

Treatment of Sandifer Syndrome with an Amino-Acid–Based Formula

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Abstract

Keywords

- ▶ Sandifer syndrome
- ▶ cow's milk protein allergy
- ▶ pediatrics
- ▶ GERD
- ▶ infants

Objective To study the presentation and treatment in two infants who presented with refractory Sandifer syndrome (SS).

Study Design We retrospectively reviewed the cases of two infants who presented to our outpatient clinic with SS who were refractory to conventional treatment.

Results We report two patients with refractory SS who responded to treatment with hypoallergenic formula.

Conclusion It is important to consider a diagnosis of milk protein allergy responsive to hypoallergenic formula in patients with SS who are refractory to conventional antireflux treatment.

Sandifer syndrome (SS) was first described in 1964 and is a rare complication of gastroesophageal reflux disease (GERD), most commonly seen in infants and children.¹ The syndrome complex consists of sudden-onset dystonic movements with arching of the back and rigid opisthotonic posturing, mainly involving the neck, back, and upper extremities.¹ Patients may present with torticollis,² laterocollis,³ or retrocollis.⁴ The posturing is often misdiagnosed as seizures or a neurologic movement disorder.⁵

Symptoms of SS are generally improved after pharmacologic antireflux therapy or Nissen fundoplication, presumably as a result of reducing gastroesophageal reflux. We describe two infants who presented with symptoms of SS and were refractory to conventional antireflux therapy. Because previous reports had described allergic esophagitis secondary to cow's milk protein allergy (CPMA) as a cause of GERD,^{6,7} we empirically initiated a trial of amino-acid–based formula in our patients with SS. This treatment of milk protein allergy resulted in the elimination of SS symptoms.

Case Report

Case 1

A 3-month-old female child presented with a 2-month history of nonbilious, nonbloody vomiting several times each day. These episodes coincided with severe arching

and opisthotonic posturing. A family video recorded these typical symptoms of SS. The parents also reported that the child was severely irritable and cried for several hours each day. The patient was receiving ranitidine (6 mg/kg/day) and Mylanta (1 mL/kg/day) for presumptive treatment of GERD. SS symptoms persisted despite being treated for GERD, and changing from a cow's milk–based formula to a soy formula and then to the casein hydrolysate formula, Alimentum (Abbott), which was thickened with rice cereal. The patient was at the 25th percentile for weight and the 50th percentile for height. The physical examination and abdominal ultrasound were normal and the stool was guaiac negative. The patient was evaluated by a pediatric neurologist and her examination and electroencephalogram (EEG) were normal. Ranitidine was replaced by lansoprazole (3 mg/kg/day), but the patient remained symptomatic. One month later, a trial of amino-acid–based formula, Elecare (Abbott), was started and within 4 days the parents reported a significant decrease in irritability and an improvement in the patient's symptoms. Two weeks after introduction of this formula, postural arching and irritability had completely stopped.

Case 2

A 2-month-old female child presented with a 1-month history of irritability with several episodes of rigid opisthotonic

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posturing each day. Because of this behavior, the patient was given ranitidine (6 mg/kg/day), assuming the presence of GERD. After no change in symptoms, she was switched from cow's milk-based formula, to soy formula, and then to a casein hydrolysate formula (Nutramigen, Mead Johnson). Her therapy was then changed from ranitidine to lansoprazole (3 mg/kg/day). The patient was at the 25th percentile for weight and the 10th percentile for height. Her physical examination was normal and stool was guaiac negative. Additional evaluations included a neurologic evaluation, EEG, and upper gastrointestinal (GI) series, all of which were normal. Despite treatment with lansoprazole for 1 month, there was no improvement of her irritability and abnormal posturing was still present. A trial of amino-acid-based formula, Elecare (Abbott) was started, and 2 weeks after introduction the parents reported complete resolution of all symptoms; postural arching and irritability had completely resolved.

Discussion

Though not typically described, SS symptoms in these patients may have been a result of CMPA, as their symptoms resolved rapidly after introduction of a fully hydrolyzed, amino-acid-based formula. Although antireflux therapy (lansoprazole) was continued in both patients, it was unlikely that GERD was the cause of SS, because proton pump inhibitor (PPI) therapy affords its maximal effect by 5 days,⁸ and each patient had been treated with PPI's for at least 4 weeks. Unsuccessful outcomes after 1 month of PPI therapy is usually considered treatment failure.

The usual symptoms of CMPA are thought to be secondary to immunologic responses to milk proteins that can be IgE and/or non-IgE mediated. These can include eosinophilic gastroenteritis, food-protein-induced enterocolitis, as well as vomiting, diarrhea, blood streaked stools, excessive crying, irritability, and eczema.⁷ The presentation of SS, as in our patients, is not a common presentation of this condition. The diagnosis of CMPA is largely based on clinical history; though skin prick and in vitro IgE testing can be useful in IgE-mediated reactions, diagnostic testing for non-IgE-mediated reactions is limited.⁶ If CMPA is suspected, initiating a trial of amino-acid-based formula is recommended as it is benign, and symptom resolution is potentially diagnostic of CMPA.⁶ SS, as a consequence of GERD, is treated with antireflux therapy and in severe cases by antireflux surgery.

It has been suggested that dystonic posturing is a learned behavior, which increases the velocity and amplitude of esophageal peristalsis, thereby promoting acid clearance and symptom relief.⁹ Another explanation suggests that in patients with a hiatal hernia and coexisting acid reflux, local diaphragmatic irritation occurs, resulting in referred dystonic spasm of the neck.¹⁰ This may be due to the shared sensory nerve roots for the diaphragm and esophagus.

Though esophageal irritation has typically been associated with GERD, several studies have noted that food allergies, resulting in esophageal eosinophilia, can result in a clinical presentation similar to GERD.^{2,5} Kelly et al described 10 infants with GERD, refractory to medical management, who

responded favorably to a 6-week dietary trial of amino-acid-based formula.¹¹ None of these patients had SS. Their symptoms were thought to be secondary to allergic esophagitis, defined as at least 20 eosinophils per high-power field (hpf). The esophageal histology paralleled the clinical presentation; the median number of eosinophils per hpf decreased from 44 to 0.5 after the dietary trial.¹¹ This study suggests that symptoms commonly attributed to GERD in infants, such as vomiting, irritability, and poor feeding, may also be caused by a hypersensitivity reaction to intact dietary proteins. We now report that SS, usually associated with GERD in the pediatric population, may also be due in part to an allergy that responds to an amino-acid-based formula. The time for symptom resolution in CMPA of 2 days to 2 weeks⁷ is similar to that seen in our patients when SS was treated with an amino-acid-based formula.

Because our patients responded to an amino-acid-based formula in the appropriate time course, there was no need for further testing. However, upper endoscopy and pH impedance probe studies may have provided additional information regarding the pathophysiology of this process. Thus, based on the clinical response in these two patients, we recommend that a trial of amino-acid-based formulas should be tried in patients who present with SS, in whom traditional antireflux therapies have failed. This should be tried before considering surgical intervention for GERD.

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