CASE REPORT OPEN ACCESS

# Super Refractory Status Epilepticus Secondary to Salmonellosis: A Case Report

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The term super-refractory status epilepticus (SRSE) refers to status epilepticus (SE) that lasts for 24 hours or longer after the administration of anesthetic agents, including situations in which the status epilepticus recurs after the anesthetic agent is reduced or removed. Status epilepticus is most frequently brought on by acute brain damage or insult. It can also occur as a primary idiopathic disorder in patients without an established epilepsy diagnosis and refer to as new-onset refractory status epilepticus (NORSE). The etiology of SRSE is multifaceted, and the majority of the time, after rigorous investigations, the root cause is discovered within 24-72 hours. The etiology can be attributed to autoimmune, paraneoplastic, and infectious origins in more than 50% of cases. In the example presented here, non-typhoidal salmonellosis led to the development of SRSE in a 22-year-old female patient, and the infection was resistant to a variety of broad-spectrum antibiotics. The patient was given numerous anti-epileptic medications (AED), anesthetic drugs, and then culture-specific antibiotics. These treatments eventually stopped the seizures, which momentarily resulted in great clinical improvement.

***Keywords:*** Super refractory status epilepticus; new onset refractory status epilepticus; anti-epileptic drugs

## INTRODUCTION

Status epilepticus (SE) is a convulsive state that lasts more than 5 minutes or two or more seizures without returning to the neurological baseline [1]. It is classed as early, established, refractory, and super refractory. RSE is a persistent seizure despite two antiepileptic drugs (AEDs), including a benzodiazepine [2]. Data suggest that 31% to 35% of epilepsy episodes are refractory [3,4]. Super status epilepticus (SRSE) is a state lasting 24 h or longer after anesthetic drug administration, including situations in which seizure recurs on reduction, withdrawal, or tapering [5]. About 15% of SE patients become SRSE [1]. It typically, but not solely, occurs in two situations: 1) Patients with serious brain injuries and 2) patients with no previous epilepsy history in whom SE develops without any overt cause [6]. Status epilepticus has multiple causes, including metabolic abnormalities and sepsis [table 1]. Energy failure, excitotoxicity, inhibitory neurotransmitter malfunction, network reconfiguration, and inflammation are some postulated cases of SRSE [5]. Controlling seizures and preventing damage are therapy goals [5]. SRSE therapy goals include control of seizure and their recurrence, cause treatment, and systemic consequence prevention. Neuro-intensive facilities are best for its treatment [7]. Anesthetic drugs (midazolam, thiopentone, propofol, ketamine as well as inhalation anesthetic agents), newer antiepileptic drugs, magnesium, immunotherapy, pyridoxine, ketogenic diet, neuromodulation, hypothermia, and surgery are used to manage seizures. Herein, we present a case of SRSE which developed secondary to non-typhoidal salmonellosis and the organism was resistant to a wide range of broad-spectrum antibiotics.

## CASE REPORT

### Case Presentation

A 22-year-old woman with no notable medical history presented to the ER with five days of high fever (>102°F) and 30 hours of continuous convulsions. She was treated for status epilepticus with intravenous dextrose-0.9% saline, IV diazepam (10mg IV every 10 minutes), IV acyclovir (10 mg/Kg every eight hours), IM artemether (3.2 mg/Kg), and IV sulbactam and cefoperazone (0.08

g/Kg each). Initial therapy failed. A head CT scan revealed no gross anatomical defect, bleeding, or space-occupying lesion and was confirmed by an MRI of the brain ruling out any abnormalities. EEG suggested encephalopathy without epileptiform discharges. CSF analysis from a lumbar puncture was normal. Patient was intubated upon arrival to ICU and mechanical ventilation were started. Continuous fits anD low GCS (6/15, E1V1M4). On exam, she showed fever (>102°F), BP (100/70 mm Hg), HR (>100 beat/min), RR (16/min), coarse crepitations in right basal lung areas, and mute plantar reflexes bilaterally. Daily laboratory studies included CBC with differential, serum electrolytes, blood glucose, renal function tests, liver function tests, PT/aPTT/INR, CRP, HbsAg, and HCV and HIV antibodies. CRP started at 70 mg/dl and rose to 340 one week later. Routine urine examination and culture were negative. HSV 1, HSV 2, and COVID-19 screenings were negative. AFB and gram stains, ANA, and other autoimmune antibody profiles were negative. Blood culture showed high development of salmonella susceptible to gentamicin and tigecycline. She was given IV Tigecycline (100mg IV loading dose followed by 50 mg every 12 hrs), gentamicin (4mg/Kg/day q 8 hrs), propofol (40 mg), topiramate (50 mg per day), oral phenytoin (15 mg per Kg), IV valproic acid (10 mg per kg q 12 hrs), and IV midazolam (0.4 mg per Kg per hour). Treatment stabilized her seizures. The airway was secured with endotracheal intubation and mechanical ventilation. Her electrolytes were checked and any abnormalities were treated. Her low serum phosphate was corrected. Magnesium sulfate was also provided (for control of seizures with a dose of 3 mg IV loading dose followed by 1 mg hourly). On day 6 of hospitalization, she developed Malena, which resolved after heparin was stopped. She was advised to wear TED stockings to prevent deep venous clot formation. A clinical exam and CXR results showed her left lung collapsed on day 7. Portable bronchoscopy dislodged mucus additionally, resulting in lung expansion. The patient was recovering well until day 10 of admission when she developed right-sided ventilator-associated pneumonia (VAP). Her temperature (>102°F) and seizures returned. Tracheal aspirate showed pseudomonas and Citrobacter growth, which was handled per culture and sensitivity report. On day 15, the patient became hypotensive and needed intermittent norepinephrine infusions. On day 20, her brainstem, papillary, conjunctival, and corneal reflexes disappeared. Cough and gag reflexes remained. A repeat CT showed no herniation or bleeding. 21-day EEG indicated epileptiform discharges without lateralization.

## Diagnostic Evaluation

Initial laboratory tests revealed:

**Table 1. Results of the laboratory investigations**

| Parameters | Day of admission | Day 7 | Day 14 | Day 21 |
|---|---|---|---|---|
| **WBC (× $10^3$/µL)** | 9.6 | 9.8 | 30.7 | 30.9 |
| **Hemoglobin (g/dl)** | 9.2 | 7.8 | 8.5 | 7.3 |
| **Platelets (× $10^3$/µL)** | 332 | 304 | 173 | 276 |
| **Random blood glucose (mg/dl)** | 133 | 105 | 227 | 253 |
| **CRP (mg/L)** | 70 | 297 | 387 | |
| **Na (mmol/L)** | 137 | 142 | 140 | 148 |
| **K (mmol/L)** | 3.1 | 3.25 | 3.7 | 4.13 |
| **Cl (mmol/L)** | 110 | 102 | 111 | 105 |
| **Mg (mg/dl)** | 2.14 | 1.78 | | 1.77 |
| **PO4 (m**mol/L) | | 1.1 | | |
| **Ca (mg/dl)** | 7.2 | 7.9 | 7.22 | 7.08 |
| **ALT (U/L)** | 77 | 33 | 11 | 19 |
| **AST (U/L)** | 50 | 73 | 101 | 76 |
| **Bilirubin (mg/dl)** | 0.5 | 0.56 | 0.72 | 1.08 |
| **Urea (mg/dl)** | 52 | 21 | 69 | 132 |
| **Creatinine (mg/dl)** | 0.85 | 0.41 | 1.58 | 1.77 |

## DISCUSSION

RSE and SRSE are uncommon diseases with significant clinical implications. About 15% of SE develops into SRSE [1]. From a neurointensive center in China, Jayalakshmi S et al. concluded that there was a 16.9% incidence of SRSE [8] and that among 98 patients, there were percentages of 20.4%, 12.2%, and 67.3% of RSE, SRSE, and NORSE, respectively. According to other studies, 12 to 43% of cases end up being refractory [4,10-11]. In a group of 35 patients, Holtkamp M et al. concluded that 20% of the cases recurred on drug tapering within five days, and other studies indicate that 50% of the refractory cases requiring anesthesia become super refractory [10]. According to Cuero, M.R. et al 10 to 15 percent of SE admitted cases, are predicted to become super refractory any time 10 to 15 percent of SE admitted cases, are predicted to become super refractory at any time

Nontyphoidal Salmonella was the cause of SRSE in our study. According to Tian L et al., 67.7% of SRSE cases were caused by encephalitis [9]. According to Vyas DD et al. estimated autoimmune encephalitis verus viral encephalitis as a cause of SRSE [1]. According to Arayakarnkul P et al., immune-mediated encephalitis and epilepsy were the causes of SRSE in 29.4% of cases and 29.4% of cases, respectively [13].

According to Vyas DD et al. estimated autoimmune encephalitis versus viral encephalitis as a cause of SRSE[1]. According to Arayakarnkul P et al., each of the immune-mediated encephalitis and epilepsy was the causes of SRSE in 29.4% [13].

The outcome of SRSE is unpredictable [14]. In our study, the patient passed away on day 21. According to studies, the mortality rate from SE varies between 7 and 39 percent in the first 30 days [10]. The mortality due to SRSE was around 50% compared to the 7% mortality of general SE according to 9. Tian L et al. [9]

## CONCLUSION

SRSE is an uncommon yet clinically significant disorder. A significant etiological factor is infectious causes. Although viral encephalitis cases are often reported, non-typhoidal salmonella

cases are rarely reported. Therefore, if common cases do not serve as the basis for diagnosis, patients with SRSE should have extensive workup done to rule out unusual causes.

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