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Mind Matters: Psychiatric Comorbidity in the Prodromal Phase of MS

Dr. Turck:
Did you know that according to a recent study, psychiatric issues like depression, anxiety, bipolar disorder, and schizophrenia may be early indicators of multiple sclerosis *years* before symptoms appear?

Welcome to *NeuroFrontiers* on ReachMD. I'm Dr. Charles Turck, and joining me today to help parse through this research is Dr. Anibal Chertcoff. Not only is Dr. Chertcoff the lead author of the study, but he's also a postdoctoral fellow at the University of British Columbia where his research centers on characterizing the multiple sclerosis prodrome.

Dr. Chertcoff, it's great to have you with us today.

Dr. Chertcoff:
Thanks so much, Charles.

Dr. Turck:
Well, let's start with some background, Dr. Chertcoff. Would you give us an overview of what we currently know about the multiple sclerosis prodromal period?

Dr. Chertcoff:
So basically, a prodrome is defined as an early set of signs and symptoms that are often nonspecific and that indicate the onset of the disease that occur before the more typical or classical signs or symptoms of that disease, which will eventually manifest and lead to a definitive diagnosis. So in order to arrive to a diagnosis of MS, it is required that individuals present at least one clinical episode consistent with central nervous system demyelination—for example, inflammation of the optic nerve or an episode of inflammation of the spinal cord—and this has to be associated with clinical MRI or laboratory evidence of lesions that are disseminated within the central nervous system and that also develop over time.

So up until not so long ago, it was thought that MS did not have a prodromal period, although prodromal phases were well recognized in other neurological or immune-mediated diseases, so the possibility of an MS prodrome—once again, the presence of certain symptoms before these more clearly defined symptoms that lead to the diagnosis of MS—have been recognized only recently with the emergence of data from both epidemiological-clinical as well as biological studies. And the key finding that forms the basis of the concept of an MS prodrome was that the use of healthcare, basically hospitalization, physician visits, and prescriptions for certain medications, was found to be increased during the five years before the first documented MS symptom or the first demyelinating event captured in administrative data within population-based studies. And these population-based studies found that the most frequent complaints that occur before MS onset were responsible for these physician visits, and hospital admissions were due to complaints that were regarded as nonspecific, so, for example, fatigue, sleep disorders, anemia, pain as well as gastrointestinal, dermatological, and psychiatric problems. And in addition, important supporting evidence to this concept of an MS prodrome came from other studies which showed that individuals who would later develop MS showed higher levels of certain markers of neuroaxonal degeneration in their blood compared to healthy controls, also presenting a number of years before their MS classical clinical onset.

Dr. Turck:
How did all that knowledge guide the objectives of your study?

Dr. Chertcoff:
So we knew that psychiatric problems are common after the diagnosis of MS, and we knew that they occur at higher rates than expected in the general population, but at the same time, as I mentioned before, we knew that there were some studies suggesting that

psychiatric problems may also be present prior to the medical recognition of MS. So, for example, there was a study that showed that in the five years before MS onset, those developing MS versus those who did not have approximately 50 percent more visits to a psychiatrist and were more likely to fill a prescription related to what was classified as nervous system. The aim of our study was to investigate—in this case, in much more detail than before—the frequency of psychiatric conditions and psychiatric-related healthcare use following a similar pattern, so comparing these outcomes both in individuals with MS compared to those without MS in the five years before MS onset.

Dr. Turck:
And jumping into the nitty-gritty just a little bit more, would you walk us through how your study was designed?

Dr. Chertcoff:
What we did is access a data platform of both health administrative as well as clinical information from British Columbia, Canada, and by accessing these platforms, we identified people with MS, and we matched them by sex, year of birth, and postal code with up to five controls from the general population that did not have any demyelinating disease claim. So this led to the creation of what we call an administrative cohort, which included over 6,000 individuals with MS that we captured using an evaluated algorithm to identify MS in administrative data as well as over 30,000 controls, and a second smaller clinical cohort, which included about 1,000 individuals with MS that were diagnosed in one of British Columbia's MS clinics, and we matched them with over 4,000 controls. The period we analyzed was the following: so taking into account the moment where an individual receives the diagnosis of MS, we went back to what we define as the MS onset, which was different for both cohorts. So for the administrative cohort, this was an individual's first ever registered demyelinating disease claim, and for the clinical cohort, this was the date of their first MS symptom as recorded by an MS neurologist at one of the MS clinics in British Columbia. And we also assigned for the controls from the general population the same onset date as their match MS patient. And from that MS onset date, we explored the preceding five years, and in these five years, what we examined was first a primary analysis, the yearly prevalence of psychiatric morbidity, which we identified by applying an algorithm to detect depression, anxiety, bipolar disorder, and schizophrenia altogether in administrative data; and as a secondary analysis, we determined what we call the relative burden of psychiatric morbidity in both MS cases and controls according to the yearly number of physician visits for any psychiatric morbidity, the yearly number of visits to psychiatrists as well as psychiatric-related hospital admissions, and finally, the yearly number of dispensation of a selected set of psychotropic prescriptions, which consisted basically of antidepressants, anxiolytics, and antipsychotics as well as mood stabilizers.

Dr. Turck:
For those just tuning in, you're listening to *NeuroFrontiers,* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Anibal Chertcoff about a study he conducted that took a look at psychiatric comorbidity during the prodromal period experienced by patients with multiple sclerosis.

So, Dr. Chertcoff, now that we have a solid understanding of how your study was designed, let's zero in on the results. What were some of the highlights?

Dr. Chertcoff:
Yeah. So the results we obtained were the following. So concerning the primary analysis, so for both the administrative and the clinical cohorts, the prevalence of psychiatric morbidity was higher in MS cases than in controls in each of the five years before MS onset, and these differences, in fact, seem to increase steadily as the MS onset date approached. So overall, for the entire five-year period, 28 percent of MS cases versus 15 percent of controls of the administrative cohort presented psychiatric morbidity, and for the clinical cohort, the prevalence of psychiatric morbidity was 22 percent for MS cases and 14 percent for the controls. And for the secondary analysis, and only for the administrative cohort, people with MS have more visits for psychiatric morbidity and more visits to psychiatrists during each of the five years before their first demyelinating event compared to controls. So, for example, the rate of physician visits for psychiatric morbidity was approximately 80 percent higher in people with MS compared to controls in the year five before MS onset to up to 125 percent higher in the year before MS onset. These differences were more pronounced, for example, for visits to psychiatrists with a rate of visits 130 percent higher five years before MS onset and up to almost 150 percent higher the year before. And we also obtained similar results for psychiatric-related hospital admissions and for psychotropic prescription dispensations. So overall, these four outcomes showed a similar pattern of continued higher rates in each of the five years before MS onset with the most notable differences occurring in the year before MS onset.

Dr. Turck:
And how might your study's findings impact the way we identify, diagnose, or manage patients with multiple sclerosis?

Dr. Chertcoff:
So we believe that trying to obtain a better characterization of the MS prodrome may be an important key to allow for earlier recognition,

diagnosis, and eventually treatment of MS. We believe this is relevant given that it has been shown that treatments for MS that can slow disease progression appear to be most effective when studied early, so for that we need an early recognition of MS. And also, we believe that this is advancing our understanding of this very early stage of MS by providing us a more comprehensive assessment of the frequency and burden of psychiatric morbidity during the MS prodrome. How best to apply this observation to benefit individuals with very early MS seeking an explanation for their prodrome-related signs or symptoms, which are also common in the general population, we believe still requires some further research and some careful consideration.

Potential examples of how we can use this information could include, for example, raising awareness of the characteristics of the MS prodrome among certain medical specialties that are often sought by individuals with MS in this stage of the disease, including in this particular case, for example, psychiatrists, although it's yet early to say these specialties may play a role in the future in identifying early MS.

And finally, as we are fully aware that psychiatric problems negatively affect quality of life and progression of MS instability, the rapid identification and management may also at a certain point benefit both short as well as long-term health outcomes in individuals with MS.

Dr. Turck:
Before we close, Dr. Chertcoff, do you have any final takeaways that you would like to leave with our audience?

Dr. Chertcoff:
Further research is needed to improve our understanding and our definition of what is prodromal MS, but I think that exciting prospects for the future include, for example, developing standardized criteria for the MS prodrome, and this will be useful in order to try interventions at this very early stage of MS similar to what has been done in other chronic diseases, and this may include clinical trials for individuals with MS in the prodromal stage or at high risk of classical MS symptom onset. However, of course, in order to achieve this, having criteria for prodromal MS would be useful but only if we have strong biological markers of what is prodromal MS. I think that in order to arrive to this point, it will be important to have the engagement of all the MS community, including researchers, industry regulators, advocacy groups as well as, of course, people with MS.

Dr. Turck:
Well, this has been such an informative discussion about a truly important topic in multiple sclerosis research. And I want to thank my guest, Dr. Anibal Chertcoff, for joining me to share insights from his study. Dr. Chertcoff, it was a pleasure having you on the program.

Dr. Chertcoff:
It was a pleasure for me. Thanks so much.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!