Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting: https://reachmd.com/programs/cme/multidisciplinary-approach-to-diagnosing-and-managing-indolent-systemic-mastocytosis-the-changing-landscape/18090/

Released: 04/24/2024
Valid until: 04/24/2025
Time needed to complete: 15 minutes

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

Multidisciplinary Approach to Diagnosing and Managing Indolent Systemic Mastocytosis: The Changing Landscape

Announcer:
Welcome to CME on ReachMD. This activity, titled "Multidisciplinary Approach to Diagnosing and Managing Indolent Systemic Mastocytosis: The Changing Landscape" is provided by TotalCME, LLC.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Akin:
Systemic mastocytosis is a heterogeneous group of disorders characterized by aberrant mast cell numbers and activity. And in most cases, in more than 95% of the time, it's driven by a tyrosine kinase mutation called KIT D816V. The mast cells with this mutation remain perpetually activated, releasing mediators and causing symptoms such as flushing, abdominal pain, itching, and diarrhea. Patients with the indolent form of systemic mastocytosis, or ISM, frequently report a symptom burden disproportionate to measurable disease burden. Many are taking 3 or more medications to block mast cell symptoms.

Diagnosis and treatment of ISM requires the expertise of a multidisciplinary team including allergists, gastroenterologists, and hematologists. Today, we will be discussing the importance of the multidisciplinary team in managing ISM and the need to improve understanding of new treatments among the different specialties such as the use of tyrosine kinase inhibitors.

This is CME on ReachMD, and I'm Dr. Cem Akin. I'd like to welcome my colleagues, Dr. Dan DeAngelo and Dr. Matt Hamilton, to our discussion today, where we will address this clinical challenge.

Dr. DeAngelo:
Thank you. Glad to be here.

Dr. Hamilton:
Thanks so much. Glad to be here.

Dr. Akin:
I will begin our discussion today with a dialogue on how the allergist approaches the diagnosis and treatment of an ISM. Let's start with a patient who is a 45-year-old male who had a severe reaction with syncope requiring resuscitation shortly after a bee sting. He did not have hives or angioedema during the reaction, and physical exam is normal without skin lesions. He also reports flushing and tachycardia with exercise and alcohol intake and diarrhea several times a week. This patient has several red flags for underlying systemic mastocytosis. First of all, he had a severe allergic reaction to bee venom. Second, during this reaction, he had syncopal reaction without any angioedema or urticaria. So these patients have a high likelihood of having clonal mast cell disease or systemic mastocytosis as the underlying etiology, in addition to an IgE-mediated trigger, such as bee venom.

First, a good thing to start with this patient is to check a baseline tryptase level. Tryptase is a protease stored in mast cell granules, and at baseline, is indicative of mast cell burden. A tryptase level of greater than 20 ng/mL is a minor criterion for systemic mastocytosis,

with a normal tryptase being around 4 or 5 ng/mL.

This patient's tryptase came back at 25, which is clearly elevated. At this point, because of the several red flags that I mentioned and an elevated tryptase level, I would refer this patient to a hematologist to establish the diagnosis of systemic mastocytosis with a bone marrow biopsy and aspiration.

If the diagnosis of systemic mastocytosis is established, then I would discuss with this patient an anti-mediator treatment approach. I would start with H1 antihistamines. Most commonly used ones are second-generation antihistamines, which can be used once or twice a day. In patients with gastrointestinal symptoms, we add an H2 antihistamine. And in patients with suboptimal symptom relief, we sometimes consider leukotriene blockers.

In some patients, we also consider omalizumab, or anti-IgE therapies, especially in people with venom allergies and if they are not able to tolerate venom desensitizations. And if they are having reactions to the venom desensitization treatments, omalizumab could be a good preventive medication.

But if the patient is having suboptimal symptom control, still affecting his quality of life, then the next line of treatment would be to consider a D816V selective tyrosine kinase inhibitor. Currently, avapritinib is the only tyrosine kinase inhibitor that is approved by Food and Drug Administration, and it is indicated for indolent systemic mastocytosis. In the PIONEER study, in which this medication was compared to placebo, there were very few side effects observed. The most common ones being periorbital or peripheral edema.

In this part of the discussion we went over a case with a typical allergy presentation. Some of our patients present with skin lesions called urticaria pigmentosa, and these skin lesions can also cause symptoms such as itching and burning sensations, flushing. And those patients are also great candidates to consider avapritinib if they're not responding to first-line antihistamine therapies.

For those just tuning in, you are listening to CME on ReachMD. I'm Dr. Cem Akin, and here with me today are Dr. Dan DeAngelo and Dr. Matt Hamilton. Our focus today is discussing the multidisciplinary management of indolent systemic mastocytosis and how best to optimize outcomes for these patients.

Dr. DeAngelo, we have discussed the allergist's approach to a patient likely to receive a diagnosis of ISM. What is the hematologist's approach to a patient with a suspected ISM diagnosis?

Dr. DeAngelo:
Thank you, Dr. Akin. Hematologists are typically referred patients from a variety of sources, either from an allergist, such as yourself, or more typically an allergist that may require an investigation to determine whether or not a patient has systemic mastocytosis, as you've nicely outlined. So a patient with allergies, anaphylaxis specifically to bee or wasp, with an elevated tryptase, those patients are often referred to us for bone marrow examination.

However, we also see patients referred in from dermatology with skin lesions. Oftentimes the dermatologist will biopsy that skin lesion to make a diagnosis of cutaneous mastocytosis. And then the question to the hematologist is whether or not there is systemic disease. Rarely, we get patients referred in from gastroenterology with patients with irritable bowel-like syndromes, or patients with some hepatic dysfunction.

And our job is to make a diagnosis with a marrow examination to determine whether or not there's aggregates – this is a major criteria – and whether or not they're spindle formed, the mutation assessment, specifically the KIT D816V, although other activating KIT mutations are now accepted as a minor criteria, and, of course, the serum tryptase which is often already obtained. CD25 aberrant expression is also important. So a mixture of these major and minor criteria is to establish a diagnosis.

And then the hematologist needs to differentiate between patients with indolent disease versus smoldering or advanced disease on the presence or absence of what are called B findings for burden of disease or C findings for those patients who require cytoreductive therapy.

And then the question for a patient with indolent SM, that is a patient without any B or C findings, has the patient been started on agents to try and control their symptomatic disease? And if they're still having breakthrough symptoms, whether or not cytoreductive therapy with a KIT inhibitor is warranted.

And so that's the approach that a hematologist will take when referred from a dermatologist, allergist, or gastroenterologist. In a tertiary referral center like myself, I also get patients referred in from a hematology, where he or she may have less experience in making a diagnosis of systemic mastocytosis and really wants confirmation of a diagnosis, confirmation of the fact that the patient has indolent disease, and whether or not the patient has been adequately or inadequately controlled on supportive care measures and therefore warrants a KIT inhibitor.

And that's my role to try and help the community allergist, dermatologist, and hematologist through what can be a very difficult diagnosis to establish with a confusing criteria for determination.

Dr. Akin:
Dr. Hamilton, there are often very concerning gastrointestinal symptoms associated with ISM. Could you take us through how the gastroenterologist approaches such a patient?

Dr. Hamilton:
Absolutely. As we know, patients with ISM can have prominent GI [gastrointestinal] symptoms, and it's important to be able to recognize what these symptoms are and to potentially come up with a treatment plan and even strategies to help with diagnosis. So what are those GI symptoms that would suggest mast cell disorder, and specifically, ISM? Typically, these patients are triggered by something and classically will get the symptoms of abdominal cramping followed by loose stools. These are sort of the classic GI symptoms associated with mastocytosis. So intermittent and triggered symptoms, loose stools. And classically, and what differentiates these symptoms from other disorders like irritable bowel syndrome, is the fact that these symptoms may also coexist with other mast cell symptoms.

You have the GI symptoms, but you also have symptoms like flush, itch, palpitations. So what do we do? How do we evaluate this and assess for this? Obviously, physical exam, but also, laboratory tests. We're looking for inflammation, so inflammatory markers are helpful. Tests for malabsorption, vitamin deficiencies, metal deficiencies. Endoscopy and colonoscopy with biopsy, it's really our key test. There, we can look for features of ISM, which I'll mention, but also, we're trying to rule out other conditions. We're trying to rule out inflammatory bowel disease, for instance, maybe peptic ulcer disease, and others. Cross-sectional imaging can also be extremely helpful, especially in those with abdominal pain, and other GI tests that can be ordered. So the endoscopy and colonoscopy, anyone can order those, and the GI will do this for you. Or if the patient was seen in the GI clinic, the GI will set this up. Endoscopy and colonoscopy in patients with ISM, this is a very safe test that can be done. We typically do involve an anesthesiologist to help with the sedation and propofol is very safe. The procedure itself does not upset the ISM. So the endoscopy itself, we're looking at the upper GI tract and colon typically, with both an endoscopy and colonoscopy. The stomach, small bowel, colon look pretty normal in ISM. So really, it's the pathology that's going to help us with regards to diagnosis and to rule out other conditions. The pathology can be patchy in the GI tract, so typically, you want your endoscopist to take random biopsies throughout the tract, so throughout the upper tract and throughout the colon. And then once the biopsies are done, we ask the pathologist to stain for mast cells specifically with the KIT stain when you're highly suspecting ISM. We also want to do the CD25 stain, which can look for clonal mast cells in the GI tract.

So the pathologic feature that we're looking for is clusters of mast cells, so 15 or more mast cells per cluster in a section. That really makes the diagnosis for you. It's not so much the numbers of mast cells that we're looking for; it's those clusters. And then typically within those clusters, you'll see the CD25 staining. That's really the key. And then, as mentioned, we're going to rule out other conditions as well, like inflammatory bowel disease. Interestingly, the pathology doesn't necessarily correlate with the degree of symptoms; the GI symptoms, those mast cell mediator-type symptoms I mentioned, don't always correlate with the pathology.

The treatment, fortunately, standard mast cell treatments do work well, such as antihistamines and stabilizers, like cromolyn. But, as mentioned in other talks, the patients that are intolerant or on many meds, the TKI therapies can be very helpful, particularly the approved avapritinib. Some of the older therapies had GI toxicities that we had to monitor for. But fortunately, avapritinib, we have not seen that.

So that's it, Dr. Akin. Thank you again for involving me.

Dr. Akin:
We looked at the multidisciplinary approach to managing patients with suspected ISM. We hope you found our presentations useful and can apply them in your clinical practice. Unfortunately, that's all the time we have today, so I want to thank you, our audience, for listening in. And many thanks to Dr. Daniel DeAngelo and Dr. Matthew Hamilton for joining me and for sharing all their valuable insights. It was great speaking with both of you today.

Dr. DeAngelo:
I want to thank you again for allowing me to participate. I hope this was helpful.

Dr. Hamilton:
Absolutely. Thank you so much. This was great.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by TotalCME, LLC

To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.