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www.reachmd.com
info@reachmd.com
(866) 423-7849

A Review of Autoimmune Hepatitis in Patients

Dr. Buch:

This is GI Insights on ReachMD. I'm your host, Dr. Peter Buch. And today we'll be discussing autoimmune hepatitis, also referred to as AIH, with Dr. Alan Bonder. He's the Director of Liver Transplantation at Beth Israel Deaconess Hospital and an Assistant Professor of Medicine at Harvard Medical School.

Welcome to the program, Dr. Bonder.

Dr. Bonder:

Thank you, Dr. Buch. It's a pleasure to be with you.

Dr. Buch:

Let's dive right in, Dr. Bonder. How does AIH usually present in patients?

Dr. Bonder:

So I would say there is different presentations. We have what the conventional abnormal liver chemistry is as an outpatient, and that leads to workup, including autoantibodies, and then we find them positive, and that leads to a biopsy that leads to diagnosis of autoimmune hepatitis, but also, we have to be aware about the presentation of liver failure. So there is patients that can present with acute liver failure related to autoimmune hepatitis, and of course, these patients need to be admitted to a liver transplant center because they will need a liver transplant. We find now that we have the patients in between, patients who come with severe autoimmune hepatitis that don't meet that liver failure criteria yet, but they need to be admitted, get IV steroids so we can treat them right away and prevent them to actually go on and to develop liver failure.

Dr. Buch:

And with that in mind, what other liver diseases could be confused with AIH?

Dr. Bonder:

That's a great question. I would say right now we have a few of them. So if you have an underlying autoimmune disease, then you are more prone to develop autoimmune liver disease. So for example, patients with SLE or rheumatoid arthritis are more at risk of having autoimmune hepatitis, so those patients need to be checked through liver test. The one that we actually see more in our practice is basically drug-induced liver injury—for example, the use of statins or other medication that can cause liver injury—and they can mimic autoimmune hepatitis, and in those cases, sometimes a liver biopsy, sometimes doing steroids or withdrawing from steroids will tell us if those patients meet criteria for autoimmune hepatitis or other diagnosis.

Dr. Buch:

And as a segue to that, it sounds like the diagnosis provides some challenges for clinicians. So how do you tell us the challenges and how to work up these patients, especially when there are the crossover illnesses with other liver diseases?

Dr. Bonder:

I think this is one of the most important questions, Peter, that we actually get asked. So a diagnosis of autoimmune hepatitis needs the help of a liver biopsy. Without a liver biopsy, we won't be able to diagnose autoimmune hepatitis because we—again, in all of those conditions, we have abnormal liver test, we have the presence of autoantibodies—so when we put everything together, put the pieces together, we want to show that the biopsy shows autoimmune hepatitis because those patients will be on treatment for at least two to three years, and then we want to make sure that the diagnosis is correct because we don't want to start giving steroids to patients who don't meet the diagnosis, specifically for example, patients who have a positive autoimmune hepatitis, autoimmune antibody, and they

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have hepatitis C, or they have autoimmune hepatitis and they have nonalcoholic fatty liver disease. So again, a biopsy is so important, and it is, I would say, kind of the gold standard for diagnosing someone with autoimmune hepatitis.

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. Alan Bonder about autoimmune hepatitis, or AIH for short.

So now that we've had some background on the presentation of AIH, Dr. Bonder, let's switch to liver biopsies. First of all, do all AIH patients need a liver biopsy? And the second question, how are biopsies helpful in clinical decision-making for AIH patients?

Dr. Bonder:
So again, this is two very important questions, Dr. Buch. Number one is the answer to your first question will be yes. Every patient that we suspect autoimmune hepatitis needs a liver biopsy to get stagnant, to get diagnosed with autoimmune hepatitis. So again, if we go through the presentations and we have a patient who presents with abnormal liver chemistries, we want to put the pieces together. The presence of abnormal liver test, the presence of a positive autoantibody, and the presence of a histologic inflammation related to autoimmune hepatitis gives you the diagnosis of autoimmune hepatitis. And it's so important, again, to look at these three things together because we are committing these patients to two to three years of immunosuppression, and some of them—we will talk about flare—some of them will need lifelong therapy with immunosuppression, so we want to make sure that these patients really have a diagnosis of autoimmune hepatitis.

As far as the second question, is the biopsy so important in the clinical decision, and the answer is yes. And the reason why, is autoimmune hepatitis, when we look at the specifics of inflammation, can look at plasma cells, lymphocytes, but that also can be found in other diseases, so this is when we actually, clinically, we have to make sure that we look at their presentation, we look at biochemical or lab abnormalities, and we put out the histologic diagnosis—and again, specifically, in overlap syndromes where you have not one autoimmune diagnosis but you have multiple. For example, if we have biliary injury and you have a patient who looks to have autoimmune hepatitis based on inflammation that can look like, for example, overlap between autoimmune hepatitis and PBC, or if we have, for example, lymphocytic cholangitis and presence of neutrophilic cholangitis, that can be also the presence of PSC and autoimmune hepatitis, and also the presence of eosinophils that can be, for example, drug liver injury causing an autoimmune reaction.

Dr. Buch:
And are there ever any false-negative biopsies when evaluating a patient with autoimmune markers for AIH and doing a liver biopsy?

Dr. Bonder:
That's a great question, Dr. Buch. I would say the answer is no. So when a biopsy has no presence of inflammation-related autoimmune hepatitis, patients cannot have a diagnosis of autoimmune hepatitis, and it's so important because, remember that patients can have positive autoantibodies, but that doesn't mean they have autoimmune hepatitis; but again, the biopsy is so useful in those cases because we ruled out completely. And again, we want to make sure that we take it back to our patient. Is the etiology that the patient has a metabolic syndrome? Does the patient have any other etiologies, like IV drugs or alcohol, anything else that can cause any harm to the liver? So that's one way we put it into context.

Dr. Buch:
Thank you for that. So let's move on to treatment. And what are the current treatment options available for patients with AIH?

Dr. Bonder:
So also, this depends on the presentation, Dr. Buch. For example, if you have a patient who comes in as an outpatient with abnormal liver test, the current guidelines from our society recommend using budesonide as an induction therapy, so we do nine milligrams, we make sure that the liver tests are coming down, and once we have biochemical remission, which means normal ALT, normal AST, normal immunoglobulins, we can start immunomodulator therapy. So we put those patients on either azathioprine or 6-mercaptopurine to keep them actually from having any relapses, and that therapy will last between two to three years, but we want to make sure they get normal biochemistry, which is biochemical remission.

In the setting of a patient coming in with liver failure, there is really certain criteria because at some point, if your liver failure is that severe, maybe the steroids will not be an option, and maybe the only salvage therapy that we have in those patients will be liver transplantation. And again, the patients that are in between we will use IV steroids because IV steroids have shown to get induction and try to calm the inflammation kind of like in the more rustic term. And then once we have actually some more biochemical remission or coming into more chemical remission, then we can actually start or start thinking about using immunomodulators. So again, I think the current therapies—and again, we switched from having prednisone to budesonide based on our more current clinical guidelines—and they have been shown that they are similar in outcome. So budesonide is better because they have less systemic effects, so if

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you're able to use them, then I think we should actually try to use budesonide as much as we can.

Dr. Buch:
And taking this a little further, how do you approach brittle diabetic patients who have AIH?

Dr. Bonder:
Really great question. And again, this also depends on the liver chemistries and the inflammation in the liver. For example, I have had patients that they have minimal elevation of liver chemistries, but they have a really nasty inflammation on liver biopsy, so those patients, instead of putting them on induction therapy with either budesonide or steroids, I will start right away immunomodulators and follow their liver tests to see if they actually get into biochemical remission. Those patients are really hard to treat, but again, if you have really bad inflammation with really elevated liver tests, some of those patients, we will need to decide if using PO steroids with actually increasing the insulin or starting insulin to try to get them in both ways treated without having any major disadvantage from the diabetes.

Dr. Buch:
Now I would like to hear from your vantage point, Dr. Bonder. What has been your experience with patients relapsing after being taken off of therapies?

Dr. Bonder:
When I have a patient with autoimmune hepatitis and when we are ready to take him off of immunosuppression around the two- to three-year mark, so there is two school of thoughts. One of them was you need a liver biopsy. You want to make sure that, first of all, you have biochemical remission, as I told you, a normal ALT, normal AST, and normal IgG. And some people, like myself, still believe that a liver biopsy without inflammation will give you the best chance to actually not have a relapse. The relapse rates are between 50 to 90 percent, so I tell my patients, "There is a good chance you'll be relapsed, but the good thing about it, if we caught you early, then we're going to be using less steroids for induction again," so I usually tell this to my patients. Some of my patients say, "Do you know what? I don't want to go over to the steroids. I don't want to have the side effects of steroids, so I will prefer to remain on immunosuppression for the rest of my life." And then we have the other patients who we should not be thinking about taking off immunosuppression. For example, the advanced stage of fibrosis or cirrhosis should never, ever try to think about actually taking them off of immunosuppression because if they have a relapse, they might go on and have liver failure, so we have to be very careful about that.

But one more important thing, Dr. Buch, is we need to tell our patients—because they are on immunomodulators, they are on immunosuppression—we need to make sure they see their dermatologist on a yearly basis, and this is a good reason we need to start thinking about taking them off of immunosuppression. So if a patient has multiple skin cancers in the past, this is the right patient to try to take him off of immunosuppression. So it depends on, again, on the clinical scenario what patients are the right patients for immunosuppression withdrawal. But we should try to give it a chance as much as we can to everyone quoting that that number will be between 50 and 90 percent.

Dr. Buch:
Thank you. And lastly, are there any other thoughts you'd like to share with our audience today?

Dr. Bonder:
I just want to send the message, Dr. Buch, that autoimmune hepatitis is a combination of a biochemical and histologic diagnosis. We do see a lot of referrals from community gastroenterologists or even primary cares that we have a patient, they have an elevated liver test, they have a positive ANA, and they start on steroids right away. I want to make sure that we send the message that patients with autoimmune hepatitis need a liver biopsy for diagnosis because it really implicates a lot for treatment, and also, actually will tell us exactly is there any other etiology that are possible that they could have?

Dr. Buch:
This was a superb review of autoimmune hepatitis. I want to thank my guest, Dr. Alan Bonder, for sharing his insights. Dr. Bonder, thanks so very much for joining us today.

Dr. Bonder:
Again, it's a pleasure to be with you, Dr. Buch, and hopefully, I can be with you in the near future.

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 looking forward to learning with you next time.

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