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Do You Know Farber Disease? A Lysosomal Storage Disorder

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.

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Dr. Harmatz:
Hello, welcome today. I'm Paul Harmatz, a pediatric gastroenterologist at UCSF Benioff Children's Hospital Oakland, Oakland, California. And you might wonder how a pediatric gastroenterologist became involved in lysosomal storage disease. Most of my background is with mucopolysaccharidosis, which is a collection of diseases that are much more common than Farber, but have very strong similarities in the biochemistry and disease manifestations and some of the possible therapies. So I will give you some background from my MPS to help tide you over and understand a much less common Farber Disease. Just a bit of background to set the framework, where Farber disease resides as a clinical problem, you probably are well aware that there are estimates of 5000 to 6000 mendelian genetic diseases.

Of this large number, a much smaller number of 500 are metabolic disorders, or as you could also call them, inherited metabolic diseases. And most of these are single-Mendelian-gene inherited disorders. Within that group of inherited disorders of metabolism, inborn errors of metabolism, you find 50 lysosomal storage disease, or more than 50. And this group will later show you a picture of the range of diseases that we see. But within this group of 50, we have 10 that fall into the Sphingolipidoses category.

This is a very common group of diseases, probably prevalence in 1:10,000, which, relatively speaking, is common, because you're comparing Farber, which is one of these sphingolipidoses, and you have a one in a million prevalence, or birth incidents in this category. So think of, most of the talk will focus on lysosomal storage disease, and within that group, 10 Sphingolipidoses, and then Farber disease as a component of the Sphingolipidoses group. In this slide, we're giving a little bit of background of the lysosome, which classically, was just thought of as a digestive factory breaking down cell components that could be recycled. But over the 70 years since de Duve described the lysosome as an organal, it's gained an amazingly broad range of functions and complexities, and many of these are summarized in this slide in a review article with Ballabio that is cited at the bottom. So think of the Hydrolases in the center in the acid environment that digest products.

There are also enzyme activators. There are transport proteins that move molecules in and out of the cell, all of which are critical, and a mutation on the gene that makes these proteins likely to result in a disease. But in addition, you have cell transporters on the surface for ions, hydrogen, cholesterol. You have systems for moving the lysosome around.

You have influences of the lysosome on cell membrane repair transcription. It has gone from a very simple organ to a very complex biochemical system. And now we're moving to give you a little more depth on lysosomal storage disease. Lysosomal storage disease is really categorized based on the type of material that's stored. And I said I spent most of my time looking at mucopolysaccharide diseases. In that group, the mucopolysaccharides different types of glycosaminoglycans, dermatan sulfate, heparin sulfate, keratin sulfate are stored in excess because we are missing an enzyme. With the sphingolipid, we have sugars attached to a fat. This results in

storage of materials in the sphingolipid digestive pathway, whether it's ceramide or sphingo phosphate. A variety of different compounds. There are also oligosaccharide storage diseases.

There are glycogen storage diseases. So base your categorization on the type of storage material. Overall, we mentioned that lysosomal storage diseases make up this group of 50, and they're relatively common; one in 8000 if we take the whole group of lysosomal storage diseases. It has a frequency approaching that of cystic fibrosis. So it's a major problem and is a focus of biochemical geneticists and geneticists around the world. This slide shows the same grouping based on storage material, which defines the disease, the gene that is responsible for the disease under each of the groupings. And so if you look at the group's sphingolipidoses, you'll see, very common, Gaucher disease, Fabry disease, that people are quite familiar with and make up most of the grouping. You also see Krabbe disease, well known with newborn screening. Tay-Sachs disease, but Farber disease fits within this group. And then you have other groups that you're quite familiar with.

Mucopolysaccharide storage disease, probably is your second group that you're most familiar with. Pompe disease, a glycogen storage disease. So it's not all glycogen storage disease, but the glycogen storage disease type two, Pompe disease, falls into this category. Thank you very much. It's been my pleasure to provide some background and information about a very important, but rare, lysosomal storage disease. And I hope you'll remember the triad for Farber and find a chance to identify a patient. Hopefully in the near future we will have improved therapies and ability to take care of these patients well. Thank you.

Announcer:
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