Nutrition Management of the Bone Marrow Transplant Patient Complicated by Graft versus Host Disease

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5/26/15
This case study follows a fifty year old female admitted to UC San Diego Medical Center with complications concerning for graft versus host disease following an allogeneic bone marrow transplant. The purpose of this paper is to outline the nutrition care process used during the subject patient’s clinical course and to analyze evidence-based medical nutrition therapy recommendations for this unique population.

Patient Introduction and Admission Summary

HHH was diagnosed with FLT3-positive acute myelogenous leukemia (AML) in November 2013. FLT3 is a genetic mutation that is often screened for when a patient is diagnosed with AML. This specific mutation provides a significant prognosis indicator, as the mutation is associated with a higher risk of relapse. Given the likelihood of relapse, bone marrow transplant is usually indicated with FLT3-positive AML patients. HHH also had a past medical history significant for hypertension (HTN) and Type II Diabetes Mellitus (DM).

HHH went through four cycles of chemotherapy, which were complicated by recurrent infections and clostridium difficile colitis (C-diff). She completed chemotherapy in June 2014 and underwent an allogeneic hematopoietic stem cell transplant on October 31, 2014. The patient’s sister served as a matched donor. Her hospital stay was prolonged due to steroid refractory graft versus host disease (GVHD) of the gut and skin. She was discharged on January 23, 2015 after a three-month hospital stay.

HHH continued to suffer complications post-discharge according to the outpatient team. HHH was unmarried and had limited family in the area, which limited her network of social support. She moved in with a friend after discharge and struggled with self-care. She suffered from anxiety and was nervous to ask for help from others. She became diaper dependent with very limited mobility. The outpatient team suspected poor medication adherence as well.
HHH returned to UCSD on February 10, 2015 with failure to thrive and severe acidosis. She had an elevated alkaline phosphatase and lactate, normal liver function tests and no evidence of diabetic ketoacidosis, likely indicating GVHD of the gut.

**Allogeneic Hematopoietic Stem Cell Transplant and GVHD**

Hematopoietic stem cells (HSCs) are blood forming stem cells produced in the bone marrow. These cells mature and divide into white blood cells (WBC), red blood cells (RBC) and platelets. Individuals with hematologic cancer and a variety of tumor-associated cancers can be treated by HSC transplantation either by transplanting cells from one’s self (autologous) or from a matched donor (allogeneic).

Those receiving an HSC transplant must first receive high dose chemotherapy that targets the cancer-causing cells and other rapidly dividing cells. The HSCs, which have been harvested from the patient’s own marrow (auto) or provided from a donor (allo) are then infused intravenously. The patient will then remain in the hospital after transplantation to await engraftment. Engraftment occurs when the body begins producing new WBCs, RBCs and platelets, and usually occurs two to four weeks post transplant (1). However, complete recovery of immune function can take up to two years and can be complicated by graft versus host disease (GVHD) in patients receiving allogeneic transplants.

**Epidemiology of GVHD**

An allogeneic HSC transplant is associated with an increased risk for graft versus host disease because the transplanted cells may not recognize by the patient’s own cells and mount an attack. Despite advances in donor HLA-typing methods and post-transplant immune suppression, GVHD remains a significant cause of transplant related mortality following an allogeneic transplant, even in a matched HLA-identical sibling setting (as noted in the subject patient). GVHD is a direct
result of one of the principal functions of the immune system: the distinction of self from non-self. The donor’s T-cells identify the host’s cells as foreign and mount an attack against them. Approximately 30-60% of allogeneic HSC transplant recipients will acquire GVHD (1).

The exact incidence of GVHD after allogeneic HCT is unknown, however reported incidence rates range from fifteen to fifty percent in patients who receive an allogeneic HCT from a genotypically HLA-identical sibling. This rate is even higher in matched unrelated donors (2). Studies have also identified a variety of risk factors that may increase an individual’s susceptibility in acquiring GVHD. These risk factors include HLA disparity, gender disparity, source of graft (peripheral blood or bone marrow has a greater risk than umbilical cord blood) and transplant conditioning regimen. The incidence and severity of GVHD also appears to increase with pretransplant comorbidities. In one study of 2,985 patients who underwent myeloablative or reduced intensity conditioning followed by allogeneic hematopoietic cell transplantation (HCT) for myeloid or lymphoid malignancies, the incidence and severity of acute GVHD increased with increasing hematopoietic cell transplantation-specific comorbidity index. The probability of developing grade III to IV acute GVHD was 13, 18, and 24 percent for those with a HCT-Comorbidity Index score of 0, 1 to 4, and ≥5, respectively. Patients with a higher HCT-Comorbidity Index score also had an increased risk of mortality following grade II to IV GVHD (3).

**Diagnosis**

GVHD can occur at any time point in the post-HCT setting, but most commonly occurs within the first few months after transplantation or following a reduction of immunosuppression. The National Institutes of Health (NIH) consensus criteria is often used to classify the clinical stage of GVHD (4). The NIH also specifies distinctive features significant to acute GVHD (occurring less than 100 days post transplant) and chronic GVHD (occurring greater than 100 days post transplant). These stages are:
- **Classic acute GVHD** – Cases present within 100 days of HCT and display features of acute GVHD.

- **Classic chronic GVHD**: Cases may present at any time post-HCT. Diagnostic and distinctive features of chronic GVHD are present. There are no features of acute GVHD.

- **Overlap syndrome**: Cases may present at any time post-HCT with features of both chronic GVHD and acute GVHD. On occasion, this is colloquially referred to as "acute on chronic" GVHD.

A variety of clinical findings may be observed in patients with GVHD, however it commonly affects the major organs, principally the skin, liver, and gastrointestinal tract. The diagnosis of GVHD can be readily made on clinical grounds alone in the patient who presents with a classic rash, abdominal cramps with diarrhea, and a rising serum bilirubin concentration. The skin and gastrointestinal tract and liver may also be biopsied to identify histologic abnormalities associated with GVHD. When biopsy is not feasible, diagnosis is usually performed as a process of exclusion, for example ruling out infectious causes and/or underlying comorbidities.

The severity of GVHD is determined by an assessment of the degree of involvement of the skin, liver, and gastrointestinal tract. Several systems for grading graft-versus-host disease have been developed. The most popular grading system is the Glucksberg grade (I-IV) (7).

**Table 1. Staging of GVHD**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Skin</th>
<th>Liver</th>
<th>GI tract</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No rash due to GvHD</td>
<td>Bilirubin &lt;2 mg per 100 ml or 35 mol/l</td>
<td>None (&lt;280 ml/m²)</td>
</tr>
<tr>
<td>I</td>
<td>Maculopapular rash &lt;25% of body surface area without associated symptoms</td>
<td>Bilirubin from 2 to &lt;3 mg/100 ml or 35–50 mol/l</td>
<td>Diarrhea &gt;500–1000 ml/day (280–555 ml/m²); nausea and emesis</td>
</tr>
<tr>
<td>II</td>
<td>Maculopapular rash or erythema with pruritis or other associated symptoms 25% of body surface area or localized desquamation</td>
<td>Bilirubin from 3 to &lt;6 mg/100 ml or 51–102 mol/l</td>
<td>Diarrhea &gt;1000–1500 ml/day (556–833 ml/m²); nausea and emesis</td>
</tr>
</tbody>
</table>
The estimated five-year survival rates of patients with grade III and grade IV GVHD are 25 and 5 percent, respectively (5). Both acute or chronic GVHD can also be classified as steroid-refractory. These patients present ongoing end-organ damage despite effective immunosuppression with second-line regimens. The subject patient in this case study was assessed with steroid refractory GVHD upon admission.

**Nutrition-Related Consequences of GVHD**

Patients with GVHD are at nutrition risk throughout the clinical course of the disease and as a result of treatment methods used. (Figure 1).

![Nutrition-related consequences of GVHD (5)](image-url)
Perhaps one of the most profound nutrition-related consequences associated with GVHD is the impairment of protein utilization secondary to high dose corticosteroids. Corticosteroids can negatively affect body composition by altering substrate oxidation, thus leading to an increase in body fat and a subsequent decrease in lean body mass. One large prospective study found that allo-SCT patients had a lower lean body mass than healthy controls at six and twelve months post-transplant and continued up to six years post-transplant (6).

Vitamin D deficiency is also prevalent in patients with GVHD related to long-term use of corticosteroids. In a cross sectional study in long term (> three years) survivors of allo-SCT, bone loss occurred in 73.4% of patients (7). Current research from the American Cancer Society states that more research is needed on Vitamin D supplementation in this population (14). Exact supplementation dosing for this population has not been established at this time.

Zinc deficiency is also common following allo-SCT, especially in patients with diarrhea. It is recommended that whole blood zinc be measured to assess for deficiency and if deficient to supplement with the same dosage as used in skin conditions, which is usually 220 mg of zinc sulfate daily (16). Deficiency of Vitamin B12 may also be seen in GVHD patients. GVHD of the stomach may disrupt production of IF, while GVHD of the small intestine may reduce absorption of B12. Per the American Cancer Society, there is Grade C evidence that monitoring B12 levels appears necessary in Allo-SCT patients (15). Hypo and hyper magnesaemia can also occur in patients using immunosuppressive medication.

All SCT patients, regardless of the presence of absence of GVHD, are at risk for iron overload related to multiple RBC transfusions. An iron-free multivitamin is recommended to all SCT patients for one year post transplant (14). Vitamin C (500 mg twice daily) and folic acid are also recommended in this population to meet elevated needs for adequate red blood cell production. Calcium supplementation
is recommended if the patient is deficient, with current recommendations dose dependent on severity of
the deficiency and the absence or presence of steroids (11). Vitamin and mineral status may also be
altered in GVHD patients as a result of poor intake and malabsorption of both water- and lipid-soluble
vitamins. The use of prebiotics in patients with GVHD of the gut has not been significantly
researched. The use of glutamine, arginine, Omega-3 fatty acids in this population has also not been
researched extensively (11).

Nutrition Recommendations

HCT patients will present with wide fluctuations in appetite beginning in the pre-transplant
(chemotherapy) phase and continuing until engraftment. During this time, the patient may experience
intermittent nausea, vomiting, decreased appetite, mucositis, early satiety, xerostomia, dysgeusia and
diarrhea. Therefore, the times in which the patient reports a good appetite should be taken advantage
of. Nutrition supplements, protein shakes and calorie-protein dense snacks are often recommended
while honoring the patient’s preferences.

Energy needs per guidelines set by American Cancer Society estimate calories needs at 25-30
calories per kg body weight and 1.2-1.5 grams protein per kg body weight in HCT patients (2). These
estimated needs increase in the GVHD patients to 30-35 kcals/kg and 1.5 up to 2 grams of protein per kg
bodyweight. Needs may be even higher in patients with significant malabsorption and/or protein losses
(2).

Nutrition Support

Patients unable to meet their needs through PO intake will often require nutrition support via
enteral (EN) or parenteral nutrition (PN). Because of severe mucositis, bleeding risks and excessive
vomiting, PN is often used in this population. However enteral nutrition is strongly favored, if medically feasible.

Triglycerides and liver function tests (LFTs) are closely monitored in GVHD patients receiving PN. Patients with GVHD of the liver may not be suitable candidates for PN if cholestasis and elevated total bilirubin is already of concern. This situation occurred with the subject patient as her GVHD liver progressed. Nocturnal EN or PN may also be used as the patient transitions to an oral diet. A calorie count is often ordered to assess PO intake adequacy before removing the patient from nutrition support.

Diet Advancement

GVHD patients with severe diarrhea (>1 L/day) are often NPO to alleviate GI distress. When the volume of diarrhea decreases to <500 ml/day, oral food is often restarted using UC San Diego’s GVHD diet progression (Table 2). This diet, which is based on recommendations from the American Cancer Society, is designed in four stages. Foods are introduced in a stepwise fashion and each stage is characterized by the amount of fat, fiber, lactose, acidity and GI irritants. The goal of the diet is to effectively manage and minimize stool output.

Table 2  UC San Diego GVHD diet

<table>
<thead>
<tr>
<th>GVHD Dietary Guidelines</th>
<th>Phase 1</th>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete Bowel Rest (NPO)</td>
<td>TPN + IV Fluids usually continue</td>
<td></td>
</tr>
<tr>
<td>Clear Liquids: lemon lime soda, ginger ale, gatorade, bottled water, strained fruit juices (no apple, prune, orange), broths, jello, frozen ice, popsicles,</td>
<td>*White rice or plain spaghetti noodles per MD order</td>
<td></td>
</tr>
</tbody>
</table>

Diamond 8
Phase 3
| Corn flakes, Rice Krispies, Special K, plain spaghetti noodles, steamed white rice, pretzels, plain bagel, English muffin, white bread/white dinner roll, saltines, unsalted crackers, jelly, sugar (All Phase 2 foods) | *Soy milk, Lactaid milk per MD. |

Phase 4
| Limit 2 yolks/day, flour and corn tortillas, rye bread, roast beef, turkey, ham sandwiches on white bread, 2% milk, pineapples, honeydew melon, cantaloupe, watermelon, green beans, cooked onions, sherbet (All Phase 3, 4 foods) |  |

Initial Nutrition Assessment

HHH was seen by nutrition upon admission as a skin trigger, with multiple skin tears to her lower extremities and a significant rash on her buttocks related prolonged exposure to soiled diapers.

Anthropometrics at Admission:

Height: 4’9”  Admit Weight: 167 lbs  % Ideal Body Weight: 135% of 94 lbs  BMI: 27.47. Usual Body Weight: The patient denied any weight loss prior to admission, however as noted earlier her quality of life prior to admission was fairly poor.

Family/Social History: HHH was unemployed at time of admission. She was not married and did not have any kids. She had a sister and brother and law that lived in North County.

Estimated Nutrition Needs at Admit:

Using the Mifflin St. Jeor equation and evidence-based guidelines, HHH’s needs were estimated at 1350-1575 calories per day (30-35 kcals/45 kg Adj BW) and 67-90 g protein per day (1.5-2 g/kg AdjBW).
GI and Physical Assessment

The patient endorsed frequent, loose stools at the initial assessment, which is a common symptom of GVHD. The BMT team assessed HHH at Stage 1 of GVHD of the gut upon admit. She was averaging seven bowel movements and day, and would continue to average about six bowel movements daily throughout her hospital stay. The patient tested negative to C-diff.

Initial Nutrition Diagnosis: Altered GI fnx r/t medical condition including GVHD of the gut AEB persistent diarrhea.

Goal: Patient to receive >75% of nutrition needs with acceptable tolerance.

Initial Diet and Intervention:

The patient was placed on a carbohydrate limited diet to manage both her diabetes and hyperglycemia related to steroid medications. Additional nutrition related recommendations included:

- Diet advancement per MD. If active GVHD, rec changing to GVHD diet II → III → IV → V. Goal diet is to return back to carb limited diet.
- Rec to adjust insulin regimen to maintain POCT BS goal of < 180 mg/dl
- Rec to check whole blood zinc and B12 to assess deficiency. A multi-vitamin without minerals was added. Imodium and Metamucil were also started to manage loose stools.

Nutrition Education

The patient was provided with nutrition recommendations to better manage diarrhea as outlined in the Nutrition Care Manual. These tips included avoiding lactose, spicy foods, sugar alcohols and caffeine, which can serve as irritants.

Clinical Course and Progress of Treatment
After a few days of significant diarrhea and concern of worsening GVHD, the patient was downgraded to a zero-carbohydrate clear liquid diet (restricted to one liter per day), which is in accordance with the GVHD II diet. Rice was trialed per the MD after a couple days on the clear liquid diet. HHH’s bowel movements slowly began to improve and noodles and chicken were added to the diet prescription per the MD.

**Nutrition Support: Total Parenteral Nutrition (TPN)**

After a brief period of improvement, HHH began to have up to sixteen bowel movements a day. The patient also began to present with altered mental status (AMS) likely related to steroid psychosis per the MD notes. Her mental status began to affect her ability to self-feed and dysphagia became of concern. Given increased stool output, limited per orifice (PO) intake and altered mental status, a peripherally inserted central catheter (PICC) was placed and the RD team was consulted for TPN recommendations. The patient remained on TPN from February 22nd to March 5th. The TPN prescription was for D15%, AA5% running at 55 ml/hr x 24 hrs. Lipids were initially held until a baseline level was measured given the patient’s history of hypertriglyceridemia. Once triglycerides were found to be within normal limits, 180 ml/day of 20% intralipids was added (15 ml/hr x 12 hrs). Given the patient’s history of hypertriglyceridemia and as a general practice when administering TPN, triglycerides were recommended to be measured weekly.

The patient continued on TPN for about a week given persistent diarrhea, but was allowed to restart clear liquids a few days into receiving TPN. A calorie count was then started as her diet prescription was advanced to assist the team in weaning the patient off of TPN. She was eventually taken off of TPN and restarted on a carbohydrate limited diet. A Glucerna nutrition supplement was recommended to bolster nutrition intake.
GVHD of the Liver

About three weeks into her hospital stay and after one week on TPN, the patient began to have an elevated alk phos and LFTs indicative of GVHD of the liver (Appendix A). A liver biopsy was performed (Appendix B) which found features consistent with GVHD and steatohepatitis. Diarrhea also increased around this time, after another brief period of improvement. However, given the patient’s liver function, restarting TPN was discouraged at this time given the high risk of cholestasis.

An EGD and colonscopy was performed at the end of March after six weeks of minimally improved diarrhea (Appendix C). The EGD revealed normal appearing mucosa in the duodenum and stomach. The colonoscopy found some mild loss of vascular pattern along the colon with two small erosions to the mucosa. At this time the patient was now with GVHD Stage II of the liver and GVHD Stage I of the gut. The patient also developed an AKI around this time of an unclear etiology. The doctors began to renally dose all medications and electrolytes were monitored.

Diet Progression

HHH was placed on a calorie count and bounced back and forth between GVHD II, GVHD III and GVHD IV depending on how well her diarrhea was managed at the time. Her intake widely varied for a couple weeks and then took a significant turn for the worse. A sample of the patient’s calorie count results is listed below (Table C).

<table>
<thead>
<tr>
<th>Date</th>
<th>Calories</th>
<th>Protein</th>
<th>Calorie Goal</th>
<th>Protein Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/3/15</td>
<td>305 Calories, 25g Protein (23% of calorie goal, 37% of protein goal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/4/15</td>
<td>245 Calories, 7g Protein (18% of calorie goal, 10% of protein goal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/5/15</td>
<td>280 Calories, 7g Protein (20% of calorie goal, 10% of protein goal)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table C  Sample calorie count

Given that TPN was not feasible at this time, EN recommendations were provided. Placement of an NJ tube by IR with the tip of the tube pointing into jejunum was recommended. Vital 1.2, an
elemental formula with a favorable carbohydrate content, was recommended. Unfortunately, EN was never started as the patient’s condition continued to deteriorate and a discussion regarding transitioning to comfort care was started.

Weight Change

HHH presented with a wide fluctuation in weights with an overall downward trend as her condition worsened. Her weights ranged from 167 lbs at admit to 116 lbs (Table D) at her lowest recorded weight, indicating a 30% weight loss in two months. A severe malnutrition nutrition diagnosis was delivered given HHH’s significant weight loss, poor PO intake and physical exam findings.

<table>
<thead>
<tr>
<th>Date</th>
<th>Weight (kg/Lbs and oz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>04/08/15</td>
<td>54 kg (119 lb 0.8 oz)</td>
</tr>
<tr>
<td>04/07/15</td>
<td>54.5 kg (120 lb 2.4 oz)</td>
</tr>
<tr>
<td>04/06/15</td>
<td>54.2 kg (119 lb 7.8 oz)</td>
</tr>
<tr>
<td>04/05/15</td>
<td>53.5 kg (117 lb 15.1 oz)</td>
</tr>
<tr>
<td>04/02/15</td>
<td>56 kg (123 lb 7.3 oz)</td>
</tr>
<tr>
<td>03/31/15</td>
<td>56.8 kg (125 lb 3.5 oz)</td>
</tr>
<tr>
<td>03/30/15</td>
<td>54.5 kg (120 lb 2.4 oz)</td>
</tr>
<tr>
<td>03/29/15</td>
<td>57.3 kg (126 lb 5.2 oz)</td>
</tr>
<tr>
<td>03/27/15</td>
<td>59 kg (130 lb 1.1 oz)</td>
</tr>
</tbody>
</table>

Table D  Sample weight trend

Nutritionally Relevant Medications

Administration of steroids is one of the primary treatments of GVHD. Steroids negatively disrupt protein utilization in the body by increasing proteolysis and inhibiting the anabolic effect of insulin. As a result, patients with prolonged steroid use can develop steroid myopathy, which results in a significant loss of lean body mass and can negatively affect functional movement. HHH suffered from steroid myopathy towards the end of her clinical course, which significantly affected her functional capacity. She was unable to stand, walk and effectively feed herself as her muscles continued to deteriorate. Additional nutrition related medications common to the GVHD population are listed below (Table E).
Patient Prognosis

HHH continued to suffer from severe diarrhea and stage III GVHD of the liver. Her prognosis was very poor. In mid April, the patient made the decision to be placed on comfort care. She passed on April 16th.
## Appendix A: Patient Labs

<table>
<thead>
<tr>
<th>Test</th>
<th>Ref. Range</th>
<th>10/16/2014 12:15</th>
<th>1/19/2015 00:45</th>
<th>2/11/2015 00:01</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glyco Hgb (A1C)</td>
<td>Latest Range: 4.8-5.9 %</td>
<td>7.2 (H)</td>
<td>6.0 (H)</td>
<td>5.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
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<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline Phos</td>
<td>Latest Range: 35-140 U/L</td>
<td>361 (H)</td>
<td>397 (H)</td>
<td>414 (H)</td>
<td>443 (H)</td>
<td>367 (H)</td>
<td>374 (H)</td>
<td>388 (H)</td>
<td>535 (H)</td>
</tr>
<tr>
<td>ALT (SGPT)</td>
<td>Latest Range: 0-33 U/L</td>
<td>34 (H)</td>
<td>36 (H)</td>
<td>31</td>
<td>33</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>35 (H)</td>
</tr>
<tr>
<td>AST (SGOT)</td>
<td>Latest Range: 0-32 U/L</td>
<td>32</td>
<td>34 (H)</td>
<td>22</td>
<td>22</td>
<td>24</td>
<td>26</td>
<td>35 (H)</td>
<td>38 (H)</td>
</tr>
<tr>
<td>Bilirubin, Dir</td>
<td>Latest Range: &lt;0.2 mg/dL</td>
<td>8.0 (H)</td>
<td>8.2 (H)</td>
<td>9.3 (H)</td>
<td>8.3 (H)</td>
<td>10.0 (H)</td>
<td>8.0 (H)</td>
<td>7.1 (H)</td>
<td></td>
</tr>
<tr>
<td>Bilirubin, Tot</td>
<td>Latest Range: &lt;1.20 mg/dL</td>
<td>7.86 (H)</td>
<td>9.14 (H)</td>
<td>9.15 (H)</td>
<td>10.72 (H)</td>
<td>9.59 (H)</td>
<td>11.47 (H)</td>
<td>9.09 (H)</td>
<td>8.32 (H)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>Latest Range: 10-170 mg/dL</td>
<td>276 (H)</td>
<td>219 (H)</td>
<td>270 (H)</td>
<td>199 (H)</td>
<td>196 (H)</td>
<td>217 (H)</td>
<td>465 (H)</td>
<td>160</td>
</tr>
<tr>
<td>Prealbumin</td>
<td>Latest Range: 20-40 mg/dL</td>
<td>7 (L)</td>
<td>32</td>
<td>35</td>
<td>22</td>
<td>32</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix B: Liver Biopsy

FINAL PATHOLOGIC DIAGNOSIS:
A: Liver, biopsy
- Features of graft-versus-host disease, see comment.
- Hepatic siderosis (Kupffer cells and hepatocytes), see comment.
- Bridging fibrosis (confirmed on trichrome stain), see comment.

COMMENT: The hepatic parenchyma demonstrates intact lobular architecture. The portal triads are show a minimal predominantly lymphocytic inflammatory infiltrate with rare plasma cells or neutrophils. Interlobular bile ducts show mild injury with occasional cells with cytoplasmic vacuolization, overlapping nuclei, and irregular spacing. There is focal bile ductular reaction. Interlobular portal vessels are intact, without endothelialitis or venous occlusion. There is no interface activity. There is minimal parenchymal inflammation with rare hepatocyte ballooning and without steatosis. Central veins are unremarkable. Trichrome stain shows bridging fibrosis and focal peri-cellular fibrosis. Iron stain shows iron overload of the Kupffer cells and hepatocytes, but without involvement of the bile ducts. PASD stain is negative. Reticulin stain confirms intact lobular architecture.

Overall, the features are consistent with graft-versus-host disease. The presence of rare acidophil bodies, rare hepatocyte ballooning, and bridging fibrosis with a pericellular component are highly suggestive of a component of metabolic injury (i.e. so-called "burned-out" steatohepatitis"). Clinical correlation is recommended. Dr. Peter Curtin was notified of the preliminary results on 3/6/15 (DF).

- Adequacy: >4cm, >40 portal triads
- Steatosis: None
- Stainable Iron: Patchy 3-4+/4 in hepatocytes and Kupffer cells
- PASD: No periportal eosinophilic globules
- Reticulin: Reticulin stain examined and contributory

SPECIMEN(S) SUBMITTED:
A: Liver biopsy

CLINICAL HISTORY:
ICD9 code: 276.2, 279.50, 250.00, 205.00, 790.4. History of GVHD.

GROSS DESCRIPTION:
A: The specimen (received in formalin labeled with the patient's name, medical record number and "A, soft tissue liver") consists of three red-tan to yellow-tan fragments of soft tissue consistent with needle core biopsies, measuring from 1.7 cm in length x 0.1 cm in diameter up to 2.0 cm in length x 0.1 cm in diameter. The specimen is wrapped in tissue paper and entirely submitted in cassette A1.

SD/kc

SPECIAL STAINS/PROCEDURES: Special stains and/or procedures were used in the final interpretation. All stains were performed with appropriate positive and negative controls.

The immunostain(s) reported above were developed and their performance characteristics determined by the UCSD Medical Center Department of Pathology. They have not been cleared or approved by the U.S. Food and Drug Administration, although such approval is not required for analyte-specific reagents of this type. The FDA has determined that such clearance is not necessary. This laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), this laboratory has established and verified the test's relevant performance specifications. Data collected for the verification process are available upon request.
CONFIDENTIAL HEALTH INFORMATION: Health Care information is personal and sensitive information. If it is being faxed to you it is done so under appropriate authorization from the patient or under circumstances that do not require patient authorization. You, the recipient, are obligated to maintain it in a safe, secure and confidential manner. Re-disclosure without additional patient consent or as permitted by law is prohibited. Unauthorized re-disclosure or failure to maintain confidentiality could subject you to penalties described in federal and state law. If you have received this report or facsimile in error, please notify the UCSD Pathology Department immediately and destroy the received document(s).

Appendix C:

Procedure Report COLONOSCOPY
Date/Time of Procedure: 3/18/2015 03:08 PM
Endoscopist: Barrett Levesque
GI Fellow: Michael Chang
Referring Physician:
PROCEDURE PERFORMED: colonoscopy
INDICATIONS FOR EXAMINATION: 50 yo F with a history of AML s/p double cord allo BMT with prior GVHD 11/2014. No w/wth worsening symptoms of GVHD involving the skin, liver, and gut. Here for EGD and colonoscopy for GVHD staging.
INSTRUMENTS:
MEDICATIONS: versed 2 mg, fentanyl 50 mcg (combined EGD and colonoscopy)
NEED FOR ANESTHESIA: Moderate sedation
The attending physician, Dr. Barrett Levesque, was present for the entire examination.
PROCEDURE TECHNIQUE: A physical exam was performed. Informed consent was obtained from the patient after explaining all the risks (perforation, bleeding, infection, missed lesion(s), and adverse effects to the medicine), benefits and alternatives to the procedure which the patient appeared to understand and so stated. The patient was connected to the monitoring devices and placed in the left lateral position. Continuous oxygen was provided with a nasal cannula and IV medicine administered through an indwelling cannula. After adequate moderate sedation was achieved, a digital exam was performed and the colonoscope was introduced into the rectum and advanced under direct visualization to the extent of exam. The scope was subsequently removed slowly while carefully examining the color, texture, anatomy, and integrity of the mucosa on the way out. In the rectum, the scope was NOT retroflexed to evaluate for internal hemorrhoids and anorectal pathology. The patient was subsequently transferred to the recovery area in satisfactory condition.
COMPLICATIONS: None
ESTIMATED BLOOD LOSS: None
BIOPSY TAKEN: Yes
BOWEL PREP QUALITY: 
EXTENT OF EXAM: cecum
Findings: 1. cecum/ascending/transverse colon: mild erythema and some patchy loss vascular pattern, 4 biopsies and placed in jar A
2. descending/sigmoid: mild erythema and some patchy loss vascular pattern, 4 biopsies and placed in jar B
3. rectum: normal appearing mucosa except for 2 erosions (3mm) biopsied and placed in jar C, small hemorrhoids
Works Cited


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