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Diagnosing and Treating Primary Biliary Cholangitis: Key Clinical Insights

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and joining me to discuss the diagnosis and treatment of primary biliary cholangitis, or PBC for short, is Dr. Dian Chiang, who's Section Head of Hepatology at the Cleveland Clinic Foundation in the Department of Gastroenterology, Hepatology, and Nutrition. Dr. Chiang, it's great to have you here with us today.

Dr. Chiang:
Thank you. I'm glad to be here. Thank you so much for inviting me, Dr. Buch.

Dr. Buch:
To start us off with some background, Dr. Chiang, can you please define PBC for us and how it differs from primary sclerosing cholangitis, or PSC?

Dr. Chiang:
PBC is an autoimmune disease of the liver, and it is our immune system that's attacking the small bile duct inside the liver. As a result of the injury, it can cause scar tissue to form in the liver, which is fibrosis, and as it progresses over time, it can lead to cirrhosis of the liver. On the other hand, PSC, primary sclerosing cholangitis, is largely affecting the medium and large bile duct both inside and outside of the liver. As the PSC progresses, it can cause complications, including recurrent cholangitis and in some cases cirrhosis.

Dr. Buch:
With that background in mind, how do you make the diagnosis of PBC? And what other autoimmune diseases are associated with it?

Dr. Chiang:
To make a diagnosis of PBC, usually we would see the patients and examine their past histories as well as their current symptoms to identify if they have clinical presentation that's consistent or suggestive of PBC. Once we have a clinical suspicion of PBC, we would usually perform additional laboratory testing to identify or confirm the diagnosis of PBC. That usually includes the following testing. First is their liver enzyme testing through bloodwork if they have a pattern of liver enzyme elevation that's consistent with a cholestasis liver injury, which is elevation in their alkaline phosphatase. Secondly is we will see if they have an autoimmune antibody called AMA, or antimitochondrial antibody, present in their bloodwork. Thirdly, we can consider performing a liver biopsy to see if they have liver injury on the biopsy that's consistent with primary biliary cholangitis. And typically, we don't need all three tests to confirm the diagnosis. According to the liver association guidelines, we only need two out of the three to confirm the diagnosis of PBC.

Dr. Buch:
Dr. Chiang, can you tell us when an ANA, or antinuclear antibody, might be appropriate? And what are the subtypes that might give us the information when an AMA is negative?

Dr. Chiang:
So there are several autoimmune antibodies that we can test. The AMA, antimitochondrial antibody, is the most sensitive for PBC, but there are other autoimmune antibodies, such as the ANA, antinuclear antibody, that we can see that usually would point to more of an autoimmune hepatitis presentation. In addition, there are two additional antibodies that are available for us to check right now. One is anti-SP-100; one is anti-GP-210. Those two autoimmune antibodies are more specific to PBC, and we would sometimes use it to confirm or rule out PBC as well.

Dr. Buch:

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Thank you. And getting back to the original question, what are the other autoimmune diseases associated with PBC?

Dr. Chiang:
There are several autoimmune diseases that are associated with PBC. One is autoimmune thyroid disease. Second will be Sjögren's syndrome. Third will be Raynaud's disease. We also see that patients with PBC oftentimes have rheumatoid arthritis and scleroderma as well. Those are autoimmune diseases that can be associated with PBC.

Dr. Buch:
And what percentage of patients with PBC also have thyroid disease?

Dr. Chiang:
So it is a very common association. It depends on the study population that we look at. It can range between 15–25 percent of patients that may have autoimmune thyroid disease. And if we look at all the extrahepatic manifestations of PBC, up to 73 percent of patients may have some extrahepatic manifestations.

Dr. Buch:
So let's come back to liver biopsies. Tell us when a liver biopsy is necessary to make a diagnosis of PBC.

Dr. Chiang:
Liver biopsy is usually recommended when there is a clinical suspicion of a secondary or superimposed liver disease. For example, if we suspect that the patient may not only have PBC, but they may also have overlapping autoimmune disease with PBC, or they may have overlapping metabolic dysfunction or steatotic liver disease with PBC. PBC biopsy can also be considered when the serological workup is not consistent with PBC, but patients have signs and symptoms and history that's suggestive of PBC. For example, if their AMA is negative but based on the history you suspect this is PBC, then you can also consider a liver biopsy. We do see up to 5 percent of patients who may have what we consider AMA negative PBC, and we can only make the diagnosis by performing a liver biopsy.

Dr. Buch:
Dr. Chiang, what are the complications of PBC that we should be aware of?

Dr. Chiang:
There are several complications of PBC that we should be aware of when we see the patients. Number one is it is an autoimmune liver disease. With progression, we may see worsening of liver fibrosis; we may see development of cirrhosis; and there is a possibility of developing liver cancer, especially after they have had long history of disease and development of cirrhosis. Beyond the liver, we also see patients with PBC that have increased risk of developing osteoporosis. Therefore, they have increased risk of fracture. We see them have increased risk of fatigue, depression and pleuritis, which can significantly affect their quality of life.

Dr. Buch:
So for those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Dian Chiang about primary biliary cholangitis, or PBC.

So let's move on to therapeutics, Dr. Chiang. What percentage of PBC patients respond to ursodeoxycholic acid?

Dr. Chiang:
Ursodeoxycholic acid is the first-line treatment of PBC in clinical practice as well as in published literature. We can see 40–50 percent of patients may respond to this first-line agent.

Dr. Buch:
And the follow-up question to that is, is obeticholic acid still being prescribed?

Dr. Chiang:
It is still being prescribed here in the US. There are patients who are on it, and if they are stable on the treatment without side effects, we may continue the treatment. As you know, the FDA has not made its final decision on whether to continue its approval at this point or not, and we're awaiting the decision from them.

Dr. Buch:
So tell us a little bit more about the concerns with regard to obeticholic acid.

Dr. Chiang:
In clinical practice, the most common side effect from this medication is skin itch, or pruritus. Many patients who have pruritus may have exacerbation of their symptoms, and sometimes patients who don't have the pruritus symptoms before may experience pruritus after using the medication, so many patients need to discontinue the medication. There is also concern of the long-term efficacy of the

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medication with the recently published long-term outcome data. However, there is significant dropout in those long-term follow-up studies, so there is an ongoing study on whether this medication help the patients with PBC long term or not, and I think that's why the FDA is deciding whether to continue its approval or not.

Dr. Buch:
Thank you very much for that insight. So how do you treat patients who have not responded to ursodeoxycholic acid and perhaps are not going to be prescribed obeticholic acid?

Dr. Chiang:
Fortunately, there are several second-line agents that are available to us right now. In 2024, we have two second-line agents approved by the FDA under accelerated approval process. Both agents are what we call PPAR agonists. One is elafibranor. The other is seladelpar. Both medications are available to be prescribed in the US. In addition, we also have a PPAR agonist that's fenofibrate. That's also available off-label use in the US as well. All three medications can be considered as a second-line agent at this point for patients who are not responding to ursodeoxycholic acid.

Dr. Buch:
So in the last few moments of our conversation, Dr. Chiang, is there anything else you'd like to leave with our audience?

Dr. Chiang:
PBC is a condition that can progress over time for many, many years without being detected, so it requires primary care providers to be vigilant and on the watch for signs and symptoms of PBC in the primary care setting. And many of the early signs of symptoms can be very nonspecific, so it requires long-term follow-up of the patient and good therapeutic alliance for the patients and the provider to notice the subtle early signs of PBC. Once there's a suspicion, then noninvasive testing can be performed, including the serological workup of liver function panel and autoimmune antibodies. When there is a clinical suspicion of PBC based on the initial workup, then referral to a hepatologist, a liver specialist, can be undertaken as early as possible. I think early detection of the disease and early referral would be the best way to ensure a good clinical outcome.

Dr. Buch:
Thank you. With those final thoughts in mind, I want to thank my guest, Dr. Chiang, for joining us to share strategies for diagnosing and treating primary biliary cholangitis. Dr. Chiang, it was a pleasure having you on the program today.

Dr. Chiang:
It is my pleasure, Dr. Buch. Thank you so much for having me.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in our series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.

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