Differential Diagnosis of Tardive Dyskinesia

[MUSIC PLAYING]

LESLIE LUNDT: Hello, and welcome to a roundtable discussion of differential diagnosis for tardive dyskinesia. I'm Leslie Lundt, Psychiatrist and Medical Director at Neurocrine Biosciences. I'm joined by Jeremy Schreiber, Psychiatric Mental Health Nurse Practitioner at Coleman Professional Services, Dr. Carlie Tanner, Professor of Neurology at the University of California, San Francisco, and Dr. Andrew Cutler, Chief Medical Officer at Meridien Research.

Today, we will discuss the differential diagnosis for tardive dyskinesia by highlighting some key differential conditions. Before we begin, would you please provide some background information about tardive dyskinesia. Dr. Tanner?

CARLIE TANNER: The term tardive dyskinesia refers to abnormal involuntary movements or dyskinesia manifesting in a delayed or tardive manner after prolonged use of dopamine receptor blocking agents, or DRBAs. Tardive dyskinesia, or TD, is defined as involuntary athetoid or choreiform movements. Athetoid movements are slow, sinuous, and continual, whereas choreiform movements are rapid, jerky and non repetitive. By definition, the involuntary movements must develop an association with prolonged exposure to antipsychotic or other dopamine receptor blocking agents for at least a few months. As stated, antipsychotics, also known as neuroleptics, are dopamine receptor blocking agents or DRBAs. DRBAs are used to manage psychiatric disorders such as psychosis, depression, and bipolar disorder, as well as gastrointestinal problems such as symptomatic gastroesophageal reflux, and diabetic gastroparesis.

JEREMY SCHREIBER: We should also mention that TD movements can involve the tongue, lower face and jaw, and extremities, as well as the pharyngeal, diaphragmatic, or trunk muscles. Symptoms may develop after a shorter period of medication use in older patients, and in some patients, dyskinesia may arise and persist after discontinuation change or decrease in dose of medication.

Another movement disorder called neuroleptic withdrawal emergent dyskinesia can also arise after change or discontinuation of antipsychotics, and usually lasts less than four to eight weeks. Dyskinesia that persists longer than this period is considered tardive dyskinesia.

ANDREW CUTLER: I think clinicians should also note that treatment with antipsychotics can result in extrapyramidal symptoms that may be mistaken for or coexist with TD.

LESLIE LUNDT: So what is the first step health care professionals should take in the differential diagnosis process?

CARLIE TANNER: I think it's important to clarify some terms when considering a differential diagnosis. Health care professionals may encounter the term extrapyramidal symptoms, or EPS, when considering differential diagnosis. EPS is used to describe movement disorders manifesting as psychiatric medication-related side effects.

But EPS is an umbrella term that has come to mean that some form of movement disorder is present. Yet, the movements are distinct and managed differently, so the term is fairly obsolete. Health care professionals can, instead, use the term acute drug-induced movement disorders.

LESLIE LUNDT: OK. So what are the distinguishing features of acute drug-induced movement disorders?

CARLIE TANNER: To begin with, health care professionals should note that the acute portion of the term refers to the quick onset of movement disorders after initiation of therapy, which helps separate the conditions from the tardive forms. The term tardive in tardive dyskinesia, for example, refers to the fact that the abnormal involuntary movements manifest in a delayed manner.

This is an important distinction that can be used to detect acute drug-induced movement disorders that health care professionals may falsely characterize as tardive in nature. Acute drug-induced movement disorders are characterized by a quick time to onset after drug exposure. We're talking hours to days.

ANDREW CUTLER: And the other defining feature is that the movements typically resolve after drug discontinuation rather than persisting. These traits contrast with TD, which can present after years of treatment and can persist for years or decades after drug discontinuation.

LESLIE LUNDT: Those are important points of distinction. What are the key acute drug-induced movement disorders HCPs should consider when determining whether or not the patient has TD?

ANDREW CUTLER: We will be discussing three of the more commonly seen drug-induced movement disorders that health care providers should be aware of, namely, parkinsonism, akathisia, and dystonia.

LESLIE LUNDT: So let's start with acute or drug-induced parkinsonism. What are the main drug-induced parkinsonism characteristics with which HCPs should be familiar?

ANDREW CUTLER: Drug-induced parkinsonism can be evident as early as a few days after drug initiation, but in some cases, it can take as long as several months to manifest. Symptoms of drug-induced parkinsonism include tremor, rigidity of the neck, trunk, and extremities, and bradykinesia of facial regions, extremities, and gait.

CARLIE TANNER: Yes, but unlike TD, drug-induced parkinsonism symptoms typically improve with treatment dose reduction or discontinuation.

LESLIE LUNDT: OK. I see how drug-induced parkinsonism differs from TD. Let's move on to drug-induced akathisia. What are its main characteristics?

CARLIE TANNER: Akathisia is characterized by feelings of inner tension, irritability, anxiety, jitteriness, and the urge to move. Movements manifest as restlessness with an inability to hold still.

ANDREW CUTLER: And because we're talking about the acute form of akathisia, the quick onset time and ability to resolve through drug discontinuation applies, right?

CARLIE TANNER: That's right. Acute akathisia usually develops within a few days after dopamine receptor blocking agent initiation, during dose escalation, or after patients switch to a more potent DRBA. Clinicians should also note that acute akathisia can also be caused by other drugs such as selective serotonin reuptake inhibitors, or SSRIs, antiepileptics, and recreational cocaine use. As with drug-induced parkinsonism, but unlike TD, acute akathisia typically resolves after drug discontinuation.

LESLIE LUNDT: Now let's consider acute or drug-induced dystonia. What is the condition's key phenomenology?

ANDREW CUTLER: Acute dystonia is characterized by muscle contractions that can be painful and manifest as twisting, repetitive involuntary movements, along with abnormal postures. Acute dystonic reactions can affect any part of the body, but usually involve the head, neck, eyes, mouth, and jaw.

CARLIE TANNER: And when it comes to the timing of onset, acute dystonic reactions usually develop within days of starting treatment, with half of all cases occurring within the first 24 hours of medication initiation, and almost all events occurring within five days of starting treatment.

ANDREW CUTLER: And HCPs should also note that discontinuation of the offending treatment is recommended and does result in resolution of symptoms, but anticholinergic drugs are often used and may abate symptoms.

LESLIE LUNDT: OK. So now that we've gone through a high-level description of these drug-induced movement disorders, let's talk about their phenomenology a bit more thoroughly. Should we start with drug-induced parkinsonism?

ANDREW CUTLER: Well, yes, because it's likely that this is the most important differential for non expert clinicians to consider when monitoring patients on DRBAs, since TD may coexist with drug-induced parkinsonism.

LESLIE LUNDT: What are the key drug-induced parkinsonism symptoms that HCPs should note?

ANDREW CUTLER: Symptoms of drug-induced parkinsonism include rigidity of the neck, trunk, and extremities, which may be accompanied by cogwheeling. Patients with drug-induced parkinsonism usually have low frequency resting tremors, typically of back and forth movement that is rhythmic and repetitive.

CARLIE TANNER: Right. And bradykinesia is another drug-induced parkinsonism symptom and can manifest as slowness of movement with lower blink rate, decreased facial expression, and reduced arm swing while walking. It can also manifest as soft voice, flexed posture, and small steps.

LESLIE LUNDT: How can clinicians recognize drug-induced parkinsonism and differentiate it from TD? One of the key differentiators between acute drug-induced parkinsonism and TD is tremor.