EASTERN PENNSYLVANIA GASTROENTEROLOGY AND LIVER SPECIALISTS

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IN THIS EDITION

THE MANAGEMENT OF ACUTE PANCREATITIS

Acute Pancreatitis (AP), an inflammatory process involving the pancreas, is commonly encountered in clinical practice and recently became the single most common gastroenterology-related hospital discharge diagnosis. It is responsible for an estimated $2.6 billion in health care expenditures. Its mortality can vary widely depending upon the severity, ranging from 3% to as high as 17%. Based on several GI Society Guidelines, the management of this common and potentially life threatening condition will be discussed here.

Briefly, the clinical presentation is often characterized by the abrupt onset of typical abdominal pain (mainly epigastric and/or left upper quadrant radiating to the back or flanks), with or without associated nausea and vomiting. The diagnosis has historically been made by fulfilling two of three following criteria: abdominal pain consistent with the disease, serum amylase and lipase above three times the upper limit of normal and characteristic findings on abdominal imaging. Contrast enhanced CT or MRI should generally be reserved for patients in whom the diagnosis is unclear or who fail to improve within 48 hours. Although the classic management triad of bowel rest, intravenous hydration and pain control remains mostly unchanged, the recommendations have become more nuanced over time.

AP can be classified as either interstitial edematous or necrotizing pancreatitis. Its severity can be mild (absence of organ failure and local complications), moderately severe (organ failure resolving in < 48 hours and/or local complications without persistent organ failure) or severe (persistent organ failure). This terminology has bearing on not only prognosis but also intensity of management. When the diagnosis is made, several strategies should be employed simultaneously. Predicted severity is important as it has bearing on both triage and management. Hemodynamics should be assessed. Risk assessment tools are available to help in triage. They include APACHE-2, BISAP and modified Marshall scores. No single predictive model has been found to be superior, and they can often be cumbersome. It is therefore important to utilize intrinsic patient characteristics such as age (> 55), obesity, medical comorbidities and altered mental status. The presence of organ failure should prompt admission to an intensive or intermediate care setting when possible. The single most important intervention in the first 24-48 hours is adequate IV hydration. This is a critical step due to large third space fluid losses, increased vascular permeability and, commonly, the inability to ingest fluids. Studies have shown that persistent hemoconcentration at 24 hours from presentation is associated with increased risk of pancreatic necrosis.

Historically, the rate of IV fluids had been recommended to be 250-500mL/hr (5-10mL/kg/hr) however more recent data suggest that less aggressive IV hydration (1.5mL/kg/hr) may be appropriate in mild cases. This tailoring of fluid resuscitation is why proper prediction of disease severity is important. Goal directed parameters of IV hydration include regular assessment of hemodynamics, urine output, and serial measurement of serum hematocrit, BUN and creatinine. It is important to understand that aggressive hydration after 48 hours may not be necessary due to not only lack of impact on clinical outcomes, but also to increased risk of cardiopulmonary complications. To date there is no clear evidence to suggest that lactated ringers is preferable to normal saline, with the exception being AP caused by hypercalcemia, in which case lactated ringers is contraindicated due to its calcium content.

Nutrition is an important and time sensitive element of patient care. Historically, it was thought that bowel rest was imperative until complete resolution of the pancreatitis. More recently, studies have shown that prolonged bowel rest is associated with gut mucosal atrophy, intestinal bacterial translocation and increased infectious complications. The management question, then, becomes when and how to begin enteral feedings. In general, timing depends on severity. In mild cases, and in the absence of nausea/vomiting or ileus, oral feeding can begin immediately (low residue, low fat diet). It is no longer considered necessary to start with clear liquids. In moderate to severe cases, enteral nutrition is recommended if oral diet cannot be tolerated by day five.

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SHASHIN SHAH, MD

ENDOHEPATOLOGY (THE ROLE OF EUS IN LIVER DISEASE)

Endoscopic Ultrasound (EUS) allows for evaluation of abnormalities arising from the GI tract and organs that are adjacent to the gastrointestinal lumen. In an earlier newsletter, we discussed the benefits of EUS in evaluating pancreas lesions and cysts and also evaluating for choledocholithiasis. In this article, we will explore the ability to evaluate the liver and surrounding area.

EUS for workup of abnormal LFTs
EUS can be an integral part in the workup of abnormal liver enzymes. To confirm disease processes, stage degree of fibrosis noted on a fibroscan or to stage cirrhosis, EUS with the use of a specialized fine needle biopsy technique (which we recently published) can be performed. (1) The EUS guided approach to liver biopsy allows for easy visualization to assess for fatty liver or nodular liver as can be seen in cirrhosis. Furthermore, access to liver parenchyma can be obtained with minimal complication rates by using techniques such as Doppler Ultrasound to prevent injury to interposed vascular structures.

Traditionally, liver biopsy has required a percutaneous ultrasound guided approach with the patient locally anesthetized yet awake and aware of the procedure. Patients required a prolonged period of monitoring after percutaneous approach with compression on the biopsy tract site for up to several hours to reduce the risk of bleeding. During an EUS guided liver biopsy, the patient is sedated (which patients generally appreciate) and has a standard endoscopic recovery period post procedure.

In addition to providing comparable diagnostic histology to the percutaneous approach performed by radiologists, EUS guided liver biopsy allows for endoscopic evaluation to rule out varices, common duct stones or ampullary and pancreas lesions which may be contributing to abnormal LFTs.

EUS for evaluation of hepatic masses and more
In the unfortunate situation that the patient has a liver mass found on cross sectional imaging, EUS allows for further evaluation. While benign lesions such as cysts, FNH or hemangioma do not often need further evaluation with EUS, solid or suspicious masses often do.

Suspicious liver masses most often represent metastatic foci and can be sampled via EUS- FNA. If primary liver lesions are suspected and after careful discussion with the Hepatologist, these liver lesions can also be sampled via EUS. Adequate histology and cytology analysis can be obtained from EUS guided FNA and can help to determine the malignant etiologies such as cholangiocarcinoma or hepatoma guiding further treatment decisions.

Patients with liver disease can also often have benign or malignant ascites which is often accessible for diagnostic evaluation via a trans-gastric or a trans-duodenal approach. In cases of metastatic disease, surrounding adenopathy is often present and can be sampled to help with oncologic staging as well.

Future of EUS in Liver disease
EUS guided intervention for the management of gastric varices is emerging. Though more data is needed, case series have been performed successfully using EUS guided injection of cyanoacrylate glue (CYA) or stainless steel endoscopic micro-coils placed separately or in combination into gastric varices (2). Some studies show that the combination may be superior to either option alone.

The current standard for portal hypertension measurement uses a transjugular approach to measure the hepatic venous pressure gradient (HVPG). With the use of newer EUS needles, portal pressure gradients can now be performed. As more data is collected, EUS guided portal pressure gradient measurements may complement traditional radiologic approaches and be preferable in certain conditions such as Budd-Chiari syndrome. (3)

Newer EUS processors available at our facility have the ability to perform a shear wave analysis to obtain a fibroscan to assess for degree of liver fibrosis. However, more data is needed to compare the EUS guided fibroscan to traditional, standard beside fibroscan.

Endohepatology is an emerging field in advanced endoscopy and gastroenterology. Many techniques above are a now regular part of our armamentarium for patients with liver disease. Novel techniques using various EUS needles are currently being evaluated in a study that we have ongoing at LVHN. Through this continued development of tools and techniques, and with more peer reviewed research, we and our GI colleagues hope to continue to bring several additional minimally invasive techniques discussed above to our LVHN community.

AMY JAVIA, MD

INADEQUATELY TREATED CELIAC DISEASE AND ITS COMPLICATIONS

While our understanding of Celiac Disease, a chronic autoimmune enteropathy related to dietary gluten exposure, has increased significantly in recent years, early diagnosis of this condition and prevention of its longer-term complications remains challenging. The prevalence of Celiac disease is estimated to be 1% in the general population with a female predominance. The disease can manifest at any age and can present in a variety of ways. Gastrointestinal symptoms such as abdominal pain, bloating, diarrhea, nausea and vomiting as well as extraintestinal manifestations such as chronic headaches, fatigue, weight loss, joint pains, dermatitis herpetiformis, neurologic symptoms or mood disorders may occur. This variable presentation can make Celiac Disease even more difficult to recognize, however increased awareness and advances in diagnostic techniques including serologic and genetic testing have helped. Currently, there is no cure for Celiac disease and the only treatment is a life-long strict gluten free diet (GFD). While symptoms may improve quickly on a GFD, it can take up to one year for complete resolution of small bowel inflammation.

The most common reason that Celiac patients have persistent symptoms, elevated Celiac serologies, or histologic abnormalities of the small bowel is nonadherence to a GFD. This may be secondary to poor compliance or inadvertent gluten ingestion. A small percentage of patients (~5%) will not have resolution of small bowel inflammation despite compliance with a strict GFD for at least 12 months and are considered to have refractory Celiac disease. Refractory disease is subdivided into two types – Type I has a normal population of intraepithelial lymphocytes while Type II is characterized by an aberrant or possibly premalignant population of lymphocytes. It is important to distinguish which type of refractory disease each patient has as the management for each varies and Type II is associated with a very poor prognosis in comparison to Type I.

It is also important to rule out concurrent diagnoses which may mimic Celiac disease and cause villous atrophy such as autoimmune enteropathy, tropical sprue, small intestinal bacterial overgrowth, collagenous sprue, hypogammaglobulinemia or combined variable immunodeficiency, eosinophilic enteritis, Crohn's disease, H pylori infection, severe peptic duodenitis or medication effect (NSAIDs, ARBs).

There are several potential complications of undiagnosed or untreated Celiac disease.
The most common complications include ongoing or worsening GI symptoms such as abdominal pain, bloating, and chronic diarrhea with risk of dehydration. There may be concomitant lactose intolerance due to damage to enterocytes that would otherwise produce the enzyme lactase. Persistent inflammation in the small bowel can lead to atrophy of the villi with associated malabsorption of important nutrients and subsequent hypoalbuminemia and weight loss. It is important to assess for deficiencies of vitamins A, D, E, K, B6, and B12 as well as folic acid, thiamine, magnesium, selenium, copper, and zinc. With vitamin D deficiency, patients may gradually lose bone density and develop osteoporosis. Iron deficiency is also very commonly seen with Celiac disease and can lead to profound microcytic anemia.

Though the pathogenesis is poorly understood, hyposplenism is identified in ~30% of adult patients with Celiac disease and may make patients more prone to encapsulated bacterial infections including Pneumococcus, Haemophilus and Meningococcus. Pneumococcal and Meningococcal vaccinations are especially important in this patient population.

Untreated Celiac disease has been associated with menstrual and reproductive issues in females. Delayed menarche, secondary amenorrhea, earlier menopause, infertility, recurrent miscarriages, spontaneous abortions, preterm delivery, and low birth weight have been observed. In males, there may be an increased risk of infertility related to abnormal sperm motility and androgen resistance.

Ulcerative jejunitis is a condition seen as refractory Celiac disease progresses. It is characterized by multiple ulcerations of the small bowel, predominantly in the jejunum. This can lead to strictures and other complications such as bowel obstruction which generally requires surgical management.

Malignancy is a very rare but serious complication of severe untreated or refractory Celiac disease. Patients with either Type I and Type II refractory disease are most at risk, especially for development of Enteropathy associated T-cell lymphoma (EATL), however this risk is significantly higher in Type II disease. It is estimated that less than 14% of patients with Type I refractory disease will develop EATL within 5 years of diagnosis as compared to up to 50% of patients with Type II in the same time frame. Risk factors for developing EATL include older age at presentation, male gender, HLA-DQ2 homozygosity, presence of ulcerative jejunitis or aberrant T-cell population. There may also be an increased risk of small bowel adenocarcinoma in patients with longstanding Celiac disease however it is generally not preceded by refractory disease and occurs more frequently in female patients.

Although our awareness and knowledge of Celiac disease has substantially increased over the past few decades, it remains a challenging disease. Most patients will do well if compliant with a strict gluten free diet, however it is important to monitor these patients closely to recognize uncontrolled Celiac disease as early as possible to prevent or monitor for complications.

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Nasojejunal (NJ) feedings have been favored in the past, due to the idea of physically introducing feeding distal to the duodenum, however more recent studies have compared NJ to nasogastric feedings and found no significant difference. As nasogastric tube placement is both easier and cheaper compared to nasojejunal, the former is generally considered preferred as a first line.

Antibiotics are not considered necessary for prophylaxis, regardless of both type (i.e. interstitial vs necrotizing) and severity. The notable exception is infected necrosis, which is most commonly seen in patients with necrotizing pancreatitis who clinically deteriorate or fail to improve after 7-10 days.

In summary, the management pillars of nutrition, fluids and pain control remain the backbone of management of acute pancreatitis. The details of each case are variable, depending on the predicted severity of the condition. Numerous tools and patient specific factors are available to aid in this prediction. With prompt triage and appropriate early management, the morbidity and mortality of this common condition should continue to decrease over time.

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