Case Report: Serotonin syndrome in burns patients

A 16-year-old boy who sustained 45% total body surface area (20% partial thickness, 15% full thickness, 10% inhalation) flame burns was admitted to our Burn Centre on 14 June 2016, via Victoria Hospital where he received emergency treatment including escharotomy on the right lower limb. His injury was sustained on 11 June 2016 during a house fire in which other individuals died. His injuries were mostly to the lower part of his body but included partial thickness burns to arms, face and head.

His initial treatment included the standard protocols of the unit viz:- complete clinical examination – including appropriate special investigations, Ventilator Associated Pneumonia (VAP) care, head up, ulcer prophylaxis, sedation, analgesia, appropriate venous and arterial access, etc.

The patient was septic with raised inflammatory markers, positive blood cultures, foul-smelling wounds and bilateral infiltrates on chest x-ray; he was initiated on appropriate antibiotics. He underwent multiple surgical debridements and skin grafts for source control as well as definitive treatment during his stay in the unit.

During August he exhibited signs and symptoms in keeping with major depressive disorder and was seen by a psychologist in response to an interdepartmental referral. A decision was made to commence 30 mg daily oral Fluoxetine (Selective Serotonin Reuptake Inhibitor – SSRI) treatment.

Mid-August, during a dressing change, the intern doctor noted clonus of the lower limbs and investigated thoroughly. His chemical pathology was within normal limits. He exhibited no other signs or symptoms of serotonin syndrome viz:- altered mentation, diarrhoea, nausea and or vomiting. The autonomic disregulation he experienced could be attributed to pain, sepsis and the hypermetabolic response to burn pathology, but the clonus not. Therefore, clonus in the severely burned patient on multiple drug regimens (including analgesia, antiemetic, ulcer prophylaxis) on SSRI therapy, in the absence of other hard clinical signs of serotonin syndrome, should alert the clinician to the possibility of mild serotonin syndrome.

Discussion

A potentially life threatening condition known as serotonin syndrome poses a potential risk to patients admitted to a burns unit, the diagnosis of which can potentially be masked by symptoms commonly seen in burns patients.

Serotonin or 5-hydroxytryptamine is a monoamine neurotransmitter that is primarily found in the gastrointestinal tract, platelets and central nervous system of the human body. In the central nervous system, it has its main effect on mood, appetite, affective behaviour, food intake, thermoregulation, migraine, emesis, sexual behaviour and sleep, but also affects some cognitive functions like memory and learning.1,2,3,4

Serotonin is produced in the brainstem’s raphe nuclei and stored in presynaptic vesicles.1 Neuronal activation causes release of serotonin into the synapse. Reuptake of excess serotonin to the presynaptic vesicles is facilitated by an active transport mechanism, or it is metabolised by monoamine oxidase. The liver is responsible for systemic metabolism of serotonin.

A vast majority of pharmacological agents alter serotonin levels (Table 1), of which the most common would be selective serotonin reuptake inhibitors (SSRIs) or monoamine oxidase inhibitors (MAOIs) both of which are used primarily for the treatment of depression. These drugs interfere with the serotonin pathway of the brain either by increasing serotonin synthesis, decreasing serotonin metabolism, increasing serotonin release, inhibition of serotonin reuptake or...
Serotonin syndrome is a predictable complication of excess serotonin stimulation and is thus not an idiosyncratic reaction. The differential diagnosis for serotonin syndrome includes adrenergic crisis, the anticholinergic toxidrome and neuroleptic malignant syndrome. To differentiate between these syndromes, a thorough history, investigation of all medication and illicit drug use as well as a thorough physical examination is needed. The physical examination should especially focus on the neuromuscular system. 

The diagnosis is primarily clinical and there is no single test to make the diagnosis. Clinical diagnosis is also complicated by the complexity of the symptoms and that not every patient will present with all the above symptoms. In an attempt to make diagnosing serotonin syndrome easier and more accurate, people have developed numerous criteria, some more useful than others and some more accurate than others. The diagnosis is primarily clinical and there is no single test to make the diagnosis. Clinical diagnosis is also complicated by the complexity of the symptoms and that not every patient will present with all the above symptoms.

Treatment includes prompt recognition of the symptoms, discontinuation of the causative agents and supportive care, which includes fluid resuscitation, benzodiazepines for the treatment of myoclonus and hyperreflexia and external cooling for hyperthermia. In severe cases, sedation, neuromuscular paralysis and intubation should be considered. It is advised to avoid succinylcholine for paralysis if possible due to the risk of arrhythmias from hyperkalemia. There is no role for antipyretics in the management of serotonin syndrome as the hyperthermia is caused by the increased muscle activity and not by central causes.

The antihistamine Cyproheptadine, a serotonin inhibitor, should be considered in moderate cases and is recommended in severe cases, despite the lack of good evidence. With effective treatment, the signs and symptoms of serotonin syndrome should resolve within 24-48 hours. Physical restraints are not advised as this may increase the risk of rhabdomyolysis, increased lactic acidosis and
Figure 1. Serotonin Syndrome Symptom Classification
Compiled by information from Franc C6 in combination with other resources1,3,4,8,9,11

Table 2: Comparing symptoms of Serotonin syndrome and symptoms commonly seen in Burns patients

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Serotonin syndrome</th>
<th>Possible symptoms seen in burns patients for different reasons</th>
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<tbody>
<tr>
<td>Fever</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Tachycardia</td>
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<td>Diaphoresis</td>
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<td>Diarrhoea</td>
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<td>Tremors</td>
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<td>Hyperreflexia</td>
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<td>Clonus</td>
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<tr>
<td>Insomnia</td>
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Data compiled from multiple publications 1,2,3,4,5
hyperthermia. If there is a need for physical restraints it should soon be replaced with chemical restraints as needed.

Prevention of serotonin syndrome could be improved by continually educating physicians, altering prescribing practices and good pharmacological research.

A high risk patient population for serotonin syndrome is those patients who are admitted to a burns unit. Pain management in burns patients are of utmost importance, and play a cardinal role in the management of the patient. Analgesia protocols differ between units, but the one thing that all units agree on is that a multimodal approach is needed to control pain adequately. This usually involves multiple drugs from different classes and different receptor activity.

Due to the nature of the injury, burns patients are at a higher risk of developing other conditions, like depression, anxiety, chronic pain syndromes, electrolyte disturbances and wound infection, all of which are amenable and deserving of appropriate treatment, which usually involves more pharmacological agents.

The risk of severe drug interactions is increased where more pharmacological agents are used, this being the case in almost every patient who is admitted with burn wounds.

The problem does, however, come in when the patient develops a serotonin syndrome, as the symptoms are easily masked by sedation and common symptoms seen in burns patients (Table 2).

Differentiating between serotonin syndrome and common symptoms in burns patients can be difficult for various reasons. The most important principle is to keep it in the back of your mind and exclude other causes for the symptoms. Careful prescription of pharmacological agents and a thorough drug history is of utmost importance and can guide your diagnosis and early treatment which can be lifesaving.

References