# An Unusual Cause of Super-Refractory Status Epilepticus

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## Introduction

- Super-refractory status epilepticus (SRSE) is a neurological emergency defined as persistent seizure activity that lasts for 24 hours or more after the administration of continuous general anesthesia or recurring with the withdrawal of anesthetics [1].
- Common etiologies in children can include CNS infections (meningitis, HIV), traumatic brain injury, CNS malignancies, epilepsy, hypoxic-ischemic encephalopathy, and congenital metabolic syndromes [2].
- Autoimmunity is a less common cause for SRSE. About 2-3% cases of status epilepticus can be attributed to an an autoimmune etiology, and these patients tend to be more refractory to anti-epileptic drug (AED) therapy [3-4].
- We present a unique case of SRSE as the inaugural manifestation of primary Sjogren's syndrome.

## Case Presentation

- A previously healthy 15 year old female presented to the pediatric intensive care unit after being found at home with tactile fever, altered mental status, and urinary incontinence. Her clinical condition progressed to super-refractory status epilepticus while in the ICU.
- Diagnostic evaluation showed a CSF analysis with a normal WBC count with lymphocyte predominance. Her CSF, blood, respiratory, and urine cultures were negative. Repeat head CT showed multiple calcific foci of her right parotid gland (Figure 1). The patient's cardiolipin and anti-Ro/SSA antibodies were positive in the serum. Salivary gland biopsy confirmed her diagnosis with evidence of lymphocytosis and focal atrophy on pathology (Figures 2 & 3).
- Extensive workup demonstrated that the patient's refractory seizures and encephalitis were secondary to a new diagnosis of Sjogren's syndrome. Despite multiple attempts at weaning the pentobarbital, the patient continued to have seizure activity in the left temporal and frontal lobes on continuous EEG monitoring.
- After 5 weeks in a pentobarbital coma, 2 doses of IVIG, pulse dose methylprednisolone therapy, and 5 cycles of plasmapheresis, the patient was successfully weaned off pentobarbital.
- Prior to discharge, the patient was able to follow commands but had significant lower extremity weakness requiring inpatient physical therapy. She was discharged on Azathioprine and Hydroxychloroquine for management of her autoimmune disease.
- 6 months after discharge, she experiences some deficits in short and long-term memory and mild cognitive impairment. She regained lower extremity strength and ambulates with mild difficulties coordinating her steps. She was seen in the ED once for breakthrough seizures after running out of AED medications, but quickly improved and required no hospitalization. Her seizures are now well-controlled with Levetiracetam, Lacosamide, and Clobazam.

## Acknowledgements

- Dr. Robert Propst for providing the pathology report and figures for this case.
- Divisions of Pediatric Critical Care & Rheumatology.

## Discussion

- Primary Sjogren's syndrome (pSS) is an autoimmune disorder characterized by the destruction of salivary and lacrimal glands along with a hyperactive humoral response leading to the production of several autoantibodies [5].
- The injury to affected organs leads to the hallmark symptoms of dry mouth known as xerostomia, and dry eyes, or xeropthalmia. These symptoms might not present in children, due to better saliva and tear reserve. They most commonly present with fever, fatigue, and/or lymphadenopathy [6].
- 53,000 to 248,000 adult patients diagnosed with pSS currently living in the United States (2.2 to 10.3 per 10,000 inhabitants), with the female to male ratio is 6-7:1 [7-8].
- 47% - 53% of patients may have neurologic involvement as the presenting symptom of pSS with peripheral neuropathy being the most common [9]. CNS involvement occurs in 2% - 25% of patients. Seizures can be the primary manifestation of 3% - 10% of childhood-onset pSS cases [10].
- Children with autoimmune diseases had a 5-fold increased risk of epilepsy compared with normal children [10]. While the mechanism is not fully understood, it is thought to be due to excessive autoantibody production, systemic release of inflammatory chemokines, and injury to cerebral tissue and vasculature [11].
- There are no studies that identify pSS autoantibodies as a trigger for increased seizure activity. There are reports of SLE patients with elevated anticardiolipin autoantibody titers having higher epilepsy activity [12]. There are also reported cases of refractory SE in patients with elevated anti-Ro/SSA with no history or diagnosis pSS [13].
- The treatment for SRSE involves placing the patient in a pharmacological-induced coma. Plasmapheresis therapy that involves the removal of circulating autoantibodies and immune factors that may promote inflammatory processes [14]. In our patient, plasmapheresis was used in conjunction with immunotherapy (IVIG and glucocorticosteroids) to achieve better seizure control. The typical plasmapheresis therapy course is of five consecutive daily treatments. Studies report including plasmapheresis in the treatment regimen of autoimmune-induced SRSE and can reduce seizure activity by up to 51.9% of cases [15].

## Figures

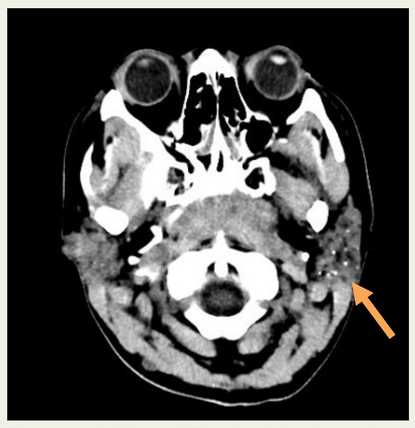

**Figure 1** Head CT with Multiple tiny parotid calcific foci, suggestive of juvenile Sjogren syndrome.

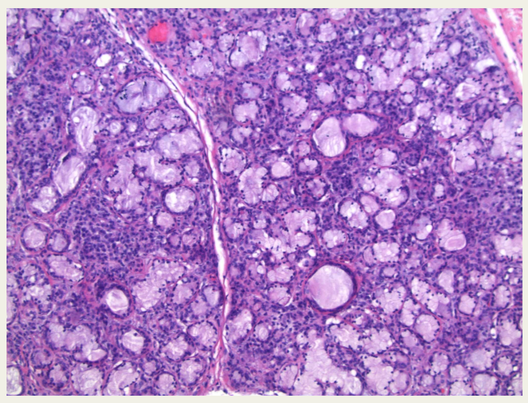

**Figure 2** (H&E stain, 4x magnification) shows a low-power view of minor salivary glands in a background of chronic inflammation and lymphoid aggregates.

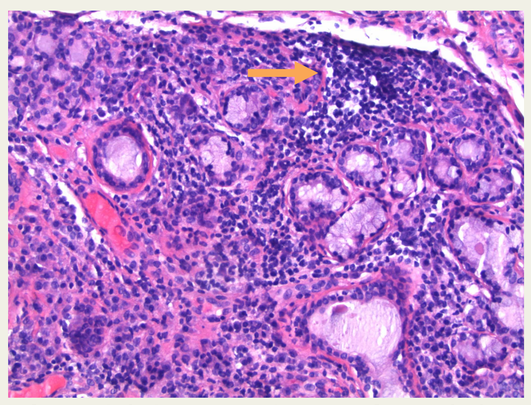

**Figure 3** (H&E stain, 10x magnification) shows a high-power view of atrophic minor salivary glands. The gland atrophy being present with the chronic inflammation suggests a chronic process rather than an acute process. The chronic inflammatory infiltrate consists of lymphocytes and plasma cells.

## Conclusion

- Although rare, autoimmune etiologies such as Sjogren's syndrome should be considered in the differential diagnosis of SRSE. It is important to recognize that neurologic symptoms can be the inaugural manifestation of such conditions, and once the diagnosis is made, it can direct the management and therapy choice.

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