



Tryptase Increase without Mastocytosis or Anaphylaxis

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Each month we present highlights from the Ask the Expert section of the American Academy of Allergy, Asthma & Immunology (AAAAI) Web site written by Dennis K. Ledford, MD. For more questions and answers, visit www.aaaai.org/ask-the-expert.aspx.

Question:

I have a question about a 74-year-old man referred to me because of an elevated tryptase level (46.9 ng/mL). The patient had been following with his gastroenterologist for chronic diarrhea and incidentally was found to have this elevated tryptase level. He has no history of drug allergies, insect sting allergies, nor anaphylaxis to local or general anesthesia. A bone marrow biopsy showed no evidence of malignancy or abnormal accumulation of mast cells and was negative for c-Kit mutations. I await results of urinary PGD2, PGF2, and N-methylhistamine. If these values are normal, what do you recommend as the next best step? Have you seen patients with this degree of elevated blood tryptase level without having mastocytosis?

Answer:

Thank you for your question. The elevation of serum tryptase is one criterion for mast cell disorders but is not a diagnostic test in and of itself. The absence of the typical findings of mastocytosis in the bone marrow, that is, clusters of spindle-shaped mast cells and/or D816V c-Kit mutation, would argue against mastocytosis. A consideration would be to ask if your pathologist could stain the biopsy sections for CD2 or CD25 to examine if mast cells express these antigens, which would be a minor criterion for mastocytosis. In light of the gastrointestinal (GI) symptoms, you may also inquire if an increased number of mast cells were noted on GI biopsies. I would caution that simply counting the number of mast cells on GI specimens may be misleading,¹ but aberrant CD25 staining of mast cells might be helpful. Persistently increased blood tryptase occurs in mast cell disorders, familial hypertryptasemia with or without mast cell activation,^{2,3} select myeloproliferative diseases, and chronic renal failure.

I have personally followed patients with blood tryptase concentrations approximating 100 ng/mL who show a decline over time, although these patients had a history of anaphylaxis. I also follow a family of patients without definitive mast cell activation who have tryptase concentrations between 11.5 ng/mL and 20 ng/mL, but not 47 ng/mL like your patient.

In summary, I think it is possible that your patient has a mast cell disorder but not mastocytosis. GI mast cells should be evaluated, but I would be hesitant to make conclusions based solely on counting GI mucosal mast cells. I would consider your patient at risk of anaphylaxis, and I would counsel on the signs and symptoms of anaphylaxis. I would prescribe an epinephrine autoinjector although I am not sure whether all consultants would agree with this prescription. I think a trial of high-dose H1 and H2 inhibitor therapy may be tried for the diarrhea. I would follow him regularly, consider repeating the tryptase and monitor for the development of a mast cell disorder.

I shared this opinion with Dr. Cem Akin at Harvard Medical School, Director of the Mastocytosis Center at Brigham and Women's Hospital and an internationally recognized investigator in mast cell disorders.

Dr. Akin Responded:

I agree with your response. I would however first make sure that the bone marrow biopsy was a good specimen and interpreted correctly, as that tryptase level is high enough to deserve a second opinion on bone marrow pathology from an expert. You may want to discuss this option with your pathologist and verify that specific stains were used for tryptase and CD117 and/or CD25 and mutation analysis was performed for c-Kit. If a review by a second pathologist is elected, you may wish to consider providing the GI biopsies as well. An interesting feature of mast cell disease in the GI tract is that mast cells can be negative for tryptase but positive for CD117 and CD25, and there could be significant accompanying blood or tissue eosinophilia.

I hope this information is of help to you and your patient.

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