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Progress in Primary Biliary Cholangitis Care: A Look at Management Updates

**Dr. Buch:**
Primary biliary cholangitis, which was formally known as primary biliary cirrhosis, is a chronic disease that progresses over time. Fortunately, much progress has been made with many patients being diagnosed and treated much earlier.

Welcome to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and joining me today to discuss primary biliary cholangitis, or PBC for short, is Dr. Hetal Karsan. Dr. Karsan is an Adjunct Professor of Medicine in the Division of Digestive Diseases at Emory University School of Medicine. He's also actively involved in clinical research. He's Chairman of Medical Education for United Digestive, and Dr. Karsan was the Associate Editor for *American Journal of Gastroenterology* for the past six years.

Dr. Karsan, welcome to the program.

**Dr. Karsan:**
Well, thank you, Dr. Buch. That's a very kind introduction. I'm very honored to be here.

**Dr. Buch:**
To start us off, Dr. Karsan, can you explain why a liver biopsy is no longer required for diagnosing most patients with PBC?

**Dr. Karsan:**
That's a great point. Before, we used to say the hallmark of diagnosing liver diseases was a liver biopsy, but now we've found new, noninvasive methods and serologic methods to diagnose liver diseases, including primary biliary cholangitis, so one does not necessarily need a liver biopsy anymore if you have clinical grounds that are highly suggestive of primary biliary cholangitis.

**Dr. Buch:**
And when might a liver biopsy still be necessary these days?

**Dr. Karsan:**
So you would need a liver biopsy if you're not sure of the diagnosis. That means, let's say, you're thinking about other conditions that may be coexisting in a patient. For example, a patient who's male, primary biliary cholangitis is predominantly female, so if you have a male and perhaps there's other comorbidities—maybe there's obesity or diabetes or you're worried about alcohol use or other liver conditions—then you would need a liver biopsy to clarify just to make sure that you are dealing with primary biliary cholangitis and not another coexisting condition.

**Dr. Buch:**
Thank you. And kind of reflecting on what we just talked about, how do you approach a patient who you suspect has PBC but whose

antimitochondrial antibody is negative?

**Dr. Karsan:**
Another great question. If someone has clinical grounds that you think they have PBC and the antimitochondrial antibody is negative, then you could check some other autoantibodies that are commonly found in patients who are AMA negative. This includes SP100 and glycoprotein-210. If those are positive and clinical grounds really look like PBC with an elevated alkaline phosphatase, female patient, perhaps in their 30s, 40s, then you may not need a liver biopsy in that scenario.

**Dr. Buch:**
How should we evaluate and treat patients who have an overlap syndrome consisting of both PBC and autoimmune hepatitis?

**Dr. Karsan:**
Well first, to diagnose overlap syndrome, you want to make sure they have both conditions and thus overlapping. One should recall that with PBC there is mild interface hepatitis that's quite common with PBC, so you may not have autoimmune hepatitis coexistent. But if you are suspecting overlap syndrome, you really need two out of three criteria —the most commonly used is the Paris criteria. For PBC, you want the elevated liver enzymes, including alkaline phosphatase, and an antimitochondrial antibody and possibly a liver biopsy, coexisting with autoimmune hepatitis criteria, which are ALT greater than five times upper limit of normal or an elevated IgG two times the upper limit of normal and antismooth muscle antibodies or a liver biopsy. So you have to have two of the three criteria for each, and then you have overlap syndrome. And the treatment is really individualized. Typically, people respond to corticosteroids in combination with ursodeoxycholic acid, primarily the mainstay of therapy.

**Dr. Buch:**
Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Hetal Karsan about the management of primary biliary cholangitis, or PBC for short.

So Dr. Karsan, now that we've discussed our diagnostic approach, let's look at some possible treatments for PBC. When should we be utilizing obeticholic acid, and what are the side effects?

**Dr. Karsan:**
So, obeticholic acid is a farnesoid X receptor agonist. It is a hundred times more potent for the endogenous ligand derived from chenodeoxycholic acid, and it is used when ursodeoxycholic acid therapy is not enough or if patients are intolerant of ursodeoxycholic acid therapy. So when you follow patients with ursodeoxycholic, you want to check their alkaline phosphatase to make sure they are appropriately responding. If they are not, then one could consider obeticholic acid therapy. The main side effect of obeticholic acid therapy is pruritus, which is dose-dependent, so you want to start patients on a low dose, such as 5mg, and then monitor them over a few months and titrate the dose upwards if they are tolerating it well and if their liver enzymes, including alkaline phosphatase, decrease.

The other thing to note is that with obeticholic acid therapy, you cannot give it to patients with decompensated cirrhosis or patients with cirrhosis with portal hypertension. So that actually includes patients with varices, patients with ascites or history of varices or jaundice, or even patients with persistent thrombocytopenia should not be receiving obeticholic acid therapy.

**Dr. Buch:**
How do you manage pruritus in PBC that's not responsive to cholestyramine or colestipol?

**Dr. Karsan:**
So pruritus is just one of the real problems with cholestatic liver diseases, including PBC, and these patients often have nighttime itching a little bit more predominant, especially with tight clothing or with heat or during pregnancy or with estrogens. The mainstay is bile acid resins. And if those fail, then one could try antihistamines, such as hydroxyzine, nightly. There's also data for sertraline, which has been

shown in a study. Again, this is off-label. That can be tried. Other medications include opioid antagonists, such as naltrexone. However, you have to watch for opioid withdrawal, and there's a little bit of a caution in patients with liver disease. That along with rifampin can be tried, but again, rifampin can cause hepatitis, so it has to be used with much caution as well.

**Dr. Buch:**
So the other trouble that we're faced with with PBC is fatigue. How do you manage fatigue?

**Dr. Karsan:**
Wow, fatigue is a real problem with PBC, and unfortunately, there is no great remedy for fatigue because our medicines don't seem to help. Even liver transplantation does not seem to help fatigue. In fact, in opposition to pruritus, fatigue is not an indication for liver transplantation because patients do not improve fatigue after liver transplant. Pruritus, on the other hand, can be an indication for liver transplantation, and you can get exception points if it's approved by a Regional Review Board. As far as fatigue goes, really one has to look for other possibilities, such as thyroid disease, which is common in patients with PBC. Also, you need to look for other conditions, such as anemia or psychiatric problems perhaps, depression. These things also can cause fatigue, and one has to be very careful and look at all things combined.

**Dr. Buch:**
Now, we've certainly covered a lot of ground today, Dr. Karsan. But before we conclude, is there anything else you would like to share with our audience?

**Dr. Karsan:**
There are a couple points I'd like to mention. One is that bilirubin is actually the best predictive factor for survival and is actually the most important component of all of the mathematical models that we use for prognosticating PBC, so bilirubin is actually quite important. In fact, having a bilirubin at 0.6 is very important. We know that when bilirubin increases, even a bilirubin of 1.0 is not necessarily a good thing, and getting your alkaline phosphatase as close to normal is important and has been shown to be predictive of longer survival and decreased risk of death and liver transplantation long-term, so those things are really important.

I'd like to also mention that liver transplantation has actually been decreasing for PBC, and that's probably due to diagnosing the disease earlier and treating it earlier. Even though the prevalence is increasing due to finding more patients with the disease. The number of liver transplants for PBC has actually been decreasing over time, which is encouraging.

**Dr. Buch:**
Those are all great takeaways. And as this brings us to the end of today's program, I want to thank my guest, Dr. Hetal Karsan, for sharing his insights. Dr. Karsan, it was a pleasure speaking with you today.

**Dr. Karsan:**
Well, thank you, Dr. Buch. The pleasure was all mine. I really appreciate you having me on.

**Dr. Buch:**
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights, where you can Be Part of the Knowledge. Thanks for listening and see you next time.