A Shared Diagnostic Stewardship Approach toward Improving Autoimmune Encephalopathy Send-out Testing Utilization

Article:
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Guest: Dr. Cierra Sharp is the quality manager and a laboratory director for Lighthouse Lab Services.

Randye Kaye: Hello and welcome to this edition of JALM Talk from *The Journal of Applied Laboratory Medicine,* a publication of the American Association for Clinical Chemistry. I'm your host Randye Kaye. Autoimmune encephalopathy and paraneoplastic disorders are autoantibody associated disorders of the central nervous system. They cause a wide variety of neurological presentations in patients. Some patients with these disorders may be diagnosed by the laboratory detection of specific autoantibodies.

The diagnostic testing options for relevant auto antibodies have greatly expanded over the past several years. However, deciding when to test and what to test for can be challenging and auto antibody testing panels can be considered as expensive. An article on the March 2021 issue of JALM describes a healthcare institution's diagnostic stewardship committee review of autoimmune encephalopathy and paraneoplastic antibody test orders. Within the article, the authors propose a diagnostic algorithm to determine what type of autoantibody testing may or may not be appropriate for each patient.

The first author of this report and our guest for this podcast is Dr. Cierra Sharp. Dr. Sharp is the quality manager and a laboratory director for Lighthouse Lab Services. Dr. Sharpe completed her clinical chemistry fellowship at the University of Louisville in 2020. Welcome, Dr. Sharp. Let's start with this, what are the differences between autoimmune encephalopathy and paraneoplastic disorders, and what makes them so difficult to diagnose?

Cierra Sharp: Generally speaking, there are more similarities between these diseases than differences, and we tend to think of paraneoplastic disorders as a subset of autoimmune encephalopathy that occurs in the present or prior to the development of cancer. As you mentioned, both of these diseases occur when the body develops antibodies against the protein in the brain and these autoantibodies cause inflammation which in turn damages or kills cells.

Where we see the most differences are in the demographic affected, the disease prevalence, and associated

autoantibodies. Autoimmune encephalopathy is more commonly seen in older adults while paraneoplastic disorders occur in younger patients and, again, there is that association with cancer.

Autoimmune encephalopathy is more prevalent in the population and affects about 14 in 100,000 people, whereas paraneoplastic disorders are rare with a prevalence of 1 in 100,000. Finally, the auto antibodies that are formed in autoimmune encephalopathy tend to target synaptic proteins, while those developed in paraneoplastic disorders target intracellular proteins.

As for the diagnosis of these diseases, it's challenging due to non-specificity of clinical presentation and findings of diagnostic studies which adds these disorders to a long list of differential diagnoses. These include infectious encephalopathy, most commonly associated with herpes simplex virus, Alzheimer's disease and dementia, electrolyte imbalances, central nervous system malignancies, and drug abuse.

The clinical presentation is highly varied from person to person and can include episodic memory loss, confusion, movement disorders, headache and gastrointestinal issues. The common diagnostics we see ordered for autoimmune encephalopathy and paraneoplastic disorders include lumbar puncture studies, MRI, and EEG but these findings are often inconclusive. Because of this, physicians will sometimes go for esoteric testing that is more specific to these diseases. Often, these are panels that test for 5 to 20 of the possible autoantibodies associated with either disease in serum or cerebral spinal fluid, and this is the testing that our project focused on.

Randye Kaye: All right. Thank you. Let's talk a little bit more about the project. The article describes the analysis of test ordering patterns for autoimmune encephalopathy and paraneoplastic antibody panels. How was this project first initiated?

Cierra Sharp: This was work that I completed when I was a fellow, and during that time our institution had a gatekeeper policy in place for any testing costing more than $500 that had to be sent out to another laboratory to perform. This is commonly referred to as send-out testing. So, as part of this policy, orders that met these criteria were reviewed by clinical chemistry fellows and anatomic pathology residents who were on call, and the goal of this review process was to determine the medical necessity of the test, ensure that the test was not ordered in error, and if there was alternative testing that would better aid in the diagnosis and treatment of the patient.

So, typically, this required having a conversation with the ordering physician to better understand the patient's past medical history and current clinical presentation. What we quickly realized with this process was that autoimmune encephalopathy and paraneoplastic disorder panels were by far one of our more expensive and most commonly ordered tests that we reviewed.

And while some orders were cancelled after discussion with the physician, in many cases these orders were ultimately approved. So, for example, in 2018 before we started this improvement initiative, a total of 77 orders were placed accruing a cost of close to $140,000. So this was an area that we identified as needing improvement. Around that same time that we started gathering information on our test ordering patterns for these panels and associated cost, our institution was starting up the diagnostic stewardship committee, and we thought this would be a perfect project for them to get their help with.

Randye Kaye: All right, thank you. So, let's talk more about this committee, the diagnostic stewardship committee, or DSC, what makes up that committee at your institution?

Cierra Sharp: So, from the very beginning, the goal for our diagnostic stewardship committee was to be as diverse as possible. It's made up of nurses and physicians across multiple disciplines, as well as pharmacists and representatives of the clinical laboratory. And we also have an open-door policy as to who can bring potential issues and projects to the group. We think this diversity is important because a lot of what our diagnostic stewardship committee does deals with appropriate utilization of laboratory testing, and the only way that you can really deem what is appropriate is with the input from the people who actually order the test and use the test results.

Randye Kaye: All right, that makes sense. And you've spoken a bit about the goals, but can you elaborate what are the goals of the DSC?

Cierra Sharp: As clinical laboratorians, we know that an issue we sometimes face is the misuse and misinterpretation of testing, as well as either under or over utilization of testing. Our diagnostic stewardship committee's main goal is to ensure the appropriate use of laboratory testing to ultimately improve patient outcomes, whether this is improving the accuracy of diagnosis, providing physicians with the information to make treatment decisions, or avoiding laboratory errors or slow turnaround times.

Personally, I think that taking this project to diagnostic stewardship committee was instrumental in its success

because prior to that, we were really only viewing it from a cost standpoint whereas the committee gave us a newfound perspective and helped us switch our goal to actually developing a system that would improve how our patients were potentially diagnosed and treated.

Randye Kaye: Wow. That sounds great. So, your article talks about that and describes the development of an algorithmic approach for the ordering of these panels. What challenges did you and your colleagues face in developing that algorithm and how did you resolve them?

Cierra Sharp: Before we started working with our diagnostic stewardship committee, one of our biggest obstacles was understanding the etiology of autoimmune encephalopathy and paraneoplastic disorders and how the corresponding panels were used for diagnosis and treatment of the patient. The existing literature on these diseases is somewhat limited, and there isn't really a consensus on how best to use these panels.

With the help of the diagnostic stewardship committee, we were able to establish a collaboration with our department of neurology and this was instrumental in not only understanding these complex diseases in a general way, but also how specifically the physicians at our institution were using the results from these panels.

In addition, when we looked at our ordering patterns for these panels, we realized that orders are being sent out several different laboratories and that the panels they offered varied in the number of autoantibodies and price. For example, one lab charged close to $4,000 for testing for seven autoantibodies, many of which were included in other panels from labs at a lower cost. So we combined this information and got feedback from our neurology physicians to streamline our selection of panels. Ultimately, what we ended up with was two main panels from the same send-out lab and this is eventually what got incorporated into the algorithm we used for test ordering.

Finally, a reoccurring obstacle we faced was which type of specimen should be sent for testing since these autoantibodies can be detected in both serum and cerebrospinal fluid. At our institution, it was common for panels to be ordered on both specimens and this was a point of contention early on. As much as we would like to have an answer to everything, this was one area where the evidence in the literature was very unclear. Some studies promote the use of both types of specimens, some promote the use of cerebrospinal fluid for specificity, while others promoted the use of serum for increasing sensitivity.

So what we ultimately decided was that our priority would be to increase our chances of detecting an autoantibody. And so, that's why initial testing and serum was incorporated to the algorithm. However, as a compromise, we decided to store cerebrospinal fluid samples for 30 days. Usually, we see the results when the serum panels come back within two to three weeks. So, if a physician wanted to confirm a detected autoantibody with cerebrospinal fluid, or still suspected one of these disorders and there were no autoantibodies detected in the initial serum, we would have the alternative specimen on hand readily available for send-out.

Randye Kaye: All right, great. Thank you. So, and that's a lot of work, what do you hope that other institutions can take away from your work?

Cierra Sharp: Well, I hope that the biggest takeaway from this project is the importance of collaboration. Even if your institution doesn't have an established diagnostic stewardship committee, it's still important to work with colleagues outside the clinical laboratory to improve the way laboratory tests are ordered and used. So, the key players in this project were Dr. Muluhngwi, who is my senior clinical chemistry fellow and was involved in the initiation of this project back in 2018, Dr. Fletcher, who was our neurology collaborator and who provided her expertise on the area of autoimmune neurology -- and ultimately, the idea to use an algorithm approach was hers -- and finally, Dr. Snyder who is the chief of microbiology and was the one who headed our institution's diagnostic stewardship committee. The success of this project really relied on their knowledge, guidance, and input all along the way.

Finally, whatever approach you choose to implement to help streamline test ordering practices, it's important to remember that the approach is not set in stone. For us, even after the algorithm was in place for five months, we realized there were several areas for improvement and because data on autoimmune encephalopathy and paraneoplastic disorders are rapidly changing and new antibodies are being discovered, there would be new information that we could incorporate to make sure that our algorithm was optimal.

So, the bottom line is that projects like this will need frequent review and updating especially because we want to make sure we are providing the best laboratory testing available to the correct population of patients.

Randye Kaye: Thank you so much for joining us today. That was very interesting.

Cierra Sharp: Thank you for having me.

Randye Kaye: That was Dr. Cierra Sharp from Lighthouse Lab Services describing the JALM article, A Shared Diagnostic Stewardship Approach Toward Improving Autoimmune Encephalopathy Send-Out Testing Utilization.

Thanks for tuning in to this episode of JALM Talk. See you next time and don't forget to submit something for us to talk about.