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ITP - Immune Thrombocytopenia

DRIP 3

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I'm glad I'm sitting on this side of the table. Nobody is in front of me because I don't want anybody to shoot me. But this is kind of a trick question because the answer to this poll question is all of the above.

And the reason I asked that question is because most clinicians and nurses think it's just about platelet surface autoantibodies targeting glycoproteins, and that's reflected in this poll question. But when it comes down to it, there are multiple mechanisms, one of which are those autoantibodies targeting platelet surface glycoproteins. But you can also have increased macrophage function and B-cell autoreactivity.

You can have dysfunctional T and B-cells that don't allow a patient to maintain self-tolerance. You can have cytotoxic T-cells. And you can even have normal-- inappropriately so-- but normal thrombopoietin level, so you're not getting that appropriate response.

Think about when you have IMHA. You're expecting a regenerative anemia because your EPO or erythropoietin level should be high, and that leads to a reticulocytosis. Well, when you don't have many platelets, you should also have an elevation in thrombopoietin levels, but that doesn't always happen. And we're going to talk about why it doesn't happen, looking at this picture.

Under normal circumstances, platelets that are aged they get desialylated as they circulate through the body by things called [INAUDIBLE]. And these "aged" platelets, these desialylated platelets, actually travel to the liver, and they interact with a specific receptor called the Ashwell-Morell receptor.

Well, when platelets are taken out by the immune system by any of those four mechanisms that have nothing to do with thrombopoietin, guess what doesn't happen? Those desialylated or aged platelets don't get to interact with the Ashwell-Morell receptor in the liver. And if there's no ligand-receptor interaction, what doesn't happen? There's no signal to make more thrombopoietin. So you've got platelets getting destroyed, and you have a lack of a platelet regenerative response, a lack of megakaryopoiesis.

Kind of cool, right? I know, I'm nerding out.

You can have essentially a scenario where platelets-- the body essentially initially loses self-tolerance, and then T helper cells promote the generation of both autoantibodies produced from B-cells, and you have autoreactive cytotoxic T-cells. And these autoantibodies opsonize the platelets, which leads to their either clearance by the spleen or clearance by a little bit of the liver, macrophages in both of those organs. And then, the macrophages end up becoming APCs. Remember, antigen-presenting cells? So they just propagate that cycle.

You get cytotoxic T-cells that can just destroy platelets in the blood or within the reticuloendothelial system. And that can even happen at the level of the bone marrow. But it seems that that bone marrow directed process based on published studies is not very common.

So who gets immune thrombocytopenia? Well, cats any age, any sex, dogs-- if you look at the studies, our middle-aged female dogs are overrepresented with some breed predispositions-- Poodles, OESes, and Cocker Spaniels. But again, any dog can get it.

Clinical signs-- usually, there's going to be some degree of hemorrhage. And not everybody is going to put all the checks in the book. In my experience, scleral hemorrhage, epistaxis, hematuria, and melena are most common after the petechiae and ecchymoses. Every once in a while, after chewing on bones, they'll report gingival hemorrhage, or they'll see the bone after the dogs chewed on it, and they'll find blood on the bone. And that will cause owners to go and investigate, and they'll find, oh, my gosh, my dog's bleeding from their gums.

Hyphema is not that common unless there's concurrent trauma. Although it can happen spontaneously. In my experience, it usually happens after trauma. And that trauma can be very minor like they're just playing.

The life-threatening issues like pulmonary hemorrhage causing dyspnea or cerebral hemorrhage they do happen. It's just not common in the average case. Because this is an immune process, they don't feel well. There's inflammation going on in their body.

They're weak. They're lethargic. They have a fever. And again, it's usually not because of an infection. It's usually because of this immune inflammation. So pay attention to your physical exam very, very closely. In that left picture, you can see iridial bleeding and then some more classic ventral abdominal, coalesce, petechiae, and ecchymoses.

Because it is an immune disease, we talk about primary versus secondary. Primary is sometimes called autoimmune, my favorite word, idiopathic-- big, fancy, pretentious way of saying, I don't know why it happened. But very, very important to recommend and ideally pursue a thorough diagnostic investigation for these secondary processes because if there is a secondary process that we don't identify and definitively treat, we're probably not going to be successful in our management of the ITP.

So what are the most common secondary causes? Well, they tend to fall into the categories of infectious diseases, neoplasia, drugs, specifically antimicrobials, and maybe some vaccines. And I can hear some of you saying which vaccines? Which vaccines? We don't know. It's really weak evidence, and this is very controversial. But the point is we're concerned.

So in terms of the infectious diseases, you can see most of these are vector-borne diseases-- mosquito transmission or tick transmission. And so what you screen for it depends on your geographic location. What our colleagues in northern Montana and northern Idaho screening for is going to be very different than what you all down in Florida are looking for, which is going to be different than what I look for here in Nebraska.

If you take a step back and say, OK, in dogs, what's more common? Primary or secondary? In cats, what's more common? Primary or secondary? This is where cats are not small dogs.

Without question, studies have shown that the vast majority of dogs have primary immune-mediated-- immune thrombocytopenia. On the other hand, cats have secondary disease until proven otherwise. Look for those infectious agents. Look for the cancer. So you need to be doing a thorough diagnostic investigation.

And I need to emphasize that the first test after documenting thrombocytopenia is being comfortable that thrombocytopenia is real. You can do a jugular stick in a patient with thrombocytopenia. And I would encourage you never to really-- never is a strong word but to try to avoid lateral saphenous veins and cephalic veins because those are catheter veins. We don't want to be collecting blood from them. You want to be collecting blood from a central vein if possible.

If there's-- if you have the ability to hold off firmly for 5 minutes-- and I don't mean putting a Band-Aid on it. I mean, you dedicate somebody to standing there and holding. That's what you need to do.