LESSON OF THE WEEK

Tetanus versus acute dystonic reaction caused by metoclopramide

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If tetanus is suspected, take a complete drug history and administer procyclidine

Although taking a travel history from patients returning from travelling abroad is important, occasionally it may be misleading. The ability to extract information that will help to establish the correct diagnosis remains the clinician's most important diagnostic tool.

Case report

A 28 year old woman presented to the accident and emergency department with tightness and twitching across the facial muscles, upwards rolling of the eyes with deviation of the head and gaze to the right, and stiffness of the neck muscles. The symptoms were associated with sweating and tachycardia at a rate of 130 beats/min. Further clinical examination and imaging were unremarkable. She had no history and no evidence of skin breaks or dental or ear infection. All the blood tests were normal, including the electrolytes, C reactive protein, and white cell count.

The patient had returned from Kenya four weeks previously, where she had been on a safari holiday. Before going to Kenya, she had had all the necessary vaccinations and had started taking Malarone (proguanil with atovaquone) for malaria prophylaxis.

Ten days before her presentation, she had had colicky left flank pain with nausea and vomiting. Her general practitioner prescribed trimethoprim followed by ciprofloxacin for a presumed urinary tract infection. She had no medical history of note. The patient was using oral contraception but had no clear history of further concomitant medication. She did not know her immunisation status for tetanus.

We believed that the symptoms were consistent with tetanus, and after discussion with the infectious diseases specialist, diazepam, intravenous tetanus immunoglobulin, and metronidazole were administered. The patient was admitted to the high dependency unit for overnight observation, where her symptoms resolved completely one to two hours after receiving the specific immunoglobulin and diazepam.

The next day, after transfer to the infectious diseases unit, it emerged that the patient had started taking metoclopramide the day before her presentation. This had

been prescribed by her general practitioner because of persistent nausea; the general practitioner confirmed that a tetanus boost vaccination had been given the previous year.

The patient's symptoms had resolved six to eight hours after onset—acute dystonic reaction caused by metoclopramide was diagnosed. A “yellow card” report was submitted to the Medical and Healthcare Products Regulatory Agency, which runs the yellow card scheme for collecting information in the United Kingdom from health professionals and patients on suspected adverse drug reactions.

Discussion

This case highlights the importance of obtaining a complete drug and immunisation history in any patient suspected of having tetanus. The report describes a case where tetanus was misdiagnosed and focuses on the main differences between tetanus and acute dystonic drug reactions. Distinguishing features include the age of the patient, presence or not of wounds, recent medication, the nature of the involuntary movements (in this case oculogyric), and the duration of symptoms.

In the absence of skin injuries, tetanus is unlikely. A diagnostic and therapeutic step in this setting would have been the administration of an anticholinergic antiparkinsonian drug such as procyclidine, which would have rapidly alleviated the dystonic symptoms.

To highlight the differences and similarities, we describe below the two conditions.

Acute dystonias and dyskinesias

Dystonia is a syndrome of sustained muscle contractions resulting in twisting, repetitive movements, or abnormal postures. Acute dystonias usually present as buccolingual (pulling sensation of the tongue), torticollis (twisted neck, facial muscle spasm), oculogyric (rolling or deviated gaze), tortipelvic (abdominal rigidity), and/or opisthotonic (spasm of the entire body).

The extrapyramidal system modulates motor function using excitatory cholinergic and inhibitory dopaminergic neurotransmitters. The inhibitory dopaminergic receptors are susceptible to blockage by antiemetics, neuroleptics, and other drug groups (table). The potential adverse extrapyramidal effects are acute

Drugs that can cause dystonic reactions

Category	Drug
Analgesics	
Opioids	Alfentanil
Antiarrhythmics	Flecainide
Anticonvulsants	Carbamazepine, phenytoin
Antidepressants	
Monoamine-oxidase inhibitors	Phenelzine, tranylcypromine
Selective serotonin reuptake inhibitors	Fluvoxamine, paroxetine
Tricyclic	Amitriptyline, amoxapine (discontinued in UK)
Antiemetics	Metoclopramide, domperidone
Calcium channel blockers	Diltiazem
Neuroleptics	
Butyrophenones	Benperidol, haloperidol
Phenothiazines	Fluphenazine, perphenazine, prochlorperazine
Sedatives	Midazolam
Stimulants	Cocaine

dystonic or dyskinetic reactions, parkinsonism, and tardive dyskinesias.

The duration of the symptoms is proportional to the half life of the drug—generally several hours. Anticholinergic medications (procyclidine, benzatropine) restore the excitatory-inhibitory balance within minutes. This step is both therapeutic and diagnostic.

Acute dystonias may be confused with partial seizures, tetanus, strychnine poisoning, and electrolyte imbalances. Often no history is offered at all: the patient may not be able to speak or make the connection between symptoms and drug, or may not admit to taking psychotropic medication.

Incidence of dystonias caused by metoclopramide

The most common adverse extrapyramidal effect of metoclopramide are acute dystonias, with an incidence of 0.2%.¹ The incidence is higher in patients receiving higher doses, in children, and in young adults. About 70% of dystonic patients are female. Only 479 reports of suspected metoclopramide related extrapyramidal reactions were reported in the UK for 1967-82: 455 were for acute dystonias, 20 for parkinsonism, and 4 for tardive dyskinesias.² The low incidence rate in the UK is the result of under-reporting of adverse reactions.³

Tetanus

The symptoms of tetanus are caused by the potent neurotoxin tetanospasmin, produced by *Clostridium tetani*. The exotoxin is disseminated through the bloodstream and the lymphatic system. It is taken up by the neuromuscular junctions, where it migrates retrograde trans-synaptically along the axons and accumulates in inhibitory synapses, resulting in the blockage of inhibitory impulses and muscle rigidity.

The toxin moves from the contaminated site to the spinal cord at a rate of 75-250 mm/day, a process which takes 3-14 days. The toxin binding is irreversible; recovery takes about one month, and it depends on the sprouting of new axonal terminals. Less than 2.5 ng per kilogram of tetanospasmin is lethal.^{4,5}

The four clinical types of tetanus are cephalic, local, generalised, and neonatal; 50-75% of patients with generalised tetanus present with trismus (lockjaw) and risus sardonicus. As the disease progresses, patients have generalised muscle rigidity. Sensation remains preserved and patients feel severe pain. Seizures, respiratory failure, glottic spasm, and sympathetic hyperactivity (tachycardia, hypertension) can result in death.

Clinical manifestation and duration of symptoms are clearly different from the oculogyric or any other dystonic movements.

Incidence

On average, 8-10 cases of tetanus are reported annually in the UK.^{6,7} The incidence decreased after national tetanus immunisation was introduced in 1961.⁸ Most cases occur in people aged over 60 years, who have not participated in the immunisation scheme.

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Endpiece

A powerful diuretic

Madame, so it is I have this night after midnight taken your medicine, for the which I heartily thank you, for it hath done me much good, and hath caused the stone to break, so that I now void much gravel. But for all that, your said medicine hath done me little honesty, for it made me piss my bed this night, for the which my wife hath sore beaten me, and saying it is in children's parts to bepiss their bed.

A letter from Edmund Howard, father of Katherine Howard, later to be wife of Henry VIII, to Lady Lisle, wife of the governor of Calais. In: Denny J. *Katherine Howard*. London: Portrait, 2005

Submitted by Philip Radford, retired general practitioner, Taunton