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Case Report

CASE REPORT

Sertraline as a rare cause of interstitial lung disease

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Abstract

Sertraline, a selective serotonin reuptake inhibitor, is commonly prescribed for the treatment of moderate-to-severe depression. We report a case of a 36-year-old male taking sertraline for 7 weeks prior to developing a dry cough, pleuritic chest pain, hypoxia and diffuse ground-glass attenuation with mediastinal lymphadenopathy on imaging. No infectious aetiology was identified and multiple causes of pneumonitis excluded. Sertraline-induced interstitial lung disease was subsequently diagnosed. Sertraline was discontinued and treatment commenced with a weaning course of oral dexamethasone, leading to a rapid reduction in oxygen requirement and successful discharge. Given the increasing prevalence of selective serotonin reuptake inhibitor use, it is vital that medical professionals can recognize sertraline as a rare, albeit potentially life-threatening, cause of interstitial lung disease—allowing for the rapid diagnosis and appropriate management of this condition.

INTRODUCTION

Anti-depressant use has markedly increased over recent years, with NHS prescriptions almost doubling from 36 million in 2008 to 70.9 million in 2018 [1]. Sertraline, first approved for use in 1991, is a selective serotonin reuptake inhibitor—a class of drugs recommended by the National Institute for Health and Care Excellence (NICE) for first line management of moderate-to-severe depression [2].

Interstitial lung disease (ILD) is a term attributed to a group of pulmonary conditions resulting in inflammation and subsequent fibrosis of lung parenchyma. Drug-induced ILD is a widely described phenomenon, with medication such as amiodarone, carbamazepine and nitrofurantoin attributed to disease development [3]. Alternative causes of ILD include idiopathic pulmonary fibrosis (resulting in progressive and irreversible pulmonary scarring) and hypersensitivity pneumonitis (an immune mediated response to inhaled allergens) [4].

Only a few case reports of sertraline-induced ILD exist and in presenting this case, we intend to further demonstrate a potentially life-threatening consequence of this drug in the hope of optimizing patient management.

CASE REPORT

In November 2020, a 36-year-old Caucasian male was admitted to a general adult psychiatric ward for the treatment of severe depression and alcohol misuse. He had not consumed alcohol for 2 weeks prior to admission. He was a non-smoker, denied use of recreational drugs and had no past medical history of note. He had no known drug allergies and took sertraline 100 mg once a day, as prescribed by his local psychiatrist 7 weeks prior to admission. The patient did not take any other medication, over-the-counter or otherwise, aside from occasional paracetamol for analgesia. There was no relevant family history. He was unemployed but had previously worked as a mechanical engineer, denying exposure to pneumotoxic substances—organic or synthetic, and did not own pets. He was independent with activities of daily living and had a body mass index of 28.1 kg/m^2.

On admission, his national early warning score was 0. Blood tests (full blood count, renal function, liver function tests and bone profile) were unremarkable. Polymerase chain reaction (PCR) testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was negative.

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Table 1: Blood results from prior to the patient's medical hospital admission through to post-discharge

	NR	A	B	C	D
Haemoglobin (g/L)	130–180	140	153	139	155
Mean cell volume (fL)	75–105	88	89	89	88
Platelets (10^9/L)	150–450	201	289	306	361
White cell count (10^9/L)	4–11	8.2	**14.1**	**15.7**	**14.3**
Neutrophils (10^9/L)	2–7.5	6	**11.9**	**13.5**	**12.2**
Lymphocytes (10^9/L)	1–4	1	**0.7**	1	1.5
Monocytes (10^9/L)	0.2–0.8	0.7	**1**	0.7	0.6
Eosinophils (10^9/L)	0–0.4	0.4	**0.5**	**0.5**	0
Basophils (10^9/L)	0–0.1	0	0	0	0
BNP (ng/L)	0–97	–	**410**	–	–
Troponin (ng/L)	<14	–	4	–	–
Serum ACE (U/L)	8–52	–	19	–	–

NR, normal range; A, pre-hospital admission; B + C, during hospital admission (6 days apart); D, post-discharge.
Numbers in bold represent values outside of the specified normal range.

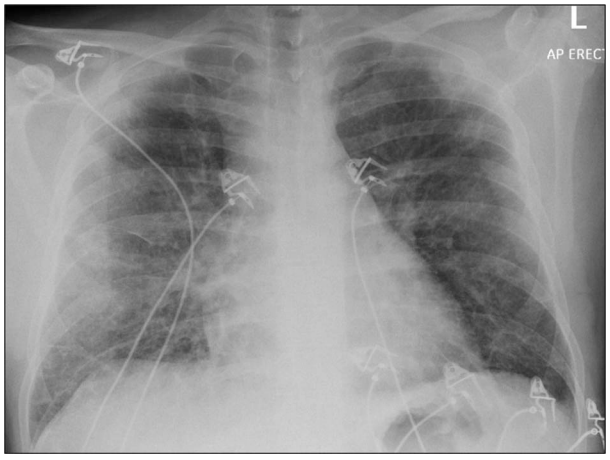

Figure 1: Chest radiograph from day of medical hospital admission showing bilateral widespread air-space opacification—more pronounced on the right, with blunting of the left costophrenic recess.

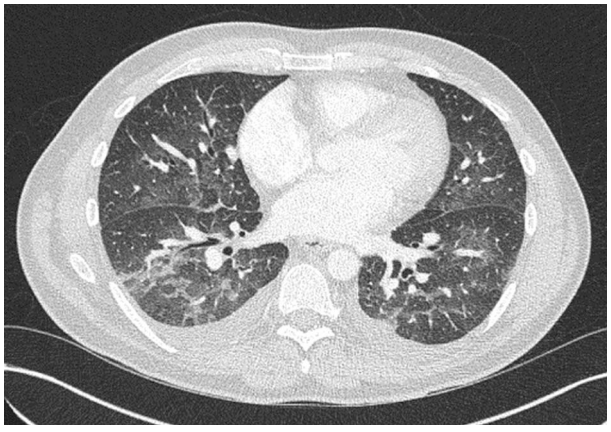

Figure 2: CT-pulmonary angiogram, axial view, demonstrates no pulmonary embolism but diffuse bilateral ground-glass attenuation with thickening of the interlobular septae and small pleural effusions—in addition to mediastinal and hilar lymphadenopathy.

Twelve days into admission, the patient developed a dry cough, dyspnoea and left sided pleuritic chest pain. Physical observations found him to be hypoxic (SpO_2 = 85% on room air, reducing to 76% on mobilizing), tachycardic (106 bpm) and febrile (38.1°C). Respiratory rate and blood pressure were within normal limits. On auscultation, air entry was reduced bilaterally and bibasal crepitations were present. Oxygen therapy was commenced and an urgent transfer made to a medical hospital.

On admission, a chest radiograph was performed (Fig. 1), showing diffuse bilateral air-space opacification. Intravenous antibiotics were commenced to cover for bacterial infection however no clinical improvement was observed over 48 h. The patient was screened for an infectious precipitant—blood cultures, sputum culture, urinary legionella/pneumococcal antigens and respiratory PCR test, including SARS-CoV-2, were negative. Table 1 displays relevant blood results from before, during and after his hospital admission. A viral screen for cytomegalovirus, Epstein–Barr virus, hepatitis B, hepatitis C, human immunodeficiency virus and mycoplasma was negative. Immunological testing for immunoglobulins, antinuclear antibody, avian precipitins and aspergillus precipitins was unremarkable. A computed tomography (CT) pulmonary angiogram was subsequently performed (Fig. 2) and whilst negative for a pulmonary embolism, showed bilateral widespread ground-glass attenuation and mediastinal lymphadenopathy.

The patient did not report specific symptoms of connective tissue disease nor display associated clinical signs. Following discussion with respiratory and psychiatric teams, sertraline-induced ILD was diagnosed. Sertraline was stopped as the risk of discontinuation syndrome was considered less harmful than exposing the patient to further medication as part of a weaning protocol. A reducing regimen of oral dexamethasone was commenced (6 mg daily for 1 week, reduced by 2 mg weekly until stopped) and his oxygen requirement rapidly improved, tolerating a switch to nasal cannuale and then ambient air over the subsequent 2 days. A repeat chest radiograph was performed prior to discharge (Fig. 3) showing near resolution of the pulmonary infiltrates. The patient reported a return to his baseline functioning and was discharged. Respiratory follow-up has been arranged for 3 months' time, to include lung function testing. A yellow card drug reaction safety report was submitted to the Medicines and Healthcare Product Regulatory Agency on 1 December 2020 [5].

DISCUSSION

A few case reports of sertraline-induced ILD exist. One describes a 47-year-old female developing sertraline-induced hypersensitivity pneumonitis, responding rapidly to drug cessation and

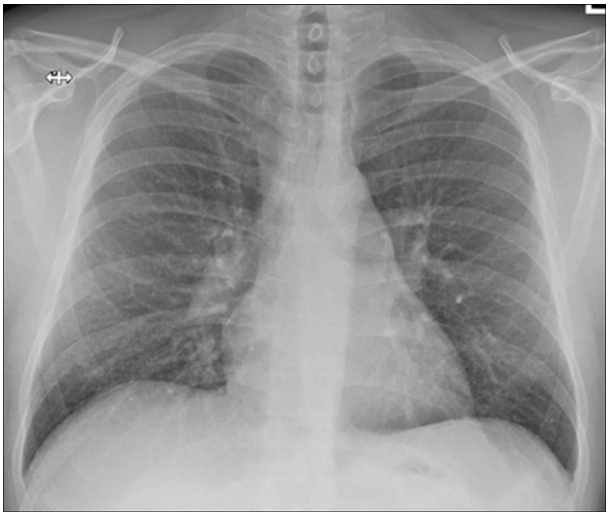

Figure 3: Chest radiograph following discontinuation of sertraline and commencement of oral dexamethasone. Marked reduction in bilateral pulmonary infiltrates compared with admission radiograph visible.

steroid therapy [6]. Another describes a 40-year-old female developing eosinophilic pneumonia just 7 days after commencing sertraline [7]. A further report describes a 33-year-old male developing pulmonary fibrosis 3 years following sertraline initiation [8]. Within these reports, the duration between sertraline initiation and symptom onset varies—with our patient's symptoms starting 2 months following drug initiation. It is possible that prolonged sertraline administration in sensitized individuals results in persistent pulmonary inflammation with increased potential for fibrosis [9].

From our case report, the importance of considering a broad differential diagnosis is evident—with the temporal association of sertraline initiation and symptom onset eventually guiding diagnosis. Various risk factors have been associated with severe drug-induced ILD including increasing age, pre-existing lung disease, male sex and smoking, and these should be considered when assessing patients [9].

In our patient, SARS-CoV-2 infection was the initial top differential as the pandemic's 'second wave' was heightening and the medical history did not elude to a more likely diagnosis. The patient subsequently had three negative SARS-CoV-2 PCR tests and the CT scan findings were not indicative of a SARS-CoV-2 pneumonitis, as discussed with a consultant radiologist. The collateral effects of the SARS-CoV-2 pandemic are gradually emerging, one example being a stark increase in cancer-related mortality from diagnostic delays [10]. It is possible that our patient's diagnosis could have been established earlier if SARS-CoV-2 was not a distractor.

In reporting this case, we hope to improve the recognition of sertraline-induced ILD amongst medical professionals to ensure that affected patients can be diagnosed and appropriately managed in a timely manner.

ACKNOWLEDGEMENTS

I am grateful to staff at Priory Hospital Roehampton and Kingston Hospital for the safe and appropriate management of the patient. Special thanks to Dr S Bishop for assistance with acquiring investigation results.

CONFLICT OF INTEREST STATEMENT

None declared.

ETHICAL APPROVAL

Ethical approval not required.

CONSENT

Informed written consent obtained from patient.

GUARANTOR

Dr Mario Lepore is the guarantor of this case report.

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