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Acute Respiratory Distress Syndrome (ARDS) – An uncommon presentation of serotonin syndrome

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ABSTRACT

Serotonin syndrome is a potentially fatal condition in which there is an increased serotonergic activity due to excessive ingestion of serotonergic drugs, an excess dose of serotonin reuptake inhibitors, drug-drug interactions etc. and is characterized by abnormal mental status, autonomic and neuromuscular dysfunction. We report a case of a 47-year-old female, with no known comorbidities who presented to the emergency room of a tertiary care centre with a history of intentional self-consumption of serotonergic drug with delirium. She was febrile and hypoxic. Her chest radiograph and CT-Thorax revealed changes suggestive of Acute Respiratory Distress Syndrome (ARDS), an uncommon presentation, as a part of serotonin syndrome. Her cardiac function was normal and pulmonary infection was ruled out. Her clinical characteristics were suggestive of serotonin syndrome and pulmonary involvement was attributed to escitalopram overdose. The patient was admitted to the intensive care unit and given high-flow oxygen therapy and supportive care. She gradually showed complete recovery.

Key words: Serotonin syndrome, acute respiratory distress syndrome, Selective serotonin reuptake inhibitors, Hunter's criteria.

INTRODUCTION

Serotonin syndrome is a condition in which there is an increased serotonergic activity due to an excess dose or intentional/ unintentional excessive ingestion of serotonergic drugs, or drug-drug interactions [1] and is characterised by abnormal mental status like lethargy, confusion, disorientation. Autonomic abnormalities like hyperthermia, dilated pupils, sweating, tachycardia, and flushing and neuromuscular abnormalities like tremors, agitation, myoclonus, and rigidity are common manifestations [1] [2]. The incidence rate is approximately 15% in patients with Selective Serotonin Reuptake Inhibitors (SSRI) overdose [3]. With citalopram and escitalopram overdose, cardiac toxicity and neuromuscular toxicity are well documented [3] [4]. Usually, lung involvement is rare. This case report describes Acute Respiratory Distress Syndrome (ARDS) as a manifestation in serotonin syndrome.

CASE REPORT

A Forty-seven-year-old lady, with no known co-morbidities, was brought to the emergency room with a history of intentional self-consumption of 300mg of escitalopram. She had consumed 30 tablets of 10mg escitalopram, experienced vomiting within an hour of ingestion and was delirious. Within few hours, she developed lethargy, altered sensorium and spontaneous myoclonus. She reported to the emergency department with acute dyspnea and decreased consciousness. On examination, her Glasgow Coma Scale (GCS) was decreased (10/15). She had moderate hypoxia and febrile Features suggestive of autonomic dysfunction was also present, such as tremors, dehydration, flushing and nausea. Respiratory system examination revealed bilateral basal coarse crackles. She was put on high flow oxygen therapy with Non-rebreather mask (NRBM). There was no significant past medical or family history.

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Initial hemogram, renal function with serum electrolytes, serum proteins and liver function tests were within normal range. Arterial blood gas analysis revealed hypoxemia with moderate ARDS (Pao2/Fio2 <200) and metabolic acidosis. ECG (12 Lead) showed sinus tachycardia and initial chest radiograph showed bilateral costophrenic angle blunting with bilateral hilar opacities. A high resolution computed tomographic (HRCT) analysis of thorax revealed bilateral pleural effusion with central peri-bronchovascular ground glass opacities and alveolar opacities consistent with ARDS (Figure - 1), (Figure – 2). 2D Echocardiography revealed normal left ventricular systolic function with normal chamber dimension and no regional wall motion abnormality. Cardiac Biomarker (NT Pro-BNP) was within normal range. Sputum culture showed no growth of organisms and nasal swab for Sars-Cov2 and H1N1 were negative. Pleural Fluid analysis was suggestive of exudative effusion and culture did not grow any organism. All common infectious etiology were ruled out.

Her sensorium improved from second day of admission. Dyspnea was however persistent. There were no further episodes of spontaneous or inducible clonus. She continued to have febrile episodes till the following day. Since all the signs and symptoms satisfied the Hunter's criteria, a diagnosis of serotonin syndrome was made and ARDS was attributed to it.

She was treated with high flow oxygen therapy with NRBM, intravenous fluids, antipyretics and supportive symptomatic management. A short course of empirical antibiotic was given for 5 days. She improved clinically and oxygen therapy was tapered gradually. A psychiatric evaluation and counselling was sought as part of her comprehensive management. She was discharged on room air after 5 days hospital stay. Post-discharge she experienced generalised weakness and decreased appetite. She was advised adequate hydration and bed rest. The patient recovered completely after 8-10 days.

DISCUSSION

Serotonin syndrome is caused by increased serotonergic activity in central and peripheral serotonergic receptors due to the ingestion of more than one serotonergic drug or excessive dosage in case of poisoning or interaction with other drugs. [1]

SSRIs are the most common group of drugs causing the serotonergic syndrome [2]. The other class of drugs that can potentiate this fatal condition are Serotonin-norepinephrine reuptake inhibitors, Monoamine oxidase inhibitors [9], Triptans, 5HT-3 receptor antagonists, Tricyclic antidepressants, and other drugs like linezolid, tramadol and fentanyl [1] [5].

Serotonin modulates attention, behaviour and thermoregulation, also in regulation of nociception, vascular tone and motor tone. Patients with serotonergic syndrome can present with a range of mild symptoms to severe delirium, convulsions and hyper-tonicity. A triad of altered mental status, autonomous and neuromuscular abnormalities are characteristic of this syndrome [1] [2]. Altered mental status includes anxiousness, lethargy, and disorientation. Autonomic hyperactivity includes diaphoresis, tachycardia, hyperthermia, and hypertension. Neuromuscular abnormalities manifest as tremors, restlessness, agitation, myoclonus, and hyperreflexia [1] [8].

The diagnosis of serotonin syndrome cannot be conclusively established with laboratory testing. Instead, the diagnosis should be inferred by clinicians based on the patient's medical history and physical examination when tremor, clonus, or akathisia are present without any other extrapyramidal symptoms [1].

Diagnosis of serotonin syndrome is made with Hunter's criteria [7]

1. Presence of a serotonergic agent
2. Presence of one or more of the following
    - Spontaneous clonus
    - Inducible clonus with agitation and diaphoresis
    - Ocular clonus with agitation and diaphoresis
    - Tremors and hyperreflexia
    - Hypertonia
    - Hyperthermia (>38degree Celsius)

The use of illicit drugs/substances, and over-the-counter medications should be asked by physicians while getting the patient's drug history because such substances can lead to excess serotonergic activity in central nervous system. A thorough evaluation of muscular rigidity, inducible clonus, and reflexes should be included in the physical examination.

Escitalopram overdose causes more serotonergic toxicity as compared to cardiac toxicity. Around 15-20% of patients with escitalopram overdose land up with serotonin syndrome [3]. Escitalopram ingestion causes QRS and QTc widening and also ventricular dysrhythmias [3], [4]. Respiratory involvement is very rare [5] [6].
The direct effects of serotonin on pulmonary epithelial cells/endothelial cells are attributed as the cause of acute lung injury. Although the exact pathogenesis of serotonin syndrome causing ARDS is still unclear [6].
Management depends on the severity of the syndrome and usually involves withdrawal of the serotonergic agent and administering supportive treatment, adequate hydration and antipyretics [1]. Oxygen therapy is vital in the management of patients with ARDS and some patients might also require mechanical ventilator support. [1].

CONCLUSION

This article brings to light a rare pulmonary manifestation of serotonin syndrome. Early recognition of ARDS with proper diagnosis and treatment prevents the worsening of the condition in the first 24 hours. A detailed clinical history and correlation with the clinical findings are indispensable, especially when rare manifestations are presented. Sufficient knowledge of the common serotonergic drugs and interactions is needed as overdose potentiates serotonin syndrome.

CONFLICTS OF INTEREST

There are no conflicts of interests.

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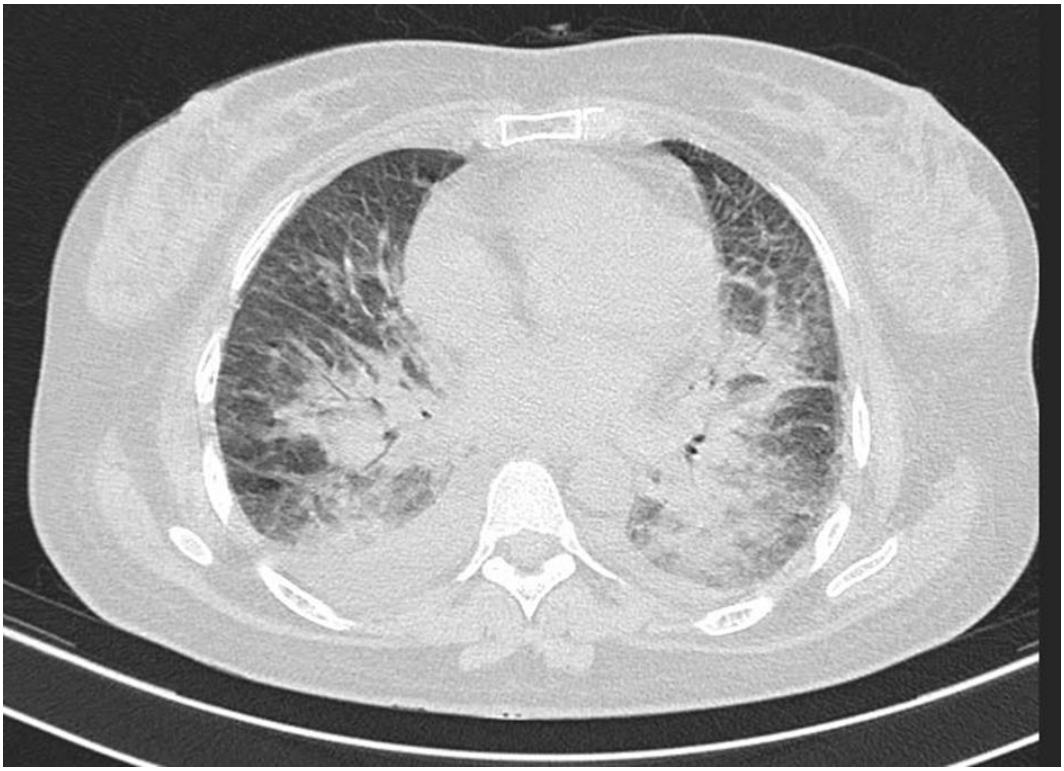

Figure 1: Axial section of HRCT Thorax showing bilateral central peri-bronchovascular Ground glass Opacities (GGO) predominantly in lower lobes with bilateral pleural effusion.

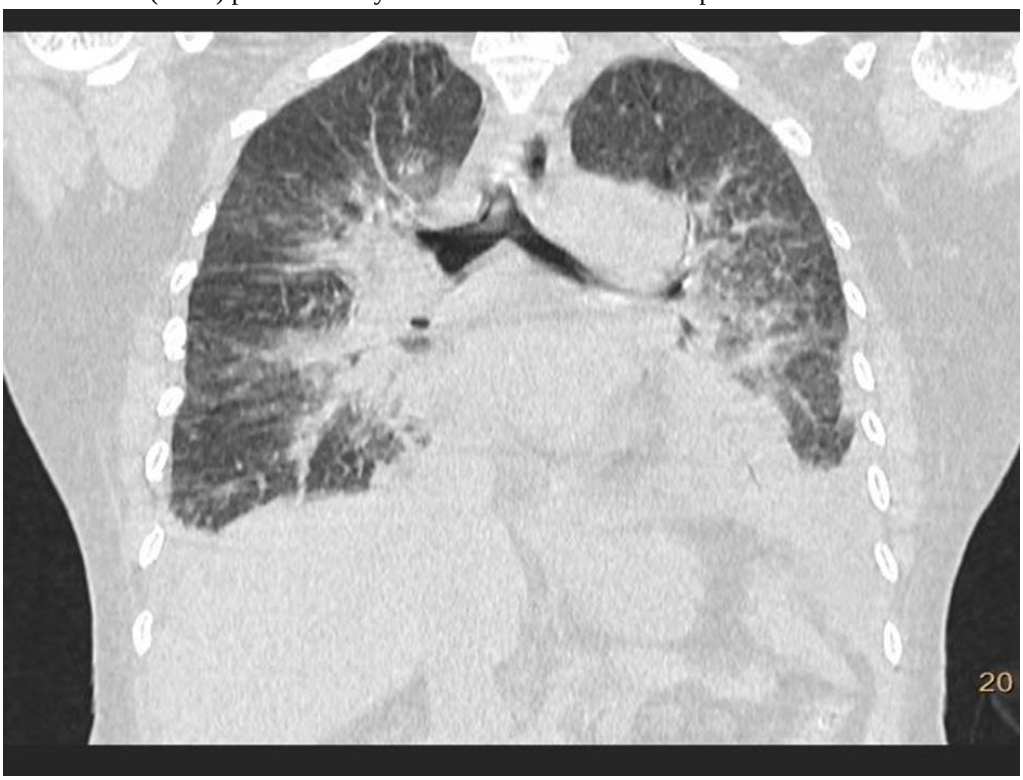

Figure - 2: Coronal section of HRCT Thorax showing diffuse bilateral central peri-bronchovascular Ground glass opacities.