PATIENT SAFETY REVIEW COMMITTEE

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Name of Deceased: Joshua PATEY
Date of Death: June 12, 2012
Age: 25 years
File number: 2012-7219 (PSRC-2013-01)

History:

The decedent was a 25-year-old male with a history of bipolar affective disorder who was also known to be a binge drinker of alcohol. He was brought to the emergency department (ED) of a community hospital (Hospital A) at 0425 hours on June 5, 2012; he had taken an intentional overdose of his medications at approximately 0300 hours after drinking six bottles of beer. He stated at that time that he had done so because, "things were not going well." His stated intent was to commit suicide. He told his care providers that he had taken the following medications:

Present Prescriptions:
Aripiprazole 10 mg tablets x 12
Venlafaxine extended release 150 mg tablets x 12

Old Prescriptions:
Valproic Acid 500 mg tablets x 10
Methotrimeprazine 5 mg tablets x 10

Initial vitals signs were: Pulse 160, BP 175/74, respirations 18, temperature 36.8°C and oxygen saturation 94% on room air. Physical examination was that of a 98 kg male and

was essentially normal with the exception of superficial lacerations to one wrist. Glasgow Coma Score was 15 (normal).

An intravenous was started with normal saline at a rate of 150 ml/hr. Bloods were drawn for routine hematology, biochemistry (including magnesium and calcium), and a venous blood gas. Serum ammonia and serum valproic acid levels were sent out to another hospital. A urine toxicology screen was also sent to a regional hospital lab. The patient was placed on a Form 1 (Application by Physician for Psychiatric Assessment, allowing for involuntary admission for up to 72 hours).

The Ontario Poison Information Centre (OPIC) was contacted for the first time at 0445 (approximately 20 minutes after initial presentation to the ED). Initial advice was given to perform a full toxicology screen and to treat the patient with standard supportive care. OPIC continued to follow the patient closely throughout his hospital stay.

Initial labs were essentially normal, with the exception of an elevated valproic acid (VPA) level of 1094 and an ethanol level of 31. Serum was negative for salicylates and acetaminophen. Urine was negative for all toxins with the exception of cannabis.

Blood testing was repeated at frequent intervals until the VPA level fell below 300.

	5/6 0455	5/6 1105	5/6 1452	5/6 1910	6/6 0800	6/6 1305	6/6 1910	6/6 2300	7/6 0515	7/6 1445	10/6 0305	11/6 1100	12/6 1600
Pt location	ED	ED	ED	ED	ED	ED	Psych	Med/ Tele	ICU	ICU	ICU	ICU	Med/ Tele
WBC	7.3							7.0	8.3		11.0	18.9	24.6
Hgb	154							138	130		126	132	121
platelets	208							180	183		157	199	139
AST	30 (19-48)		30					22	23			120	87
ALT	36 (21-72)		28					22	21			68	56
GGT	(15-73)							56	52			258	
INR	1.0							1.0	1.0			1.1	1.3
NH_3	92 (9-33)	238	279	499	18	100	358		53	78	71	23	71
VPA	1094 (350-700)	>1040	4115	2620	<69	701	661		443	299	L		
Lactate	(0.5-2)		3.1						1.0			4.4	11.1
CK	118 (55-170)								230			1536	1345

At 0700 hours, care of the patient was transferred to the incoming emergency physician. Further blood work was done, including liver function tests and repeat serum valproic acid. A single dose of 100 g activated charcoal was given by mouth.

At 1330 hours, the treating physician called the OPIC again with concern about the rising ammonia and valproate levels. After consultation with the consultant toxicologist, advice was given to treat the patient with L-carnitine IV. However this could not be started until

approximately 1800 hours as it needed to be obtained from another hospital 20 km away.

Over the course of his first 36 hours in hospital, the patient remained in the ED. Vital signs were stable throughout this time and the patient gradually became more lucid. At approximately 1500 hours on June 6, 2012, the patient was reassessed by the internist caring for him and was felt to be medically stable. The IV L-carnitine was discontinued after a total dose of 9 grams had been administered. He was then assessed by a psychiatrist and removed from the Form 1 prior to transfer to the mental health ward at approximately 1800 hours that day.

Soon after arriving on the mental health floor, OPIC contacted the nursing staff and recommended that the patient continue to be closely monitored on telemetry and have VPA and ammonia levels done every six hours until back in the normal range. For this reason, the patient was transferred to a monitored bed and placed under the care of another internist, as the internist who had provided initial care was not available. The L-carnitine infusion was restarted.

Soon after arriving in the telemetry unit, the patient developed a tachycardia of 160 and was hypoxic with an O_2 saturation of 58%. A Code Blue was called. It was noted that his O_2 saturation improved quickly with airway positioning. He was immediately transferred to the ICU where he was extremely agitated, requiring eight people to restrain him. It was decided to intubate him using propofol and succinylcholine. Despite a propofol infusion at 3 mg/kg/hr, his agitation proved difficult to control in the ICU so he was also started on an infusion of midazolam at 3 mg/hr. Other ICU care was rendered as appropriate. This included heparin 5,000 u SC given every 12 hours.

In order to rule out a structural intracranial cause for his agitation, a CT head was performed early on June 7, 2012; the results were normal.

The patient's vital signs stabilized. On June 8, 2012, he was noted to be febrile to 38.4° C. Intravenous ceftriaxone and metronidazole were started for presumed aspiration pneumonia; however, his chest x-ray remained clear. On the morning of June 9, 2012, he was noted to be more restless and demonstrated mild hypoxemia necessitating an increase in the FiO_2 to 0.55 and an increase in sedation.

By June 10, 2012, his serum levels of ammonia and valproate levels had returned to relatively normal levels. After weaning his sedation throughout the day of June 10, he was extubated on the morning of June 11, 2012. Shortly thereafter, he had a brief episode of unresponsiveness, hypoxia and tachycardia that was felt to be related to residual sedation; he was given flumazenil 0.1 mg IV and he appeared to become more alert after this. An ECG taken at that time showed an $S_1Q_3T_3$ pattern that had not previously been present on his ECG. The patient remained in the ICU for observation for another 24 hours after this episode and was transferred to a telemetry bed the following day.

At the time of transfer out of the ICU to a medical telemetry bed, the patient remained febrile and tachycardic at 120. He was also noted to be hallucinating and appeared paranoid. Olanzapine 10 mg po TID [by mouth, three times daily], was initiated.

At approximately 1555 hours on June 12, 2012, the patient once again became more tachycardic (160), diaphoretic and cyanotic. His pulse was lost and he became unresponsive. CPR and a full resuscitation ensued, however the initial supraventricular tachycardia and pulseless electrical activity deteriorated to asystole and he could not be resuscitated.

Post Mortem:

Cause of death was reported to be bilateral pulmonary emboli secondary to a right popliteal vein thrombosis.

Discussion:

1. *Could part of this patient's clinical course have been related to alcohol withdrawal?*

   It is difficult to comment definitively without knowing more about the patient's prior alcohol use history, such as frequency used, amount, time of last drink, etc. Of note, the patient had none of the typical markers of chronic alcoholism (i.e. macrocytic anemia; thrombocytopenia; elevation of liver enzymes).

   While it is certainly conceivable that some aspects of his clinical condition (in particular, tachycardia, fever, confusion/agitation) could have represented an alcohol withdrawal syndrome, there are a number of other possibilities to explain this as well. There does not appear to be any formal documentation of objective measures of alcohol withdrawal (such as the CIWA score), and it is not clear whether this possibility was actively considered by the care team.

   Even if his agitation 44 hours after admission to hospital was on the basis of ethanol withdrawal, one could argue that he was at least partially treated for this with IV sedation including benzodiazepines - the treatment of choice for alcohol withdrawal. The amount given for sedation may have been insufficient to effectively treat symptoms and signs of alcohol withdrawal, if this indeed was present.

2. *Was the discontinuation of L-carnitine therapy on June 6, 2012 premature?*
   The patient appeared clinically stable at that time, although the ammonia level (i.e. 358) had risen from a level of 100 over the preceding six hours since the

discontinuation of the L-carnitine infusion. It is unclear if the rising ammonia level that evening resulted in his severe agitation that necessitated his intubation in the early hours of June 7, 2012. Unfortunately, there is no ammonia level in the chart between 1910 hours on June 6 (i.e. 358) and 0515 on June 7 (i.e 53) that might have helped to determine if the L-carnitine was a significant factor.

3. *Was it necessary to keep the patient sedated in the ICU for a little more than four days?*
   It would appear from ICU nursing notes that attempts were made to keep the propofol and midazolam infusions to a minimum, in concert with orders written by the attending physician. It is very difficult to determine from the chart whether or not an earlier extubation and hence patient mobilization might have been possible.

4. *Was prophylaxis for venous thromboembolism (VTE) appropriate?*
   Standard therapy for VTE prophylaxis includes heparin 5,000 u S/C Q12H [subcutaneous every 12 hours] as one option. This is the dose that this patient received. It may have been prudent for this prophylaxis to be initiated in the ED, if indeed he were immobile at that time.

5. *Was timing of discharge from the ICU appropriate?*
   The episode of hypoxia and tachycardia shortly after extubation on June 11, 2012 was thought to have been related to hypoventilation as a result of residual sedation. With hindsight, this may have been the result of a significant but non-fatal pulmonary embolus, and the response to flumazenil coincidental.

Recommendations:

To Hospital A, the Ontario Hospital Association, and the Ontario Medical Association:

1. Venous thromboembolism (VTE) prophylaxis should be initiated as soon as possible after presentation to hospital for any patient in whom it is indicated.

2. Greater consideration be given to the possibility that sudden and unexplained hypoxia and tachycardia could be the result of a pulmonary embolus in any patient who has been immobilized for a period of time, even if conventional anticoagulant therapy to prevent venous thromboembolic disease has been part of the treatment regimen.

3. Hospitals should review the antidotes they stock on a regular basis, and at least annually. If a given antidote is not stocked by a hospital, a plan should be in place and readily available to staff in order to ensure that this antidote can be obtained rapidly from another institution or source, on a 24/7 basis.

4. Alcohol withdrawal should be considered in any patient admitted to hospital within the last five days who demonstrates signs or symptoms such as tachycardia, hypertension, tremor or confusion / disorientation / hallucinations. If alcohol withdrawal is suspected, this should be assessed and managed using accepted protocols, such as the CIWA-Ar score and symptom-triggered therapy with benzodiazepines.