroid hormone metabolism
- Alpha1 antitrypsin deficiency rule out
- Defects of fatty acid metabolism ruled out by acylcarnitine profile
- Defects of peroxisomal metabolism ruled out by normal urinary bile acid levels and liver biopsy
- Defects of mitochondrial function and energy generation ruled out by normal lactate and pyruvate levels and liver biopsy, no acidosis and normal acylcarnitine profile
- Defects of aminoacid and organic acid metabolism rule out by acylcarnitine profile and plasma amino acid profile
- Niemann-Pick type C rule out with normal acid lipase level
- Defects of glycosylation pathways ruled out by transferrin testing
- Cholesterol, triglycerides, HDL and LDL do not indicate any defect of lipid and lipoprotein metabolism

What other types of metabolic disease are they worried about ?

Maybe he is not a common case, some symptoms are not so apparent on him? We checked his pictures, jaundice is never apparent on him until several days before being accepted in ER on Apr 9. There are no common cases in infant liver diseases

Before the biopsy, Dr. Horslen told us that the biopsy could either telling us the damage source or pointing to the right direction for further testings. We just wonder what testings are we going to do and when. See answer to first question above in regard to what the biopsy told us. There are no more tests to do, he has cirrhosis secondary to a presumed defect in fetal or embryonic development of the liver – some such as ARPKD and Alagille (and no he does not have either of these conditions) we know the defective gene but for most we do not.

The important thing to concentrate on now is keeping Jianhua as well as possible so that he is ready to undergo transplant when a suitable organ becomes available.

From: Cella, Ellen
Sent: Friday, May 10, 2013 14:31
To: Horslen, Simon
Subject: FW: J. Xie

Simon,
I received this email from Jianhua's father. I am not very familiar with this child since he is followed by Vickie and he was seen by Jorge yesterday in clinic. Are you able to answer or decipher his questions. If not I will let him know Vickie will address his concerns when she is back on Monday.

Thanks.

Ellen

From: 永 谢 [mailto:yong.xie@outlook.com]
Sent: Friday, May 10, 2013 10:29
To: Cella, Ellen
Subject: FW: contact info

Ellen,

Could you please convey our questions to Dr. Hsu or Dr. Horslen?

Thanks

Yong

From: yong.xie@outlook.com
To: victoria.kuiper@seattlechildrens.org
CC: yong.xie@outlook.com
Subject: RE: contact info
Date: Fri, 10 May 2013 10:25:49 -0700

Vickie,

While we are happy to see that Jianhua has been very stable at home waiting for his liver transplant, there are some big concerns that we want to ask Dr. Horslen and Dr. Hsu. It's difficult for any parents to wait every two weeks for an answer.

Our biggest concern is the reason of his liver damage. Without the reason, the damage in his body may not be limited to his liver only (spleen is still big while liver data are improving), and there might be other things happening while he is waiting. "Fat in Stool" is still observed everyday at home, could this be a serious problem?

His blood test is continuously improving slowly while taking his medicine and Pregestimil, which is given to babies with metabolic diseases. We didn't see many metabolic testings in the lab list, how can we be certain that it's not related to metabolic things? Maybe he is not a common case, some symptoms are not so apparent on him? We checked his pictures, jaundice is never apparent on him until several days before being accepted in ER on Apr 9.

Before the biopsy, Dr. Horslen told us that the biopsy could either telling us the damage source or pointing to the right direction for further testings. We just wonder what testings are we going to do and when.

Vickie, please re-word my questions if they are not clear or not so nice. We just cannot stand still long while Jianhua's condition could get worse for some unknown reason.

Thanks

Clinic Note XIE, JIANHUA DRACO - 1275567

Result Type:	Clinic Note
Result Date:	29 April 2014 0:00
Result Status:	Modified
Result Title:	GI Clinic Outpt Report
Performed By:	Horslen, Simon P, MB ChB on 06 May 2014 14:19
Verified By:	Horslen, Simon P, MB ChB on 06 May 2014 14:19
Encounter info:	95113223, CHMC, Outpatient, 4/29/2014 - 5/4/2014
Contributor system:	SOFTMED

GI Clinic Outpt Report

Document may Not be Signed/Finalized. See End of report for Electronic Authentication of Signature.

OUTPATIENT NOTE

XIE, JIANHUA DRACO
DOB: 09/16/2012 M -MR #: 01-27-55-67

CLINIC: GI

DATE OF SERVICE: 04/29/2014

CHIEF COMPLAINT: History of micronodular cirrhosis.

HISTORY: Jianhua is a 19-month-old boy who was accompanied by his father and paternal grandmother. We first met him in early 2013 when he presented with what looked initially like acute liver failure and then appeared to be more chronic in nature. A surgical biopsy showed micronodular cirrhosis and the cause was not apparent. Since that time, he has had a very detailed workup without finding a specific diagnosis including full exome sequencing and a very detailed metabolic workup. His liver disease, however, has become less and less obvious to the point where his jaundice cleared completely many months ago, and his transaminases have settled down almost to normal. In spite of this, his father has refused to believe there is not a diagnosis and that he has some form of fat lipid metabolic defect. This, in spite of all the evidence to the contrary, and the care is somewhat pathologic. He has this abnormal diet which is very precise measurements of Pregestimil and hot water and chicken that he got from some Internet sources and he is feeding him on this. We are having a

nutritionist meet with him to ensure that there are no essential deficiencies in this, but we have explained to him both here in Hepatology Clinic and by Dr. Merritt in Metabolic Clinic that there really is no justification for him to be on an abnormal diet. He is kept from the outside world. The child hardly ever leaves the house. This is a restricted family. Dad has given up work. He did share with me that he has significant depression, himself, and I think that this problem that dad has in understanding and believing the medical advice he is given is really disrupting the family's overall wellbeing. Recently Jianhua has not had any significant acute intercurrent illnesses. He is taking his feeds well. He is very anxious around people and cries freely when having his vital signs measured or being examined and he is not particularly interactive for a 19-month-old. Apparently, he does walk, and he has a word or two. He had been seen in Developmental Clinic, but I think they have had difficulties following up with the advice Dr. Zinner had recommended that he see them again 3 months after their last visit in February.

REVIEW OF SYSTEMS: Other than his history of micronodular cirrhosis, etiology unknown, we do not have any other concerns about his health, but we do have worries about his family's response to his illness and his diet, and we will have our nutritionist evaluate his current diet carefully.

PRESENT MEDICATIONS:
1. Vitamin E in the form of Aquasol E 50 units once a day.
2. SourceCF 1 mL once a day.
3. Cholecalciferol 1000 units once.
4. Ursodiol 80 mg twice a day.

ALLERGIES: He has no known allergies, although dad thinks he is allergic to eggs.

SOCIAL HISTORY: Unchanged. The family lives in Redmond. Paternal mother is visiting from China. Mom works as an optical engineer. Dad is no longer working.

FAMILY HISTORY: There is a significant family history of depression on the father's side, but there is no family history of liver disease.

PHYSICAL EXAMINATION: Today, Jianhua looks well, but he is very anxious about being examined. His weight today is 10.94 kg, which puts him on the 40th percentile, and his height is 80.15 cm, which puts him just above the 10th percentile. His heart rate is 120 beats per minute, but he was not sufficiently cooperative to have his blood pressure recorded today. He has no pallor, no jaundice, no significant lymphadenopathy. He has conjugate gaze and equal pupils. ENT examination is normal. His

neck is supple. No enlargement of his thyroid gland and no significant lymphadenopathy. His chest is clear on auscultation. Heart sounds are normal with normal peripheral pulses. His abdomen is soft and nontender with no hepatosplenomegaly. He has no ascites, no peripheral edema. Neurological and musculoskeletal examination is unremarkable.

LABORATORY DATA: Today show normal electrolytes, normal renal function. Normal calcium, magnesium, phosphorus, and iron profile. His conjugated bilirubin is 0, AST 69, ALT 57, alkaline phosphatase 407, GGT 26. His triglycerides are 92, cholesterol 133. Albumin 4.7. Platelet count is 291, hemoglobin 13.3, and INR 1.1. His urinalysis is essentially normal. He does have somewhat low immunoglobulin levels that were measured back in March in Metabolic Clinic with an IgM of 15 and an IgG of 267 and Dr. Merritt was recommending that he get worked up for possible combined immunodeficiency syndrome, but the family so far are resisting this.

ASSESSMENT AND PLAN: From a liver point of view, I think Jianhua is doing well. We can stop his ursodiol, his multivitamin and his vitamin E because his levels have been adequate in the past. He should continue on his vitamin D supplementation. I have told dad that there is no justification to keep him on anything but a normal diet. I do not think the father believes me or any of us and is hoping to go to Pittsburgh for further opinion. We are happy to see him again in 6 months' time from the liver point of view if the family is willing to come see us. I have a feeling that his liver injury may have been a subacute event and that the micronodular cirrhosis that we saw may have been a regenerative phase given that he has done so well subsequently, but at this stage there is no further investigations that we are able to do. I look forward to hearing how he progresses, and if there is anything further we can do to help with his care we are always here.

Electronically Authenticated by
Simon P Horslen, MB ChB 05/06/2014 02:19 P

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Simon P Horslen, MB ChB , Attending Physician, Gastroenterology

Clinic Note

XIE, JIANHUA DRACO - 1275567

SPH/cf Doc #3431051 d: 04/29/2014 03:24 P t: 05/01/2014 10:05 A (1890152-)
Location: TXP
cc: Evelyn K Hsu, MD
Peggy J Kulpa, MD

Completed Action List:
* Perform by Horslen, Simon P, MB ChB on 29 April 2014 0:00
* Transcribe by on 29 April 2014 0:00
* Perform by Horslen, Simon P, MB ChB on 06 May 2014 14:19
* VERIFY by Horslen, Simon P, MB ChB on 06 May 2014 14:19