Neonate with Seizures After Consuming Star Anise Tea

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ABSTRACT

Chinese Star Anise (*Illicium verum*) is a common spice used in many cultures as an herbal treatment for infant colic.[1,2] Often, it has been found to be contaminated with Japanese Star Anise (*Illicium anisatum*) or is used in high doses resulting in neurotoxicity and gastrointestinal disturbances.[1,3,4] Here we present a case of a previously healthy 2-week-old male who was evaluated in the emergency department for abnormal movements, irritability, and emesis after ingestion of star anise tea for the treatment of colic.

KEYWORDS: neonatal seizure, star anise, neurotoxicity

BACKGROUND

Abnormal movements and seizures in infants may be caused by a variety of pathologies, such as infection, trauma, metabolic derangements, stroke, inborn errors of metabolism, primary neurologic conditions such as brain malformations and epilepsy syndromes, and toxic ingestions or exposures, among others. Specifically, toxic ingestions are a less common but potentially fatal cause. As infants with abnormal movements and/or seizures often present to the emergency department (ED) for initial evaluation, it is paramount that ED clinicians consider the broad differential diagnosis and complete a careful history and exam, making note to assess for any possible toxic ingestions or exposures.

Chinese star anise (*Illicium verum*) is a well-known spice and is used around the globe as an herbal remedy for infant colic[1] (**Figure 1.**). While Chinese star anise has a reputation for being safe and benign at low doses, its relative, the Japanese Star Anise (*Illicium anisatum*), has been shown to cause neurologic and gastrointestinal toxicity.[1,5] The toxin in this species, anisatin, acts as a non-competitive GABA-antagonist which can lead to hyperactivity of the nervous system, causing seizures.[6,7] This hyperactivity, without inhibitory mechanism of the GABA receptor, causes excess neuronal firing in the form of seizures and may be lethal.[2] In some cases, ingestion of star anise tea with resultant toxicities has been traced back to contamination of the Chinese species with the Japanese species.[4,8] However, it should be noted that Chinese star anise also contains toxic compounds (veranisatins) that can be neurotoxic and lethal high doses.[9] Chinese star anise also contains high content of anethole and estragole, essential oils which are neurotoxic and can cause irritability, nystagmus, and lethargy.[2]

Star anise intoxication has been documented in isolated cases around the globe but is not well documented in children. Previously published case reports, describe the toxidrome characterized by both neurologic and gastrointestinal toxicities.[4,8] Neurologic toxicity has been characterized as an acute onset of jitteriness, hyperexcitability, nystagmus, myoclonic movements, and seizures.[1] Gastrointestinal toxicity usually involves emesis, as well as diarrhea and abdominal distension.[2] The onset of symptoms typically occurs between 30 minutes and 4 hours following ingestion.[8]

Figure 1. Chinese Star Anise *(Illicium verum)*

CASE PRESENTATION

A two-week-old, full-term male born by spontaneous vaginal delivery (SVD) to a 17-year-old G1P1 with an unremarkable prenatal, delivery, and immediate postnatal course, presented to the ED with concern for abnormal movements, irritability, and vomiting. The described movements included vertical eye deviation, jitteriness, and holding arms outstretched with rhythmic shaking. These episodes were brief, self-resolved, and occurring every 5–10 minutes.

This patient was described to be a fussy baby since birth by his mother and another caregiving family member present at the bedside. He reportedly had small volume, non-bloody, non-bilious emesis with each feed. He had no documented or tactile fevers. Given his fussiness, the family raised concerns for colic. Multiple dietary changes

had been made without consultation with their primary care provider, including switching to a soy-based formula and adding Pedialyte. Over the course of the two days leading up to presentation he developed large volume emesis after every feed, poor urine output, and watery bowel movements. Additionally, he developed the abnormal movements described above, prompting the visit to the ED.

Vital signs upon arrival to the ED revealed a pulse of 126 bpm, SpO2 of 100% on room air, temperature of 98 °F (36.7 °C), and a respiratory rate of 34. The patient's weight was 4.35 kg. An initial blood pressure was not documented. The infant was observed to have more than 5 episodes of abnormal movements with tonic outstretched arms, intermittent episodes of nystagmus, tongue thrusting, and eye deviation accompanied by tachycardia lasting 5–10 seconds before self-resolving. He was noted to be fussy when not being held but was consolable. His exam otherwise revealed an open and flat anterior fontanelle, clear lungs without increased work of breathing, a normal cardiac examination without murmur and 2+ radial pulses, a non-distended abdomen without hepatosplenomegaly, a normal penis and testes, well perfused extremities, and no outward signs of injury.

Concern for seizure was raised based on the clinical presentation. Given the broad differential of irritability, vomiting, and seizures in a neonate, a workup including CBC, BMP, blood culture, urinalysis, and urine culture was initiated. Laboratory findings were unremarkable. Additionally, per institutional imaging practice guidelines, a non-contrast CT of the brain was obtained to assess for any evidence of intracranial pathology such as hemorrhage, skull fracture, and/or hydrocephalus; this was also normal. (**Table 1.**)

On further questioning during the course of evaluation, the patient's grandmother added that she had been feeding the baby star anise tea for colic. She disclosed that she had fed him 4 ounces of this tea at four different time periods over the course of the days prior to presentation. Poison control was contacted who noted that the patient's presentation was very consistent with star anise toxicity, a rare toxidrome. Per their recommendation, the patient was given one dose of lorazepam which resolved the abnormal movements. The infant remained hemodynamically stable throughout the ED course without desaturations or apnea.

The patient was admitted to the pediatric intensive care unit for further monitoring. Based on the clinical presentation and rarity of star anise toxicity, a lumbar puncture was performed to complete a full septic workup, with resultant normal cell counts, glucose, protein, and negative gram stain and culture. All cultures remained negative at 48 hours. An abdominal ultrasound was performed to evaluate for pyloric stenosis given the frequent large volume emesis and was found to be normal. The patient was subsequently discharged home, tolerating feeds and without any recurrence of seizures.

Table 1. Laboratory and Radiologic Diagnostic Results

Diagnostic test	Result	Normal Range for age
CBC	WBC 9.1	4.4–16.0 x10^9 /L
	RBC 5.15	3.90–6.10 x 10^12 /L
	Hemoglobin 15.7	14.0–20.0 G/DL
	Hematocrit 47.2%	42–67%
	MCV 91.8	88.0–122.0 fL
	MCH 30.5	28.1–37 PG
	MCHC 33.2	28–37 g/dL
	RDW 15.5%	11.5–14.5%
	Platelets 335	150–400 x10^9 /L
	MPV 10.0	7.4–10.4 fL
	Normal differential	
BMP	Glucose 82	50–80 mg/dL
	BUN 12	5–27 mg/dL
	Creatinine 0.26	0.30.–1.00 mg/dL
	Na + 131	131–142 meq/L
	K+ 5.3	3.7–5.9 MeQ/L
	Chloride 98	99–116 meq/L
	CO2 16	22–32 meq/L
	Anion Gap 17	3–13
	Calcium 10.3	9.0–10.9 mg/dL
Magnesium	1.9	1.3–1.9 meq/L
Phosphorus	6.0	3.4–5.9 mg/dL
Acetaminophen Level	<10	11–20 ug/mL
Salicylate Level	<2.5	15.0–30.0 mg/dL
Blood culture	No growth after 5 days	
CSF Gram Stain and Culture	Gram Stain: No Polys, No squamous epithelial cells, No Organisms Seen Culture: no growth at 48 hours	
Urinalysis	pH 5.0	5.0–8.0
	Specific gravity 1.020	1.010–1.030
	Bilirubin negative	negative
	Blood negative	negative
	Glucose negative	negative
	Ketones 1+	negative
	Leukocyte esterase negative	negative
	Nitrite level Negative	negative
	Protein 30	<10
	Urobilinogen negative	negative
	WBC none seen	0–4 per HPF
	RBC none seen	0–3 per HPF
	Renal Epithelial cells: few transitional epithelial cells present	0–3/HPF
	Calcium Oxalate crystals: present	absent
Urine Culture	No growth after 5 days	
Non–contrast CT Brain	Impression: Normal Non–contrast CT of the brain	
Abdominal Ultrasound	Negative for pyloric stenosis	

DISCUSSION

This case illustrates the risk of star anise tea consumption in infants due to the significant degree of potential toxicity. While serum and urine confirmatory testing were not completed, the neurologic and gastrointestinal effects demonstrated by this patient, along with the resolution of seizures, and return to baseline with withdrawal of star anise, was highly suggestive of a toxidrome due to star anise consumption. In the 18 months following the patient's initial presentation, there were no return visits for any neurologic or gastrointestinal complaints.

There is no current antidote for star anise intoxication or specified treatment guidelines. The active agent anisatin is a neurotoxin with GABA antagonist activity, and so benzodiazepines are recommended as a first-line treatment for abortive therapy for seizures. Supportive treatment with fluid replacement for emesis as well as withdrawal of the offending agent are also paramount. After one dose of lorazepam and discontinuation of star anise tea, the described patient recovered without need for further treatment.

Although Chinese Star Anise (*I. verum*) has been considered safer due to its lower veranisatin content, it is prudent to avoid use in infants and children due to the risk of neurotoxicity or overdose in high concentrations, potential for contamination with Japanese star anise (*I. anisatum*),[7,10] and the challenge of differentiating between the two species. Of note, due to reported cases of star anise toxicity, the FDA has issued an advisory statement on the risks from all remedies that contain the name star anise.[11] Point-of-care education in the primary and acute care setting is important for families to inform them of the potential adverse effects of this home remedy.

Toxic ingestion, including ingestion of star anise tea, should always be included in the differential for infants presenting with abnormal movements and/or seizure. Taking a thorough history including herbal/traditional treatments and home remedies is key to creating a thorough differential diagnosis and deciphering a probable toxic agent causing abnormal movements in an infant.

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