Case report

Psychiatric symptoms post intensive care unit admission

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SUMMARY

A 53-year-old woman was admitted to a tertiary intensive care unit (ICU) with acute respiratory distress syndrome secondary to severe community-acquired pneumonia that necessitated maximum supportive care with venovenous extracorporeal membrane oxygenation. Her medical history included bipolar disorder on quetiapine and sertraline, as well as a previous ICU admission, approximately 2 years prior, for non-cirrhotic hyperammonaemic encephalopathy that was complicated by prolonged post discharge anxiety and post-traumatic stress disorder-like symptoms, consistent with post-intensive-care syndrome. Here, we present a case, and explore the outcomes for a patient who had two separate admissions with life-threatening illnesses, but had distinct differences in the psychological outcomes following each illness.

BACKGROUND

Post-intensive-care syndrome (PICS) is an increasingly recognised syndrome that affects intensive care unit (ICU) survivors of critical illness. PICS is defined as new or worsening impairments in the domains of physical, cognitive and/or mental health, that occur following critical illness and continue post-acute care hospitalisation.¹ Psychiatric-related symptoms include anxiety, depression and post-traumatic stress disorder (PTSD),¹ which, if unrecognised, can affect long-term health and health-related quality of life.² We present the unfortunate, yet relatively unique case of a patient who had two critical illnesses, approximately 2 years apart, with a self-reported discrepancy in the psychological outcomes following her two critical illnesses, and discuss factors that may have impacted this.

CASE PRESENTATION

A 53-year-old woman was brought in by ambulance to a tertiary hospital emergency department with a 1 day history of worsening shortness of breath, fever and confusion. This was on the background of a 6 day history of lethargy and coryzal symptoms.

Medical history included type 2 diabetes mellitus on metformin and sitagliptin, bipolar disorder on sertraline 100 mg mane and quetiapine 25 mg mane and 225 mg nocte (i.e. total daily dose of 250 mg) and migraines on amitriptyline 50 mg nocte. She also had an ICU admission approximately 2 years prior, previously reported,³ for non-cirrhotic hyperammonaemic encephalopathy thought to be

due to a combination of a *Klebsiella pneumoniae* urinary tract infection with bacteraemia and sodium valproate therapy.

On presentation, her vital signs included oxygen saturation of 80% on 15 L/min oxygen via non-rebreather mask, respiratory rate 40 breaths/min, blood pressure 150/125 mm Hg, heart rate 140 beats/min (sinus tachycardia) and temperature 40.7°C. The examination was significant for widespread bilateral crackles on auscultation; however, the patient was warm and well-perfused, jugular venous pressure was not elevated, there was no lower limb swelling and her Glasgow Coma Score was 14 (E3, V5, M6).

INVESTIGATIONS

Initial investigations showed type 1 respiratory failure with a mild, normal anion gap metabolic acidosis and mild hyponatraemia (pH 7.28, pCO₂ 42 mm Hg, pO₂ 59 mm Hg, bicarbonate 21 mmol/L, base excess -7 mmol/L, sodium 131 mmol/L, potassium 3.9 mmol/L, chloride 107 mmol/L and lactate 2.3 mmol/L), plus hyperglycaemia (glucose 27 mmol/L). She also had elevated inflammatory markers (white cell count 19.92×10⁹/L with neutrophils 19.32×10⁹/L, and C-reactive protein 490 mg/L) and mildly elevated liver enzymes alanine aminotransferase (ALT) 197 U/L (<35), alkaline phosphatase (ALP) 141 U/L (30–110), gamma-glutamyl transferase (GGT) 75 U/L (<40) but normal renal function (urea 4.9 mmol/L, creatinine 87 μmol/L). Chest X-ray showed bilateral multifocal consolidation consistent with multilobar pneumonia.

TREATMENT

The patient was diagnosed with acute respiratory distress syndrome secondary to severe community acquired pneumonia and required intubation in the emergency department for persistent type 1 respiratory failure. Despite maximal therapy with FiO₂ 1.0, sedation and paralysis, open lung ventilation with airway pressure release ventilation (pressure high 30 cmH₂O, pressure low 0 cmH₂O, time high 6 s, time low 0.8 s), inhaled nitric oxide up to 10 parts per million, bronchoscopy and prone positioning, the patient had refractory hypoxaemia and required bifemoral venovenous extracorporeal membrane oxygenation (VV-ECMO) within 8 hours of presentation. On VV-ECMO, the patient was sedated predominantly with fentanyl, propofol and midazolam, and at times paralysed with vecuronium.

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Broad spectrum antimicrobials consisting of Tazocin (piperacillin/tazobactam), azithromycin, vancomycin and oseltamivir, plus a stat dose of gentamicin, were commenced. On day 2 of admission, the bronchoalveolar lavage (BAL) PCR was positive for both *Legionella pneumophila* DNA and *Rhinovirus* RNA. At this time ciprofloxacin was added. The BAL cultured *L. pneumophila* group 1, and the urinary antigen for *L. pneumophila* serotype 1 was also positive. Of note, influenza PCR was negative.

OUTCOME AND FOLLOW-UP

This patient required VV-ECMO for 14 days, at which time she was successfully decannulated, and required intubation via an endotracheal tube for 20 days and was then extubated. She remained in the ICU for a total of 23 days and was subsequently stepped down to the general high dependency unit for a further 8 days. Following this, the patient spent 3 days in the general respiratory ward before being transferred to an offsite rehabilitation unit.

Despite severe respiratory failure, the patient did not develop multiorgan failure. The patient's 14 days on VV-ECMO were mostly uncomplicated except for some difficulties achieving therapeutic heparinisation due to an acquired antithrombin deficiency that necessitated several doses of antithrombin concentrate, as well as minor oozing at the ECMO cannulation sites. The patient completed 21 days of dual treatment for *L. pneumophila* with azithromycin and ciprofloxacin, and, while on ECMO, was on meropenem and vancomycin for empiric cover for indwelling cannulae. Additionally, the patient had a 4 day course of fluconazole for empiric cover while awaiting cultures due to fevers on broad spectrum antimicrobials. Despite severe type 1 respiratory failure, the patient did not have documented periods of prolonged hypoxaemia, with mean and median PaO₂ 81.5 and 76 mm Hg, respectively, with a range of PaO₂ between 52 and 123 mm Hg between days 1 and 15 of her admission.

While still on ECMO, aware of her previous ICU admission and prolonged post discharge anxiety and post-traumatic stress-disorder-like symptoms, the treating intensive care specialists recommenced her quetiapine at a reduced total daily dose of 125 mg/day (25 mg mane and 100 mg nocte) on day 7 of her admission that was increased to her usual daily dose of 250 mg/day by day 10, and her usual dose of sertraline was recommenced on day 16 of her admission. Following extubation the patient was documented to be orientated to person, but not place or time consistently until the day she was ready for transfer to the rehabilitation unit. The delirium screening tool, the confusion assessment method for the ICU,⁴ was recorded on 3 mornings during her ICU and general high dependency unit admission, and was reported as positive for delirium each time, and for the other days it was either not recorded or documented as not able to be performed due to deep sedation. The patient's predominant complication was critical illness weakness for which she required physical rehabilitation.

On returning home the patient sent an email describing that she felt that her 'state of mind and recovery' were much improved following this critical illness compared with the last, and that she wondered if this was due to her medication for her bipolar disorder being continued during a significant proportion of her admission, unlike during her first admission. Prior to her first critical illness, the patient was on valproate 400 mg two times per day, as well as quetiapine 300 mg/day (50 mg mane and midday and 200 mg nocte) and sertraline 100 mg daily for her bipolar affective disorder. During her first critical illness admission, her valproate was ceased due to her hyperammonaemia;

however her quetiapine was restarted on day 7 of her 10-day admission at a dose of 25 mg nocte and increased to a total daily dose of 100 mg prior to discharge, and her sertraline was restarted on day 9 of her admission at 50 mg/day and she was discharged home on this dose. The main reason that her quetiapine was recommenced at such a low dose was due to her drowsiness rather than hepatic dysfunction.

DISCUSSION

The purpose of this case report is to highlight, through this patient's unfortunate, yet relatively unique experience, that there may be benefits in continuing and/or restarting a patient's usual antipsychotics and antidepressants early on during his/her critical illness. With the aim being to reduce the subsequent development and severity of psychiatric symptoms of PICS and thus enhancing recovery in patients with premorbid psychiatric illness.

This patient had two episodes of life-threatening illness within approximately 2 years of each other. The patient presented to the same hospital and was treated predominantly by the same intensive care specialists each time. Through the patient perspective that she had written as part of the BMJ case report related to her first admission,³ we had unique insight into the issues that she had in recovering from her first critical illness. Based on this, we were able to make the informed and deliberate decision to reinstitute her usual antipsychotics and antidepressants early in her admission to hopefully alleviate some of the psychiatric issues that she had post her first critical illness. The psychiatric symptoms that this patient described following her first intensive care admission would have been consistent with a diagnosis of PICS; however, this was never formally diagnosed, and ICU follow-up clinics are not conducted at our centre. Other diagnostic possibilities could include a prolonged slowly resolving delirium, depressive relapse of her existing bipolar disorder, or acute/traumatic stress disorder. Although all of these conditions could have contributed to PICS with likely overlapping symptoms.

The prevalence of psychiatric-related PICS is not insignificant, and is estimated to affect between 10% and 50% of ICU survivors.⁵ Recognised risk factors of psychiatric complications post critical illness include female gender, younger age, pre-critical illness psychiatric symptoms, lower levels of education¹ and a pessimistic personality trait.⁶ ECMO has also been associated with a higher risk of mental health problems post hospital discharge.⁷ In relation to the development of post-traumatic stress disorder (PTSD) symptoms, there appears to be an association between early memories of frightening ICU experiences and ICU benzodiazepine use.⁸ There however appears to be no association between PTSD symptoms and the severity of illness, ICU length of stay, or the use of mechanical ventilation.⁸ Furthermore, there is evidence to suggest that a more prolonged duration of delirium is associated with greater depression and worse mental health outcomes at 12-month follow-up post critical illness.⁹

Unfortunately, despite the gravity of the issue, there is limited data on the prevention and management of psychiatric-related PICS. However, it is probably undeniable that the type and timing of interventions conducted during a patient's ICU stay will have a significant impact on the development of psychological and cognitive sequelae.¹⁰ Recommended management modalities for psychological and cognitive morbidity currently include early mobilisation and rehabilitation, reduction in sedatives, sleep enhancement, as well as the provision of psychological support

through ICU diaries, ICU follow-up clinics and early counselling.¹⁰ There is also preliminary evidence to suggest that abrupt discontinuation, rather than continuing chronic antidepressants in patients admitted to the ICU, is associated with an increased risk of symptoms consistent with antidepressant discontinuation syndrome such as agitation, delirium, mood changes, insomnia as well as nausea, vomiting, dizziness, paraesthesia and headache, and that the risk of developing these symptoms is higher in women.¹¹ At present there are no studies that have investigated the effects of stopping versus continuing a patient's usual antipsychotics during his/her critical illness.

An important consideration for restarting a patient's usual antidepressant and antipsychotic medications is timing and dose. Critical illness is commonly associated with multiple organ dysfunction syndrome. This organ dysfunction may range from mild and subclinical all the way to profound failure. As a result, it is not uncommon practice to withhold all of a patient's non-essential usual medications when a patient is critically unwell, and to then reintroduce the medications when clinically required and/or once the associated organ dysfunction has improved. The majority of psychiatric medications are metabolised by the liver,¹² and as such these medications are also associated with a risk of hepatotoxicity.¹² It goes without saying that drugs associated with hepatic toxicity should be avoided in liver failure; however, the recommendations are less clear in patients with mild-to-moderate hepatic dysfunction. A reasonable approach is start at a low-medium dose and increase as tolerated.

This patient had a clear subjective difference in the psychological outcomes following her two critical illnesses, and although psychotropic medications were continued during most of her second admission, the impact of this on her psychological state and the difference between the two admissions is not quantifiable. There are also other contributing and potentially confounding factors that need to be considered. Importantly, her first admission involved hyperammonaemic encephalopathy. Ammonia is neurotoxic and this may have contributed to her more severe psychiatric symptoms. Her prolonged delirium after the first admission may have represented a relapse of her bipolar disorder, which may have been clinically indistinguishable from psychiatric-related PICS, and additionally, may have contributed to her slower PICS recovery.⁹ The patient's improved recovery in her second admission may have also been due to higher resilience acquired from her first critical illness. A pilot study by Maley *et al*² looking at resilience in critical illness survivors showed that resilience was normal in 63% and high in 9% of ICU survivors, and that resilience inversely correlated with neuropsychiatric impairment as well as pain and difficulty in self care. A limitation of this case report was that formal cognitive assessments were not performed in either of her admissions, and therefore we are unable to comment on this aspect of PICS for this patient.

In conclusion, PICS is an increasingly recognised entity affecting a significant proportion of ICU survivors, and yet remains poorly understood. More specific and directed preventative and therapeutic methods to reduce the development of PICS and improve recovery of patients affected by this syndrome are required. This case report highlights a gap in the ICU management of critically ill patients on regular psychiatric medications. Thus, while there is no existing research that looks at the specific question of continuation and cessation of patients' usual antipsychotics and antidepressants during critical illness, we encourage clinicians to consider continuing or restarting these medications as soon as appropriate. Lastly, this case emphasises the importance of patient follow-up post critical illness. This process enables patients to reflect on their experiences to assist them

with their healing process, to identify gaps in our knowledge that require further research, and most importantly to be able to individualise patient care if the patient regrettably has another episode of critical illness in the future.

Patient's perspective

Email from the patient to one of the treating intensive care specialists post discharge.

Subject: Thanks Again

Hi...

Apologies for my tardiness, but I just wanted to express my gratitude and appreciation to you, and to everyone involved in my treatment while in ICU this time around. Please convey my heartfelt thanks to all concerned.

I was discharged from hospital on... My physical rehab has been quite good since then, despite a lot of muscle spasms and pain during the night. I am walking almost normally now, but still have a lot of weakness—need to increase my stamina. The most disturbing after effect is that I feel like I am in a 'dream state'. To give you an idea of what I mean, I feel like I could run my car into a brick wall, but nothing would happen—I would be OK because I am not really here. Although I do know better and would never do such a thing, it is still disturbing and quite frightening to be experiencing this all the time I am awake. Even when I am relaxing and watching TV, I still feel 'out of body'. Not to put a label on it, but being so 'detached' I almost feel like I am in a fugue state—hopefully this sensation will soon pass.

FYI, leaving me on my psych meds during my admission made a significant difference to my state of mind and recovery. Everybody who sees me has noticed that I'm handling this little stint far better than during and after my last admission. Some of my friends have even started calling me Lazarus!

Once again, thank you so much for your care and your kindness—I hope you know how much it is appreciated. I really hope NOT to do this again—that is it for me (as far as getting so unwell; I am done)!

Many thanks.

Kindest Regards,

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Learning points

- ▶ Post-intensive-care syndrome is an increasingly recognised syndrome that affects intensive care unit survivors, and is defined as new or worsening impairments in physical, cognitive and/or psychiatric domains.
- ▶ Patients with precritical illness psychiatric symptoms are at increased risk of psychiatric complications following critical illness including anxiety, depression and post-traumatic stress disorder.
- ▶ Clinicians should consider continuing or restarting a patient's usual antipsychotics and/or antidepressants as soon as appropriate during their critical illness.

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