What doctors wish patients knew about amyotrophic lateral sclerosis

JUN 2, 2023

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Lou Gehrig—the New York Yankees’ first baseman known as the “Iron Horse”—was one of the greatest players in baseball history. But his career was tragically cut short when he was diagnosed with amyotrophic lateral sclerosis (ALS), a progressive neurodegenerative disease that slowly robs people of their ability to move, speak and eventually breathe.

In Gehrig’s case, the disease ended his record-setting consecutive games played streak at 2,130 in 1939. He died two years later, though his endurance record remained unbroken for 56 years. Recent advances in understanding ALS—aka Lou Gehrig’s disease—and potential therapies offer hope for those living with the disease and their families.

There are more than 31,000 patients with ALS in the United States with about 5,000 new diagnoses of this disease each year. Most people who develop ALS are between 55 and 75 years old and live between two to five years after symptoms develop, according to the Centers for Disease Control and Prevention. But the disease also can afflict people in their 20s and 30s, or even younger.

Additionally, ALS is 20% more common in men than women, and about 90% of ALS cases occur without any known family history or genetic cause. The remaining 5–10% of ALS cases are inherited through a mutated gene with a known connection to the disease, says the ALS Association. For unknown reasons, military veterans are more likely to be diagnosed with the disease than the general public.

The AMA’s What Doctors Wish Patients Knew™ series provides physicians with a platform to share what they want patients to understand about today’s health care headlines.

For this installment, two neurologists took time to discuss what patients need to know about ALS. These AMA members are:

- Ryan Hakimi, DO, MS, a neurointensivist, director of Transcranial Doppler Ultrasound Services, and chair of pharmacy and therapeutics at Prisma Health in Greenville, South Carolina. He is also a professor at the University of South Carolina School of Medicine-
Greenville and a delegate in the AMA House of Delegates for the American Society of Neuroimaging.

Amir H. Sabouri, MD, PhD, a neurologist and a neuromuscular subspecialist and medical director of The Permanente Medical Group Multidisciplinary ALS Clinic in Martinez, California. The Permanente Medical Group is a member of the AMA Health System Program.

It’s weakness, but not pain

“The key is that ALS gradually starts with weakness in some skeletal muscles. It can be in the hand, leg, tongue or affect breathing,” Dr. Sabouri said. “We classify ALS into two main categories. One we call limb-onset ALS, which means arm and leg. Or there is bulbar-onset ALS, which means it starts from the tongue or affects breathing. So, it’s either weakness or difficulty with speech and swallowing or breathing.”

“ALS typically presents with painless, gradually progressive asymmetric motor weakness. So, if somebody comes and tells me they have pain and weakness,” then there is no worry about ALS because pain doesn’t fit with this disease, he said. “Or if somebody comes and tells me that they have weakness, and also numbness on the same location, I’m happy because ALS doesn’t cause numbness.

“But if someone comes and tells me they have weakness in their hand that’s been gradually going on for some time and there is no pain or numbness, I get worried. That could be ALS,” Dr. Sabouri said.

ALS worsens over a person’s lifespan

“It’s a neurologic disease that's progressive, meaning that it continues to get worse over the course of the person’s lifespan,” Dr. Hakimi said. “It has some early symptoms of asymmetric weakness in the limbs, meaning one side is much greater than the other or one side only; most commonly in the upper extremities, particularly hand weakness.

“So, somebody might notice that they have a hard time gripping things or they might be dropping things. They may notice having difficulty with something like using their keys,” he added. “However, it could involve the shoulders and therefore affect the person’s posture and range of motion.”

“In the lower extremities, it very commonly leads to weakness of one of the ankles leading to what’s called a foot drop where the ability of the individual to raise their foot as they walk is impaired so their toe catches and therefore can lead to falls,” Dr. Hakimi said. “Then, lastly, the least common initial
presentation is what we call bulbar symptoms that are related to the head and neck. Those can be things like somebody having slurred speech or difficulty swallowing, but are much less common.”

As the disease progresses, it “often can lead to some slowness because part of the brain—the frontal lobe—which is involved with executive function, for example writing checks or remembering to pay your bills or those types of things that require a lot of thought,” he said. “Then a little bit later you get rigidity called spasticity where a joint is difficult to move, so it becomes tighter and that can lead to falls because somebody’s balance is affected.”

Then “as it progresses further, you start seeing muscle atrophy or shrinkage of the muscles. And so, you might notice that somebody has very asymmetric arms or legs,” Dr. Hakimi said.

**Diagnosis can be delayed**

“Unfortunately, it takes about a year on average to make the diagnosis because you have to keep in mind that those initial symptoms are extremely common neurologic symptoms for a variety of different diseases,” Dr. Hakimi said. “For example, hand weakness is most commonly due to carpal tunnel syndrome. So, when somebody presents with hand weakness, that's sort of the first thought.”

With ALS, “it's the evolution in the person’s symptoms because the symptoms spread from one location to an adjacent location,” he said. “And then once you start getting involvement of the forearm or at the elbow or even the shoulder, then you know that that's not carpal tunnel syndrome.”

Furthermore, “the weakness of the person’s foot on one side is a very common presentation for somebody who has a pinched nerve in their low back, which we all develop arthritis as time goes on and there’s a reasonable chance that we can develop that kind of symptom,” Dr. Hakimi said. “And when somebody has those symptoms, that’s the first thing people think about as opposed to ALS. Therefore, that leads to difficulty in making that diagnosis.”

**ALS is fatal**

“Unfortunately, ALS is a fatal disease and recognizing that endpoint is always going to be the same, which is death. That's not a very good outlook,” Dr. Hakimi said. “Some of the medicines that are out there can slow the progression of the disease by about three to six months.”

Those few months can mean so much, the doctor noted.
“That might be very valuable for a given person. For example, if their child is going to graduate from high school or they’re going to be a grandparent.”

**There’s a test for familial ALS**

“Overall, familial ALS is relatively uncommon. It’s about 5–10% of all ALS,” Dr. Hakimi said. “However, in patients who have a positive family history—if there’s a family member who has that—then those are the individuals who we would potentially offer genetic testing to.”

That’s “because the majority of times it’s what we call autosomal dominant, meaning that if I have it then my children are going to have it. If my children have it, then they’re going to pass that on,” he explained. “It’s important to keep in mind that ALS is part of a collection of neurodegenerative disorders such as Alzheimer’s disease and Parkinson’s disease.

“So sometimes if you have a number of family members who have these degenerative conditions, that might be a clue that you should be thinking about testing somebody,” Dr. Hakimi added.

**Time is the best diagnostic tool**

“We don’t order genetic testing for every ALS patient as part of the initial workup,” Dr. Sabouri said. “However, this approach may change in light of the recent Food and Drug Administration approval of the ALS medication called Tofersen, which is specifically indicated for a small minority of familial ALS patients with a particular mutation known as SOD-1.”

“It’s cruel to say and think, but it’s true that sometimes time is the best diagnostic tool for ALS, since there is no specific test to confirm the diagnosis,” he said. “Some families come in and want to know immediately whether it is ALS or not, but it’s about ruling out other conditions first and the time to determine gradually progressive disease course.”

“And we typically avoid from mentioning ‘ALS’ or ‘Lou Gehrig’s disease’ to patients or families until we achieve a reasonable certainty, ruling out other potential diagnoses,” Dr. Sabouri said, emphasizing that “the concept of time is the best diagnostic tool for ALS.”

**The ice bucket challenge helped**

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“As of 2022, the ice bucket challenge raised $115 million for research for ALS and support for clinical trials,” Dr. Hakimi said.

Through the ice bucket challenge, participants helped deliver AMX0035, which is the first newly developed treatment approved for ALS in years. While this isn’t a cure, it does slow progression of the disease and extends life for people living with ALS.

“Anything that brings awareness to a disease that people don’t know a lot about improves the time to diagnosis,” Dr. Hakimi said. “That education provided, and awareness is extremely helpful.”

Management is multidisciplinary

“There’s no cure for ALS, but several treatments can control symptoms, prevent complications, and ease living with the disease,” Dr. Sabouri said, emphasizing that “ALS management requires a multidisciplinary approach with interventions tailored to disease progression.”

"Speech therapy is initiated at—or often before—the onset of speech issues. Physical therapy is needed when mobility problems, particularly leg weakness, emerge. Occupational therapy helps maintain independence, especially when hand function declines,” he explained. “Additionally, social workers provide emotional and psychological support, and assistance with social and financial matters as needed by patients or their families.”

“There is a very well-structured system in the U.S. and many parts of the world known as multidisciplinary ALS clinics, effectively a ‘one-stop-shop,’ Dr. Sabouri said. “You go there, you see all relevant specialists in one place avoiding the need to spend your valuable time visiting them at different sites on different days.”

For example, Kaiser Permanente has several ALS clinics across the health system, Dr. Sabouri said, noting “if you go to the ALS Association or the Muscular Dystrophy Association website, there is useful information and locations for clinics, including our center inside Kaiser in Northern California.”

Make appropriate lifestyle changes

While there is no cure for ALS, “the main management is lifestyle modification, so things like exercise,” Dr. Hakimi said. “And if you know that you’re going to develop some element of weakness, maximizing your capability to have strength, coordination, muscle control and things like that with exercise before the disease has progressed very far is very good.”
“The other lifestyle modifications include just making sure your home is safe, using assistive devices like a cane or walker,” he said. “And in some cases, once it involves your respiratory situation, using things like a BiPAP, which are like the CPAP machine—similar concept, but the machine helps you breathe so that you don’t develop oxygen problems.”

“And there’s a number of other things, of course, that need to be considered. One is nutrition. For some of these patients, as the disease progresses, they will develop swallowing difficulty,” Dr. Hakimi said. “Therefore, one would consider putting a feeding tube in that individual to make sure that they get enough nutrition because if your muscles are already shrinking and becoming weak, not getting enough nutrition is surely going to affect that as well.”

“There are medicines also to treat muscle spasms, weakness, depression and things like that. And of course, there’s sort of the bigger picture kinds of things which are family planning type of things or getting your affairs in order because unfortunately it is a fatal condition,” he said.

Stick with a neurologist

“Consult with your neurologist or multidisciplinary clinic team before making any significant health-related decisions.” Dr. Sabouri said. “Be vigilant about businesses that may unfortunately exploit the vulnerability of those affected and steer clear of ‘hope shops’ or ‘miracle stores’ that offer expensive, yet unapproved treatments that may look scientific.”

“It breaks my heart whenever I reflect on the journey of an ALS patient who was devastated by the absence of a cure and had a hard time accepting the harsh reality,” he said. “Tragically, she fell into the trap of those who peddle false hope. In her case, she placed all her trust, along with her entire fortune, into a ‘cleansing diet’—an unproven and potentially harmful pseudo-treatment.

“Ultimately, she succumbed to the disease earlier than expected,” Dr. Sabouri said. That is why “it’s important to stick with a neurologist who you trust and follow the clinic for all-in-one care.”

Family support is essential

“It’s obviously extremely emotionally taxing recognizing that somebody is going to get worse as time goes on regardless of what you do for them,” Dr. Hakimi said. “What you’re impacting as a family member is that trajectory of how quickly they’re worsening and also giving them emotional support. So, making sure that you keep a positive outlook for them and do whatever you can.”
Additionally, “patients often get to the point that they need to be fed even though they’re adults. So, as a family member, ensuring that you sit with that person and very slowly feed them much like you would a child is important,” Dr. Hakimi said.

Families “can help by being present to listen to their loved one with ALS, to support them physically and emotionally,” Dr. Sabouri said. “As ALS doctors, we gain valuable insights into the dynamics of the patient’s family and the best thing to do is reach out to the neurologist and multidisciplinary team members and share the struggle either physically, emotionally or financially. Everything. Any challenge—not only about the patient, but also the family.”