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Multiple Sclerosis & Aging: Considerations for Diagnosis & Treatment

Announcer:

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Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:

When it comes to managing patients with multiple sclerosis, there are several factors we need to address that affect the course of this disease. But how can we manage the impact of something that is inevitable like aging?

This is ReachMD and I'm your host, Dr. Jennifer Caudle. Joining me today are Dr. Weinstock-Guttman, Professor of the Department of Neurology at Jacobs School of Medicine and Biomedical Sciences, and Dr. Riley Bove, Assistant Professor of Neurology at the University of California-San Francisco Weill Institute of Neurosciences. Thank you both for being here today.

Dr. Weinstock-Guttman:

Thank you.

Dr. Bove:

Thank you.

Dr. Caudle:

So, why don't you start us off, Dr. Weinstock-Guttman, providing us with a brief overview of the demographics of MS in the United States.

Dr. Weinstock-Guttman:

Sure, new estimates obtained from administrative health data claims obtained from different data sets that suggest that nearly one million patients are living with MS today in the U.S. The prevalent rate estimated in 2010 was as high as 300 patients per 100,000 while in 2017 it was up to 360. Women continue to be disproportionately affected by MS as compared to men. The ratio obtained recently ranged between 2.5:1 up to 3:1. Patients with relapsing/remitting disease are actually seen much more in women than in men and seems that the conversion to secondary progressive is also seen less frequent in women that have, as mentioned, more relapsing/remitting disease than progression as compared to its men. Men have a faster consideration of progression.

But the most important an amendment that came from this new analysis evaluating the prevalence on age specific group is that the highest prevalence was actually seen in the age group uh affecting 55-64 year old patients and the next one would be 65-74, suggesting that the increased prevalence is actually related probably to longer survival of MS patients.

Dr. Caudle:

Excellent. Now, obviously, changes within the human body occur naturally with aging. So, Dr. Weinstock-Guttman, in your opinion, which are the most pertinent to patients with MS?

Dr. Weinstock-Guttman:

So, as you already mentioned, aging affecting all human body or um the organs and different systems as MS is an autoimmune disorder the immune system and the aging of immune system is very important. This is known also as immunosenescence. The immune cells as number decreases in aging population. There are also activity decreased and that is associated with increased risk for infection in all the population. In addition, we do have an increased um so-called memory cells or B-cells that is also associated often with increased risk for developing autoimmune disorder and consider also as the base for developing of comorbidities of cardiovascular disease

So, the increased um immunodeficiency or immunodysregulation in aging population is increasing; therefore, the risk for infection, possibly also opportunistic infection as well as cancer. And this is very important to consider especially in MS population treated with immune moderator and especially immunosuppressive medication. In addition, a second element we have to really pay attention is that the repair processes in aging population is decreased as compared to its uh younger population; therefore, any kind of injury in aging population will be associated with much more irreversible damage. Another event and element that we have to pay attention is actually the decrease in production of sex hormones. We have menopause in women, andropause in men. we know that um sex hormones have beneficial affects on protection tissue. They have a crosstalk with the immune system; therefore, a decrease on the secretion of the sex hormones may have a clear impact on the neuroprotection of the tissue as well as um immune resistance.

So, an important element more toward ensuring MS patients and especially in aging population is the brain volume. We know that uh aging is associated with brain tissue loss, MS itself is associated with tissue loss. We know that uh in general MS patients not treated they may lose between 0.7 to 1% per year, clearly treatment intervention may decrease this and going towards the normal considered tissue loss is 0.1 to 0.3% per year.

The cognition is primarily uh related to uh tissue loss, brain tissue loss, and, therefore, uh monitoring the cognitive function in uh MS patients including the aging population is very important way to monitor the disease um preservation or progression.

Dr. Caudle:

As patients with MS age, Dr. Bove, let's turn to you, how might their disease course be affected?

Dr. Bove:

So, if we think about the various mechanisms that Bianca just outlined, and their impact on MS course, we think of sort of three categories. Conversion from the relapsing/remitting form of MS to secondary progressive MS; accumulation of disability and comorbidities, or all the other medical conditions that a person can accumulate over time.

So, conversion is certainly not inevitable. In about one-third of patients will remain with the relapsing/remitting MS category over time. But onset of progression is more dependent on age than the presence or duration of a pre-progression symptomatic disease course. If we look at people with MS and their likelihood of having progressive forms of MS, in a younger population about 60% of patients have relapsing/remitting MS. But in patients over 65 years of age, over 60% of them will have progressive forms of MS. If we think about the risk of converting to secondary progressive MS, at age 20, the odds ratio is about 2 and, if we look at age 50, the odds ratio of converting to secondary progressive form of MS is 6. So, three times more than age 20. Age of MS onset is significantly earlier for patients who develop secondary progressive MS relative to primary progressive MS but age of progression onset, whether that's primary progressive MS progression or secondary progressive MS onset, does not vary. It's about the age of 45.

Now, if we turn to disability accumulation, age is independently associated with more rapid disability development and this is in part due to what I just described, the increasing age-related risk of converting to secondary progressive MS. Older age in onset of relapsing/remitting MS is associated with a greater risk of reaching advanced disability scores, especially when we think about ambulatory disability or other forms such as cognition as well. Younger age of conversion to secondary progressive MS is associated with a shorter time from conversion um to reaching high disability scores. Older age in the primary progressive MS cohort does not affect disease progression compared to secondary progressive MS. So now, if we turn to those comorbidities, patients with MS who are age 60 or above do have marginally higher rates of these comorbidities. So the rate ratio ranges somewhere between 1.07 to 1.6, compared to age and sex matched controls. We also see higher rates of epilepsy, depression, fibromyalgia, irritable bowel disease in um these older populations. Those rates are two to threefold higher.

So, if we hone in sort of the many comorbidities that a person can develop to the vascular comorbidities, so, specifically, hypertension, hyperlipidemia, diabetes; what we see is that patients with MS who have these vascular comorbidities actually have a 1.5 fold higher risk of having problems with walking, so ambulatory disability. And they can experience a decrease in time to developing this ambulatory disability um by six years compared to people with MS who don't have these vascular comorbidities.

Dr. Caudle:

Turning to you now, Dr. Weinstock-Guttman, does the disease course for patients who develop MS after age 50, or also known as late onset MS, differ from that seen in patients diagnosed at younger ages?

Dr. Weinstock-Guttman:

Yes, indeed. The percentage of patients diagnosed late, so after 50, is only 4.5%. There are very few studies showing possible up to 12%. The diagnosis late, so after age 50, often is related to a delay in diagnosis. And the delay in diagnosis already mentioned before could be related to the presence of comorbidities. So, a delay sometimes up to three years or even more in patients with late onset from the uh first presentation of symptoms versus the uh patients with the younger onset. So, the presentation of the late onset MS usually associated with more walking difficulties supporting much more um spinal cord involvement as well as also cognitive impairment. Now, if we're looking, as already mentioned before, on the time to increase disability in patients with late onset versus early onset we do see.

In regard to treatment for late onset MS, in general, the recommendation would be to use the same disease-modifying therapy as for young onset MS. We do have more primary progressive and late onset MS for which only, at the moment, we have one DMT approved.

Dr. Caudle:

You know, because women are most often diagnosed with MS during their reproductive years, health care providers will inevitably be managing women with MS going through menopause, whether that's naturally or clinically induced, so let's shift gears for a bit now and talk about older women with MS. Uh, Dr. Bove, let's go back to you. You know, what impact does menopause have on a patient with MS and is there an interplay between MS and menopause?

Dr. Bove:

To tease out the impact of menopause specifically on MS, um, it is a little challenging but um there's a lot of research ongoing. The first thing we have seen so far is that MS does not appear to affect the age at natural menopause in women. So it seems to be about 51.5 years old which is typical for age at natural menopause in western societies, but the long term use of some MS therapies could reduce menopausal age in subsets of women with MS. Natural menopause does seem to be a turning point um where we see that women um after menopause tend to have perhaps a reduced risk of uh relapses but may also have worsening disability with a more steep course of um disability accumulation and also um these findings align with the increased risk of converting to progressive forms of MS with age. Um, if we think about menopause and disability accumulation specifically, um, so women age 50 or older, have reported lower physical functioning levels compared to younger women. Um, whether women go through uh natural or surgical menopause, um the earlier age at the menopause does seem to be associated with worse self-reporting of MS severity scores even when you adjust for chronological age in MS type menstruation.

Dr. Caudle:

And lastly Dr. Bove, what may be considered as some of the potential benefits and risks of hormone replacement therapy in menopausal women with MS?

Dr. Bove:

As with any decision, this has to be an individual decision between the patient, her MS doctor, and her general clinician, um, and to think about some of the benefits, those may include prevention of activation of inflammatory genes, their affect on bone density loss that are positive. Um, there are also affects on general wellness, quality of life, as well as on uh bladder and vaginal wellness. Um, there have been observational studies that have suggested that hormonal therapy does have a protective affect on cognitive function when initiated early in the post-menopausal time period. women with MS specifically, there are just a few self-report studies that have shown that women who use hormonal therapy did report beneficial affects on their MS-related disability and symptoms and also on their physical functioning. When we think about some of the risks of hormonal therapy those can include cardiovascular disease, forms of cancer including endometrial and breast cancer, um and stroke, especially when given to women well beyond the perimenopausal window. It's really important to weigh the type of dose, the timing of initiation, duration of use, um and anticipated benefits and risks in individual women as a team.

Dr. Caudle:

If you could summarize what has been your approach really to managing and treating older patients with MS, um, I'd love to hear your thoughts Dr. Weinstock-Guttman if you'd like to begin.

Dr. Weinstock-Guttman:

We have to be aware about, as already mentioned, of the increased risk of infection for uh aging populations using high efficacy DMTs medication so, clearly, we have to be more vigilant for aging population, you know, regard to choice of disease-modifying therapy, the consideration of switching taking consideration not only the benefit that can be seen or not in aging population but also on their uh safety.

Um, in addition to disease-modifying therapy, we have to provide a much more uh comprehensive um approach to aging population, much more considering the uh comorbidities, being in um direct evaluation with um the primary physician uh as well as providing wellness recommendation, physical therapy, social interactions for our patients that is so important for quality of life and uh healthy aging.

Dr. Caudle:

Excellent and, Dr. Bove, what are your thoughts?

Dr. Bove:

Yeah, so I echo what Bianca said um and I would just add that, in addition to being really vigilant and careful here, we also have to be really anticipatory meaning as our patients come to us in their 40s and 50s, we have to think about what the next 20, 30, 40, 50 years are going to look like for them, and we have to help set them on their path to more healthy aging, to wellness.

Dr. Caudle:

Well this has been so informative, and I'd like to thank our experts for sharing their knowledge on the affects of aging on our management approach to MS. It was wonderful speaking with both of you today.

Dr. Weinstock-Guttman:

Thank you.

Dr. Bove:

Thank you for shedding light on this topic.

Announcer:

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