Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/unexplained-hematologic-abnormalities-could-it-be-type-1-gaucher-disease/11343/

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

Unexplained Hematologic Abnormalities: Could It Be Type 1 Gaucher Disease?

Announcer:
Welcome to ReachMD.

This medical industry feature, “Unexplained Hematologic Abnormalities: Could It Be Type 1 Gaucher Disease?” is sponsored by Sanofi Genzyme.

Here’s your host, Dr. Matt Birnholz.

Dr. Birnholz:
Have you ever encountered a patient with splenomegaly and unexplained hematologic abnormalities such as anemia and/or thrombocytopenia? Now, you might assume that these are indicative of a malignancy or infections, and they can be, but could it be Type 1 Gaucher disease instead? And how can we tell the difference in order to reach a timely and accurate diagnosis? This will be the focus of our discussion today.

This is ReachMD, and I'm Dr. Matt Birnholz. Joining me to share insights on Type 1 Gaucher disease is Dr. Joel Weinthal, Medical Director at Texas Oncology, Medical City Dallas Hospital in Dallas, Texas.

Dr. Weinthal, welcome to the program.

Dr. Weinthal:
Thank you, really, really nice to be here.

Dr. Birnholz:
So, Dr. Weinthal, let's start from the top. Can you just give us a refresher on Gaucher disease and some key details we should know?

Dr. Weinthal:
Absolutely. Gaucher disease is a rare genetic disease in the lysosomal storage disease family that causes the accumulation of a substrate called glucosylceramide, or glucocerebrosidase, in the cells of the monocyte or macrophage lineage resulting in a progressive multiorgan dysfunction. It's a progressive, lifelong genetic disease, and when the diagnosis is missed or not diagnosed in a timely fashion, a patient with Gaucher disease may experience a diagnostic delay for up to 10 years, and this can lead to some serious implications or consequences.

Type 1 Gaucher disease often mimics the signs and symptoms of many other hematologic malignancies and conditions, such as leukemia, myeloma and many others, so hematologists/oncologists play a pivotal role in identifying and diagnosing these patients because >85% of the patients are seen at some point by hematologists or oncologists in the pursuit of a diagnosis.

Dr. Birnholz:
Interesting. So, what then are some symptoms hematologists and oncologists should look for? And can you also speak to the consequences of diagnostic delays that you mentioned before?

Dr. Weinthal:

The hallmark symptoms are the symptoms that you mentioned at the top: splenomegaly, or a big spleen, anemia, and/or thrombocytopenia, or low platelets. These are among the most prominent and frequent presenting symptoms of Type 1 Gaucher disease. Some patients may be asymptomatic despite having these manifestations, which include cytopenia, splenomegaly,

hepatomegaly or a big liver, or bone involvement as we'll discuss in just a few minutes I suspect. With missed or delayed diagnosis, you can delay disease management and therefore increase the chances of symptomatic disease progression which unfortunately can lead to irreversible damage.

So, let's start with the skeletal impact because skeletal involvement is often the most debilitating aspect of Type 1 Gaucher disease: 94% of patients with Type 1 Gaucher disease, as documented in the Gaucher registry, which is sponsored by Sanofi Genzyme, had radiologic evidence of bone disease at diagnosis. At the time of diagnosis, many patients can present with bone marrow infiltration, Erlenmeyer flask deformities, pathologic fracture, and, as the disease progresses, patients may develop focal lytic or sclerotic lesions with joint collapse and secondary degenerative arthritis. Bone crises are common, and these episodes of deep bone pain, often with fever and leukocytosis, neurologic complications secondary to the bone disease such as osteopenia or vertebral compression, emboli following long bone fractures can be quite symptomatic. This bone pain and pathologic fractures are also associated with bone malignancies, which a bone marrow aspirate and biopsy can help rule out. Many patients, including children, present with bone-related symptoms.

Bone damage aside, as the disease progresses, patients can experience progressive visceral enlargement, mostly in the spleen and liver, growth failure in children, hepatic, splenic and marrow fibrosis, lung disease including pulmonary hypertension, bleeding and bleeding complications including anemia, fatigue and pallor. Furthermore, Gaucher disease can also lead to a reduction if quality of life, a shortened lifespan, and even an increased risk of cancer.

The important thing to remember is that this disease is manageable, and there are multiple treatment options available. Regardless of how a patient presents in terms of symptoms or severity, Type 1 Gaucher disease is progressive, so it is important to diagnose it as soon as possible and initiate therapy in a timely fashion.

Dr. Birnholz:
That was an excellent review, Dr. Weinthal. Thank you. Let's focus then on the genetics of Gaucher disease for a moment. What's the inheritance pattern? And are there any population groups more susceptible to it?

Dr. Weinthal:
Gaucher disease is an autosomal recessive genetic disorder that affects males and females equally. It is panethnic, but we see a higher incidence in individuals of Ashkenazic Jewish decent. In this population the incidence is about 1 in 850 as compared to the general population where it's about 1 in 40,000. As you may know, 90% of American Jews are Ashkenazic, so to put this in perspective, in patients of Ashkenazic ancestry, the frequency of Gaucher disease is about 1 in 850. Compare this to the incidence of hematologic malignancies where the incidence is about 1 in 2,500. Therefore, in this ethnic group it is prudent to test for Gaucher disease as a first-line investigation in any patient presenting with splenomegaly and cytopenias without a clear diagnosis. It is important to keep in mind that the most common mutation in the Ashkenazic population is the N370S variant, and those with homozygous N370S mutations are often characterized by mild cytopenias, mild splenomegaly that can escape easy detection.

Because of the inheritance patterns associated with Gaucher disease, family screening and history is important to identify at-risk family members. As I mentioned before, it is common for patients to go undiagnosed for years while their disease is progressing in an insidious fashion. It should be remembered the most common disease variant among Ashkenazic Jews is the N370S, and most patients with this homozygous pathogenic variant are asymptomatic. These patients can experience adult-onset disease and a disproportionate burden of progressive skeletal disease without major visceral or hematologic involvement. And so, again, it is important to include the Gaucher enzyme test as part of the differential workup and send an enzyme assay if a diagnosis of Gaucher Type 1 disease is contemplated.

Dr. Birnholz:
For those just tuning in, you're listening to ReachMD. I'm Dr. Matt Birnholz, and with me is Dr. Joel Weinthal to talk about why hematologists-oncologists should include Type 1 Gaucher disease in their differential diagnosis.

So, Dr. Weinthal, earlier you talked about how Gaucher disease often mimics the signs and symptoms of hematological malignancies, such as leukemia and many others. Now, given that challenge, can you explain how you test for and diagnose Gaucher disease?

Dr. Weinthal:
A blood-based enzyme assay for glucocerebrosidase, which is also known as acid-beta-glucosidase, is the gold standard for a definitive diagnosis of Gaucher disease. Molecular testing including DNA testing can be used to confirm the Type of Gaucher disease as well as carrier status. Now, while bone marrow biopsy continues to be an important part of ruling out malignancy or identifying other comorbid conditions or malignancies, a bone marrow exam is neither necessary nor sufficient for diagnosing Gaucher disease, so you have to order the enzyme assay as part of the differential workup.

Case studies can underscore the diagnostic difficulties of Type 1 Gaucher disease, and because Type 1 Gaucher disease prevalence differs among populations, diagnostic approaches should differ as well. There are simple diagnostic algorithms that may help hematologists-oncologists identify when to test for Type 1 Gaucher disease. In any patient of Ashkenazic ancestry presenting with splenomegaly and/or thrombocytopenia, test for Type 1 Gaucher disease as a first-line investigation. For all other patients, test for Type 1 Gaucher disease after ruling out other malignancies and conditions.

There is detailed information on these 2 diagnostic algorithms and other information about Gaucher disease available at many websites including gauchercare.com/hcp, which is a Sanofi Genzyme sponsored website, and there are many publications that speak to this approach as well.

Dr. Birnholz:
Great. And just to bring all of this together, Dr. Weinthal, what takeaway thoughts on Gaucher disease do you want to make sure we come away with today?

Dr. Weinthal:
I'd like to remind hematologists-oncologists that Type 1 Gaucher disease is a lifelong genetic disease that is characterized by an extreme diversity in phenotype, age of onset and disease severity. The disease course can be progressive and is unpredictable. It is important to diagnose Gaucher disease as soon as possible and initiate treatment in a timely fashion. Hematologists/oncologists play a pivotal role in identifying, diagnosing and helping these patients because most often they come to us first or they are referred to us, so we see them in our offices in a frequent fashion. Rule out malignancy and test for Gaucher disease in patients who present with splenomegaly, anemia and/or thrombocytopenia, and for patients of Ashkenazic decent, you can test for Gaucher disease first or simultaneously because it is more common in this particular population. Testing and diagnosing or ruling out this disease is easy with a simple blood-based enzymatic assay available in most commercial labs. Gaucher disease is a serious disease with long-term implications if left undiagnosed or unmanaged, but it is manageable, and multiple treatments are available.

Dr. Birnholz:
Well, you've given us a great new vantage point on this disease, Dr. Weinthal, so I really want to thank you for sharing these insights on Type 1 Gaucher disease and the key roles that hematologists/oncologists play in recognition, testing and diagnosis. Dr. Weinthal, it was great speaking with you today.

Announcer:
This program was sponsored by Sanofi Genzyme. This is ReachMD. Be part of the knowledge.