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Well, I’m very pleased to be talking about a topic that most physicians are familiar with, but oftentimes, causes a lot of confusion when you get into the nitty-gritty of trying to figure out what the syndrome is and what the best way of treating a patient is. How do you evaluate them and manage them?

When you talk about Lennox-Gastaut Syndrome, about one to ten percent of all epilepsy clinics will have a patient with Lennox-Gastaut Syndrome in them. The reason that the range is so wide is because it depends on the level of the clinic. If you have a new onset seizure clinic, you’re going to see Lennox-Gastaut Syndrome very rarely. But if you have a chronic epilepsy patient clinic, you’re going to see a lot of Lennox-Gastaut patients. In a tertiary care epilepsy center, the incidents would be about ten percent.

When you look at population-based surveys, the incidents are a quarter of one in a thousand. So it would be .26 per 1,000 patients is what would be in the general population. Of course, most of you who have worked in neurology clinics will realize that they occupy a significant portion of our time and resources. To try and understand that, we could go to the next slide.

What is Lennox-Gastaut Syndrome? It is, in its traditional form, a triad of seizures including tonic seizures, atonic seizures, and myoclonic or absence-like seizures. These would be atypical absence seizures. There is some confusion between the word typical and atypical. Really, the difference between the two is an EEG-related difference. With typical absence, which you see in childhood absence epilepsy, the frequency of the spike wave index is about three to four hertz per second. In Lenox-Gastaut Syndrome, when you see an atypical absence, there are usually two spikes in wave discharge per second, also called slow spike in wave discharges on the EEG.

Now, Lennox-Gastaut Syndrome is a syndrome so it’s not a disease. There are many causes for it and the causes can be very varied. They can be associated with neonatal in utero types of conditions. They can be associated with cerebral palsy. They can be associated with other types of etiologies that cause significant neurologic deficits. One very big
hallmark of the syndrome is that patients usually have mental retardation of cognitive impairment. The degree may vary, and there are certainly come patients that have mild impairment of their cognition. This still would be one part of the triad for the Lennox Gastaut syndrome.

The EEG, as I mentioned, is usually the hallmark. When you do see a very clear EEG, the pike wave index is about two to three hertz per second, usually 1.5 to 2 hertz and it’s referred to as slow spike in wave discharge, and you will see examples of this in future slides. The other very typical factor is that these patients with Lennox-Gastaut Syndrome drop. When they drop, they hurt themselves. The EEG will show you that there will be an associated electrodecremental response with this particular drop. Those are usually seen with atonic seizures.

Let’s take the slow spike in wave index. I’ve already talked to you about it. It is at two hertz, and that is the interictal discharge rate that you would see. As I mentioned earlier, when the patient actually has a spasm or has a spell and falls, you actually have an electrodecremental response. There would be flattening or there will be absence of the spike wave index, which is opposite of what you’re normally used to seeing. The seizure types are tonic seizures, where the whole body stiffens, and usually, a patient is propelled forward with this type of seizure, sometimes backwards, atonic seizures, and the last type is atypical absence and not to be confused with typical absence seizures, which I talked about where the EEG is radically different. The last point is the mental retardation and cognitive impairment we spoke about.

When you put the three aspects together, the seizure type, the EEG characteristics, and the cognition, you have the Lennox-Gastaut Syndrome triad. In a particular patient, on aspect of this may not be as well developed as the others. For instance, a patient may have tonic and atonic seizures, but not have atypical absence seizures. The EEG may show slow spike in wave, but the majority of the EEG shows a very slow, disorganized background. The degree of mental cognitive impairment is a wide spectrum. It can be from mental retardation all the way to autism or pervasive developmental delays. There's a large spectrum with that.

We often say that children who have had West syndrome, which is infantile spasms plus hypsarrhythmia, grew up to have Lennox-Gastaut Syndrome. If the infantile spasms do not disappear, often times those patients will develop Lennox-Gastaut Syndrome at a later age. The causes, as I indicated to you, could be prenatal, perinatal, or neonatal, but often times, they could also be outside the neonatal spectrum.

Examples of causes would be hypoxic-ischemic encephalopathy, or it could be a congenital malformation that occurred during the second or third trimester of pregnancy, and resulted in cortical malformations. It could also result from metabolic disorders as part of the etiologies.

The classification of epilepsy syndromes is undergoing quite a transformation. In the ’89 ILAE classification, we would talk of these as symptomatic or cryptogenic causes for it. Symptomatic means it’s a symptom of another neurologic disorder or deficit. Cryptogenic means that you can’t identify a structural or anatomic cause, but there is something that is causing the diffused epilepsy plus the cognitive impairment. In the new ILAE classification, which is still undergoing some transformation, you may hear words such as structural metabolic. That refers to structural abnormalities seen on neuro-imaging or metabolic as in metabolic disorders that might be causing this syndrome. Some cases are referred to as unknown, and that probably makes up about 20-percent of patients with Lennox-Gastaut Syndrome.
The EEG is critical in this diagnosis. You need a good EEG study, sometimes a video EEG study to really characterize this syndrome properly. Atonic seizures are associated with a diffused electrodecremental response where the EEG would flatten, be suppressed for a brief few seconds, and then return to its prior background. Tonic seizures are usually fast, frontally dominant frequencies. Atypical absence, as I pointed out before, is a slow spike in wave. This is not to be confused with typical absence. So the spike in wave index would be about two hertz.

The slow spike in wave patterns can be biphasic, triphasic, but usually they’re diffused. They may be more anteriorly dominant, but they’re very diffused bilateral, bisynchronous types of discharges. If you remember what hypsarrhythmia looks like, it’s usually chaotic, multifocal. By the time you come up to three to five years of age where Lennox-Gastaut Syndrome frequently presents, the EEG is going to transform into a more bisynchronous abnormally rather than a multifocal abnormality. It’s a very interesting ontogeny that takes place with that.

The peroxisomes are more fast activity, and as I mentioned, may last for about 15 to 20 seconds. It’s usually bilaterally synchronous and frontally dominant.

Here is an example of what would be a slow spike in wave background. Notice that this is a bipolar montage left and right. You can see that there is diffused slow spike in wave discharges that dominate this EEG. There is another portion of this EEG, but unlike hypsarrhythmia, where it’s multifocal, these are anteriorly dominant slow spike in wave discharges that take place.

During sleep, the EEG will transform quite significantly and you may have fragmentation of these discharges, and you may have faster frequencies seen in these discharges, so that’s something to be aware of. The sleep patterns can significantly alter the picture, as you can see in this slide.

Now, here is what you should definitely remember. Look at the sensitivity of this. This is 1,000 microvolts per millimeter, so the EEG is very high amplitude in real time, if you had to look at it at the more traditional 17 microvolts per millimeter. Just to illustrate the point, you can see that where you see the patient with the marker saying the patient falls backwards, you can see that there is a diffused discharge and that is followed by a tree second electrodecremental discharge. Again, it’s a very characteristic feature of Lennox-Gastaut Syndrome. If you will remember, this is also seen in West Syndrome where a patient has infantile spasms, you will see the same electrodecremental response, another hallmark of these two conditions indicating some transformation over the age from where one progresses and transforms into the other, meaning infantile spasm transforms into Lennox-Gastaut Syndrome. It’s an important point to keep in mind.

Now, drop attacks are the terror of these patients. When you walk into a clinic and you see a patient in your epilepsy clinic with a helmet on, chances are that patient is dropping. Drops are caused by three types of seizures. They could be tonic seizures where the patient becomes very rigid and like a pole, propels either backwards and hits the back of their head, sometimes if they’re depending on the posture, if they’re leaning forward, they may actually propelled into the ground and hurt themselves. These are the children that damage teeth, fracture jaws, but chins, and sustain significant abrasions and lacerations with this syndrome.

If the seizures are atonic, sometimes the patient is standing and suddenly as if the wind is taken out of their feet, they just collapse to the floor. Depending on where they fall and how they fall, they may injure themselves with these
seizures. Myoclonic seizures are less typical. They are variable in the patient depending on which direction the seizure is, they could fall in that particular direction. The important point to remember is that in many of these syndromes, by the time the patient has hit the ground, the seizure has already disappeared. They are aware of them falling and unable to do anything to prevent or break their fall. It’s a very frightening condition and a very tragic condition that really highlights the importance of recognizing this syndrome.

The issue with mental retardation and cognitive impairment goes back to Lennox from the 1960’s. What he showed in a very crude fashion, is the number of seizures increases the index of cognitive impairment. Now, this is difficult to say that the seizures themselves cause the cognitive impairment because you could have a patient with severe cognitive impairment and severe epilepsy. It certainly brings up the point of being much more proactive about this condition, really recognizing it for what it is and being aware of it and treating it effectively. It's very important and you can see over here, just looking at the last bar where they have 1,000 plus seizures, this is a very devastating, a very damaging condition.

What was also studied subsequently is a very interesting phenomenon, which says that if you had earlier seizures how cognitively impaired were you as compared to later seizures. Not surprisingly, those with earlier seizures had more severe cognitive impairment compared to those that developed the Lennox-Gastaut Syndrome or other intractable catastrophic epilepsies at a later stage. Again, it’s implying the importance of recognizing this condition, possibly effectively treating it, and managing the condition in a very humanistic way, taking into consideration not just the seizures and chasing every small myoclonic jerk with more medications, but really having a balanced approach as we will talk about later in this presentation.

The other problems associated with Lennox-Gastaut Syndrome are very important. We talked about cognition. That is just one aspect of it. Bone health is another very critical issue with these patients. Remember, these patients are not moving around as much as they should because of their disability. The second thing that's very important is there are multiple medications, which may impair bone formation and bone strength leading to osteopenia. Added to this, they frequently fall, and when you fall on a weakened bone, the chance of you fracturing that bone certainly goes up. So it’s very important to be aware of the other aspects that go along with this syndrome, often cause a lot of morbidity and are not as effectively treated or managed. Thank you.