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BRIEF REPORT

Severe Rhabdomyolysis Associated With RSV

James Bender,[1] Rusheng Chew,[2] Belinda Bin Lin,[2] and Eugene Athan[3]

[1]Junior Medical Workforce, Barwon Health, Geelong, Australia; [2]Department of Infectious Diseases, Barwon Health, Geelong, Australia; [3]Department of Infectious Diseases, Barwon Health, Deakin University, Geelong, Australia

Severe rhabdomyolysis is associated with morbidity and mortality. We report on a previously well male who developed severe rhabdomyolysis, sepsis, and multi-organ failure. The patient made a complete recovery. Extensive microbiological testing was only positive for RSV, making this the first reported case of adult RSV-related rhabdomyolysis in the literature.

Keywords. acute kidney injury; respiratory syncytial virus; rhabdomyolysis; RSV.

CASE SUMMARY

A 42-year-old male presented to the University Hospital Geelong, Victoria, Australia, with a 2-day history of generalized myalgia, dyspnoea, cough, headache, chills, and fever. He was a well and active individual with no significant past medical history. He was a smoker, consuming 20 cigarettes per day on a background of at least 10 years of variable smoking intensity, but consumed minimal alcohol. He had a BMI of 33 kg/m^2, putting him in the obese range. Using BMI as a marker of adiposity in this patient was limited by his large muscle mass, and adiposity was not deemed to be a significant risk factor. His wife and children had been unwell in the week prior to his presentation, with upper respiratory tract symptoms, but they had all recovered. Further questioning revealed significant exposure to animal excretions in the course of his work as a carpet layer. He was a keen fisherman who ate his catch and regularly hunted rabbits and foxes.

On admission, his respiratory status rapidly deteriorated, with increasing work of breathing and oxygen requirements. Within 24 hours, he was admitted to the intensive care unit (ICU). In the ICU, his initial observations showed a blood pressure of 210/130 mmHg, which rapidly deteriorated to a systolic blood pressure of 90 mmHg, heart rate of 110, oxygen saturation of 88% breathing air, and respiratory rate of 30 breaths/minute. He was mechanically ventilated on an inspired oxygen fraction of 100% and required significant vasopressor support. He became anuric within 24 hours and required hemofiltration. His initial chest radiograph was suggestive of viral pneumonitis.

Initial blood tests showed a significant leukocytosis with a white cell count of 33.0 × 10^9/L (4.0–11.0 × 10^9/L) and predominant neutrophilia. He was also thrombocytopenic with a platelet count of 95 × 10^9/L (150–500 10^9/L). His C-reactive protein (CRP) was elevated to 55 mg/L (<2.9), lactate to 8.2 mmol/L (<2), and he had a severe metabolic acidosis with pH 7.11. His alanine aminotransferase (ALT) peaked at 4351 U/L, and aspartate aminotransferase (AST) at 9209 U/L on day 3 of admission. His creatine kinase (CK) levels were markedly raised, with initial testing showing levels of 26 302 U/L (39–308 U/L). His CK increased dramatically in the following days, peaking at 330 110 U/L on day 4. This CK level combined with the presence of myoglobinuria in the ultrafiltrate bags indicated extreme rhabdomyolysis. Blood and urine cultures, and urine antigen for *Legionella pneumophila* type 1 and *Streptococcus pneumoniae,* were negative.

Initial management was supportive, with broad spectrum antibiotic coverage of azithromycin and ceftriaxone being commenced empirically on the day of presentation. The initial working diagnosis was severe community-acquired pneumonia, with viral pneumonitis considered a differential. This initial treatment was broadened when he failed to improve, to include courses of ciprofloxacin, meropenem, vancomycin, clindamycin, and oseltamivir.

An extensive workup was performed, including acute and convalescent serology for Epstein-Barr virus (EBV), cytomegalovirus (CMV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), hepatitis B and C, adenovirus, Ross-River virus (RRV), influenza, *Chlamydia pneumoniae*, Q-fever, *Legionella, Brucella, Mycoplasma,* and *Leptospira* species. These were all negative. Screening IgM for *Leptospira species* was positive; however, this was not confirmed in both acute and convalescent samples by microscopic agglutination for the 9 strains tested in Victoria, and therefore was regarded as a false-positive result. Serum polymerase chain reaction (PCR) for HSV and CMV were also negative. Cultures from blood, bone marrow aspirate, sputum, and urine were negative for pathogens. Sputum multiplex PCR was negative for *Legionella* spp, *Mycoplasma* spp, Chlamydiaeceae, *Bordetella pertussis,* and *B. parapertussis*. A naso-pharyngeal swab for respiratory viral PCR detected RSV, but was negative for influenza. A computed

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Correspondence: E. Athan, Department of Infectious Diseases, University Hospital Geelong, Barwon Health, PO Box 281, Bellarine Street, Geelong, Victoria, Australia, 3220 (eugene@barwonhealth.org.au).

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tomography (CT) scan was completed on his abdomen and pelvis, which showed liver congestion and widespread muscle edema (Figure 1). Due to the muscle edema and extensive CK rise, a muscle biopsy was completed, which showed no microscopic abnormality and was nondiagnostic. PCR for influenza, parainfluenza, rhinovirus, adenovirus, metapneumovirus, RSV, enterovirus, parechovirus, EBV, CMV, varicella-zoster virus, and HSV done on the tissue biopsy specimen was negative.

He required 15 days in the ICU, during 9 of which he was sedated and required mechanical ventilation. Due to shock, he received high-dose inotropic support, and he required hemofiltration due to acute kidney injury, anuria, and a profound metabolic acidosis. Antibiotics were ceased on day 16.

After discharge from the ICU, he required extensive inpatient rehabilitation with ongoing hemodialysis. He made a good recovery and was discharged home after 14 days of inpatient rehabilitation, ceasing dialysis shortly after discharge.

DISCUSSION

Rhabdomyolysis is a clinical syndrome characterized by muscle necrosis and the release of muscle constituents into circulation. The traditional characteristics of rhabdomyolysis include myalgia and weakness, and are often associated with dark urine that results from myoglobin excretion [1]. Rhabdomyolysis ranges in severity from asymptomatic to life threatening, and complications such as acute kidney injury are more likely to occur with higher CK levels and associated sepsis and acidosis [2, 3]. While the mortality of rhabdomyolysis is variably reported in the literature, it is accepted that mortality is greater if rhabdomyolysis is associated with acute kidney injury [4], and it has been reported as high as 59% in those with acute kidney injury requiring ICU admission [3].

The etiology of rhabdomyolysis is variable and includes infection, trauma, toxins, extreme exertion, prolonged immobilization, drugs and medications, and metabolic diseases [5]. We hypothesized infection to be the most likely cause of our patient's rhabdomyolysis, as his presentation was suggestive of a respiratory viral infection and his family had recently been unwell with upper respiratory tract symptoms. Toxins were considered a differential, with many toxins including snake, spider, and bee venom, as well as carbon monoxide, being associated with rhabdomyolysis [5, 6]. A rarer cause of rhabdomyolysis is that induced by an unidentified toxin associated with fish digestion, known as Haff disease [7]. While our patient regularly eats his own catch, his family had not become ill despite eating the same fish. The other causes of toxin-related rhabdomyolysis were excluded after taking a thorough history, which failed to identify exposure to other toxins.

Infectious causes can be bacterial, viral, parasitic, or fungal in origin. The most common bacterial pathogens identified in the literature are *Legionella* spp, followed by *Francisella* and *Streptococcal* spp [8, 9]. Singh and Scheld documented creatine kinase levels associated with infection from different pathogens [8]. The only bacterial pathogens to cause levels greater than 300 000 U/L, similar to our patient, were *Legionella*, *Francisella, Brucella,* and *Leptospira* spp [8]. Leptospirosis was a differential diagnosis in our patient due to his recent exposure to animal urine combined with an increase in leptospirosis notifications in Victoria in 2016 [10]. This diagnosis was excluded on serological testing.

Viral causes of rhabdomyolysis are more common than bacterial [9]. Influenza is the most common viral pathogen, followed by HIV and coxsackie virus [8, 9]. Viral causes of rhabdomyolysis also appear to correlate with higher creatine kinase levels (>300 000 U/L) [8]. Our patient received extensive viral testing, and only returned a positive result for RSV.

There have been only 2 documented cases of RSV-induced rhabdomyolysis, both in pediatric patients. The first case was in a 2-year-old previously healthy boy who had RSV diagnosed by enzyme-linked immunosorbent assay in a nasopharyngeal

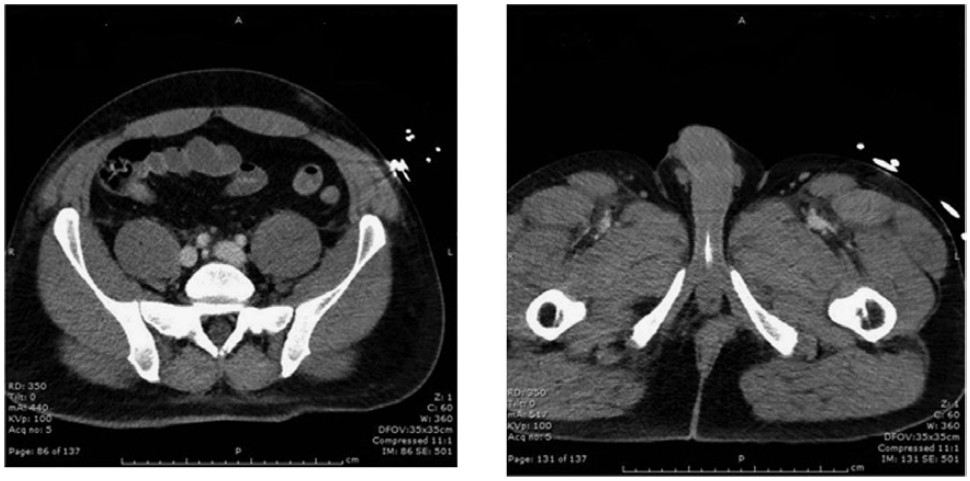

Figure 1. Increased psoas muscle size at time of raised creatinine suggestive of edema, and edematous lower limb muscle with inflammatory stranding.

sample [11]. The patient was referred to the hospital after 10 days of nonspecific symptoms including diarrhea, sore throat, fever, generalized myalgia, and weakness. Investigations showed significant CK elevation (55 000 U/L) as well as liver dysfunction with ALT elevation to 1198 U/L (10–60 U/L) and AST to 4065 U/L (10–55 U/L). While these are nonspecific findings, this case has a number of similarities to our patient, whose ALT peaked at 4351 U/L and AST at 9209 U/L 3 days after admission, and who also presented with fever, myalgia, weakness, and respiratory symptoms. The second case is documented in a German report of RSV rhabdomyolysis in a 4-month-old child [12]. This case also had similarities to ours, in that the child suffered acute renal failure and hepatic dysfunction.

Our case is significant as it is the first documented case of severe rhabdomyolysis associated with RSV infection in an adult. RSV is often a self-limiting disease in adults, and is more commonly known for causing severe illness in infants. Despite this, our patient's history of respiratory symptoms, a recent viral respiratory infection in his family, a lack of any other clear diagnosis, and only testing positive for RSV among a battery of investigations suggest that this is the first documented case of RSV-associated rhabdomyolysis in an adult patient.

CONCLUSION

We have reported on a severe case of RSV-associated rhabdomyolysis in a previously healthy 42-year-old male. It is the first documented case of severe rhabdomyolysis related to RSV in an adult patient, and only the third case in a patient of any age that can be found in the literature. While a rare cause of rhabdomyolysis, RSV should be considered a possible etiological agent in a patient with rhabdomyolysis and symptoms of respiratory tract infection.

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