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Sandifer Syndrome Posturing: Relation to Abdominal Wall Contractions, Gastroesophageal Reflux, and Fundoplication

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Sandifer syndrome designates abnormal posturing in patients with gastroesophageal reflux. To explore its mechanisms via examining relationships among Sandifer syndrome posturing, abdominal wall contractions, and reflux episodes, we studied an affected child in detail. The study utilized esophageal pHmetry, surface electromyography, and split-screen videography. The multichannel physiologic study demonstrated association of rectus abdominis contraction with onset of reflux episodes ($P < 0.001$) and association of reflux episodes with Sandifer syndrome posturing. This child's subsequent course confirmed his diagnosis and suggested mechanisms of the association of reflux and Sandifer syndrome. We conclude that abdominal wall contractions may induce reflux episodes. Sandifer syndrome may be due to gastroesophageal reflux even without hiatal hernia, macroscopic esophagitis, or reflux symptoms. Despite the absence of more typical reflux symptoms and failure to respond to very aggressive medical therapy, Sandifer syndrome may resolve after fundoplication.

KEY WORDS: gastroesophageal reflux; proton pump inhibitor; regurgitation; Sandifer syndrome; strain; fundoplication; child.

Sandifer syndrome (SS) is an uncommon syndrome of abnormal movements of the head, neck, and trunk occurring in patients with gastroesophageal reflux disease (GERD) (1–12); often the abnormal movements are temporally associated with gastroesophageal reflux (GER) episodes (2, 5). Of the 40–65 cases reported in the literature, most are young, male, neurologically normal children, although some reports describe instances in infants (1, 2), in adults (11, 12), in girls (2, 8, 9), and in neurologically abnormal children (5). SS is sometimes initially evaluated as a neurological disorder, due to the spastic torticollis and dystonia (1). The association of the SS posturing with GERD suggests a potential pathophysiological relationship, but the nature of this relationship is incompletely understood.

In contrast to SS, GERD is one of the most common pediatric disorders, prompting about 7% of all children to see a physician each year (13). One of the most frequent manifestations of GERD, particularly prominent in young children, is regurgitant reflux, in which gastric material refluxes up into the mouth and may be ejected from the mouth ("spitting up"). We have previously shown in infants that regurgitant reflux episodes are significantly associated with contraction of the rectus abdominis musculature of the abdominal wall. This is in contrast to nonregurgitant episodes, which are more likely to occur in the absence of rectus contraction (14). The additional pressure supplied to the gastric contents in this way by the somatic musculature likely promotes reflux of greater quantity and force, which is more likely to be propelled from

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the mouth. Various studies have shown similar promotion of retrograde movement of gastric contents by "voluntary" somatic (striated) muscle abdominal contractions during "strain-induced" reflux (e.g., by coughing or lifting) (15), as well as during rumination (16).

Our detailed study of a child with SS provided the opportunity to explore the interrelationships among somatic abdominal wall contractions, reflux episodes, and SS posturing.

METHODS

Case Report. This child presented to the Pediatric Gastroenterology Division of the University of Pittsburgh School of Medicine at Children's Hospital of Pittsburgh in January 1998 as a very bright, developmentally normal, 4-year-old boy with complaints of several months of uncontrollable head tilting to the right, agitation after eating, and frequent swallowing and belching. Meals exacerbated his head tilting, sometimes hindering his speech at these times. While the posturing diminished after the postprandial period, and disappeared during sleep, it occurred regardless of other activities. The posturing had continued despite treatment with antacids and ranitidine. The boy's parents provided careful video recording of the head tilting, which documented him continuing his usual play and interactions at home despite obvious, and sometimes extreme, head tilting. He had vomited a few times while travelling in the car after drinking milk; his mother believed he vomited because his seatbelt prevented his twisting to assume the habitual posture. A very verbal youngster, at the initial visit he denied heartburn, chest pain, sour regurgitation, anorexia, and abdominal pain; he experienced no nocturnal awakening or discomfort; and he had no symptoms of otolaryngologic, ophthalmologic, or neurologic disease. Medical history was normal.

The patient had undergone an extensive evaluation, including subspecialty consultations by neurology, psychiatry, and allergy-immunology. Neurological evaluation was normal other than the posturing, which the consultant described as "tics" and for which he suggested psychological evaluation. A head magnetic resonance imaging study was normal except for "paranasal sinus disease" in the ethmoid and maxillary sinuses and a large normal variant cisterna magna. Allergy skin testing was positive to tomato and sweet potato (2+).

The boy was quite well grown (height, 99th percentile; weight, 96th percentile) and had a normal physical exam, including a rectal examination negative for blood.

Gastroenterological evaluation included normal barium upper gastrointestinal fluoroscopy: no hiatal hernia, no esophageal mucosal disease, and no reflux observed over a 5-min period after ingestion of barium. He had a macroscopically negative upper endoscopy; esophageal biopsies revealed only mild histologic esophagitis (papillary height, ~0.75–0.80; normal, <0.53; basal thickness, ~0.40–0.60; normal, <0.25 [17]), with fewer than five eosinophils per high-power field.

Because the patient's head-tilt posturing resembled SS, and because no other explanation for them was evident, we attempted to modulate them through treatment of reflux, despite the lack of macroscopic endoscopic or radiographic findings. We gradually intensified the antireflux regimen, as it failed to control the behaviors. The patient maintained a restrictive diet, with frequent small feedings and avoidance of food or drinks that had a low pH, were fatty or spicy, or contained chocolate. Pharmacologically, he received up to 60 mg (2.5 mg/kg) of lansoprazole daily, given 15–30 min before meals, as well as 150 mg (6.3 mg/kg) of ranitidine at bedtime. This aggressive treatment had resulted in only a modest improvement in SS posturing during the 14 months after we first saw him, and he had begun to describe symptoms of reflux.

In March 1999, to determine whether acid gastroesophageal reflux was persisting despite high proton pump inhibitor (PPI) doses, to assess any relationship between reflux episodes and the head tilting, and to assess a hypothesized relationship between voluntary somatic abdominal wall contraction and reflux episodes in this child, he underwent a protocol of investigation described below (Study Techniques). We analyzed the data for publication following approval by the Institutional Review Board of the Children's Hospital of Pittsburgh and written informed parental consent.

Study Techniques. The techniques used during the investigation were distal esophageal pH monitoring (EpHM), to characterize reflux; coding by an observer, to register head-tilt posturing; and electromyography (EMG) of the rectus abdominis, to monitor its contraction (14). These data were recorded synchronously, and with replication, by feeding the EpHM data in parallel to a paper tracing and into an Apollo workstation computer; by feeding the concurrent EMG data into the Apollo workstation; and by keystroke recording the coded behavior into the Apollo and writing it on the EpHM paper tracing. The final technique to assure accuracy, synchronization, and duplication involved split-screen video recording, depicting the Apollo monitor screen (showing the EpHM and EMG tracings and the head tilt codes) on one side and the child himself on the other, and a date/time stamp running continuously at the bottom of the screen (18). Details of the physiologic monitoring are described elsewhere (14, 18).

During 7.8 hr of monitoring, "head-tilt" posturing was coded by keystroke on the Apollo workstation, and also by writing on the pH tracing, by an observer (T.M.S.) whose undivided attention was focused on the child; the behaviors were also recorded videographically, using the monitor with a split screen. During the rest of the 24 hr of monitoring, much of it while the child slept, the behavior was coded by his mother by recording head-tilting episodes on the pH tracing.

Study Protocol. When the 24-hr EpHM-EMG study was performed, the patient had been taking 15 mg of lansoprazole twice daily (15–30 min before breakfast and dinner), ~1.4 mg/kg/day. The study began in the morning, while he was fasting and had not taken the PPI for nearly 24 hr. He fasted until he received lansoprazole, 15 mg at 30 min before a lunch of milk, pizza, and fries, consumed within 30 min. He fasted thereafter until he received a double dose of lansoprazole (30 mg), followed within 30 min by a dinner of plain pasta, a roll, and milk.

The head tilting was coded in real time by notations on the pH tracing and supplemented by the split-screen video recording; during the first 7.8 hr, when all of the head tilting occurred, this coding was precisely supplemented by the keystroke entries.

Study Analysis. Data analysis was modeled after that used in a study characterizing behaviors associated with reflux episodes in infants (18). Meal times were excluded from analysis, leaving a total of 20.2 hr. Data were coded (E.A.F.) in each of the 14,546 separate 5-sec intervals.

The intervals were scored in EpHM as reflux *onset*, *pre-onset, post-onset, no reflux*, or *unscored*. *Onset* was defined as a drop in pH >1.0 unit to a pH <4.0 during a 5-sec interval. Pre-onset and post-onset intervals were the 5-sec intervals immediately preceding and following an onset. Periods scored as no reflux were those in which the pH remained above 5.0 for at least 30 sec (i.e., for six or more 5-sec intervals). Unscored intervals were those that did not fit any of the above criteria (including periods following an onset when the pH remained <5).

For each of the 6603 scored intervals, EMG data were coded as either *EMG+* or *EMG−*. Intervals were coded EMG+ when rectus abdominis EMG activity was clearly visible above the electrocardiographic signal at any time during a 5-sec interval. Thus, EMG+ represents rectus abdominis, or voluntary abdominal muscle, contraction. All other 5-sec intervals were scored *EMG−*.

For each scored interval, head- tilt data were coded present or absent, based on the "head-tilt" keystroke entries on the Apollo workstation. Head-tilt, never having taken place during sleep, occurred exclusively during the period of multiphasic monitoring. The videographic recording substantiated the keystroke entry coding.

The significance of associations between the EMG positivity and the EpHM documentation of initiation of reflux (including onsets, pre-onsets, and post-onsets) was analyzed within the scored intervals by Fisher's exact statistic.

RESULTS

Study Results. Acid reflux (pH <4) occurred during 28% of the 20.2 hr of continuous nonmeal EpHM. In the first few hours of the study, with the patient still fasting and unmedicated, the reflux index (RI; percentage of the time with pH <4) was 78%; the RI was not much improved following his dose of ~0.7 mg/kg lansoprazole 15 min before lunch, so he received an additional ~1.4 mg/kg 15 min before dinner. During the 2 hr after dinner, the RI was 20%, dropping to 5% for the rest of the night. The RI was 28% for the whole 20.2 hr of study, largely due to daytime reflux, worsening in the absence of PPI. The EpHM had documented the patient's requirement for high daily dosing of PPI for suppression of acid reflux.

During the 20.2 hr (14,546 5-sec intervals) of nonmeal monitoring, there were 101 reflux onsets and, thus, 303 intervals scored as pre-onset, onset, or post-onset. There were 6300 intervals scored as no reflux (pH remaining above 5 for >30 sec) and a further 7943 that were unscored.

During 7.8 hr of awake-time monitoring, we recorded 83 episodes of SS posturing. None of these episodes occurred during a period scored as no reflux (pH >5 for ≥30 sec; Figure 1). Thus the "density" of SS posturing was 12.4 episodes/hr while the pH was <5, but no episodes occurred during the 1.1 hr when the pH was persistently >5. Thirteen of the 83 SS episodes occurred within 1 min after a reflux onset, with 7 of them actually occurring during a 5-sec interval coded as reflux onset.

Rectus abdominis contraction (EMG+) occurred during 603 (9.1%) of the 6603 scored 5-sec intervals. Reflux onsets occurred during 23.5% of the EMG+ intervals but

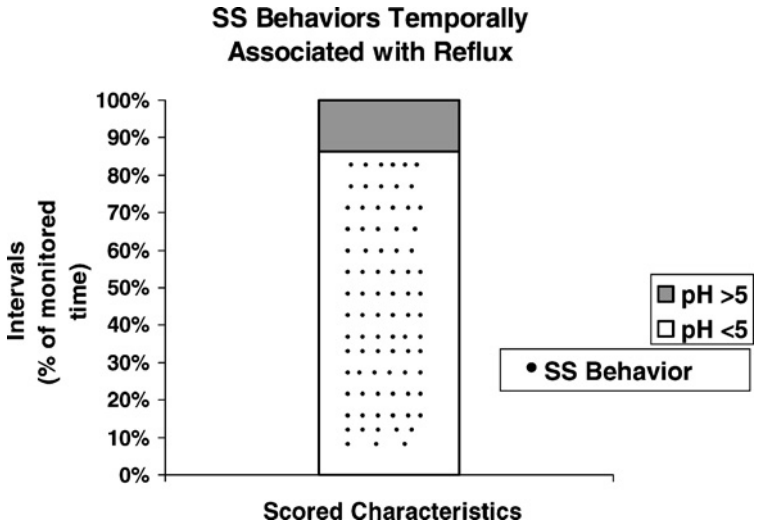

Fig 1. Sandifer syndrome (SS) behaviors are temporally associated with reflux. The darker-shaded area represents the percentage of behavior-monitored time (7.8 hr) during which the esophageal pH was ≥5 (i.e., 13.7%). The lighter-shaded area represents the percentage of time during which the pH was <5 (i.e., 86.3%). Each recorded episode of SS behavior (i.e., head tilting) is represented by a •; each episode is sorted into one of the two shaded areas according to the esophageal pH at the time of the behavior. All of the 83 recorded episodes of head tilting occurred at a pH <5.

during only 2.7% of the EMG− intervals ($P < 0.001$). Additionally, 46.9% of reflux onsets were associated with EMG+ activity, while only 7.3% of the "no reflux" periods were EMG+.

Although EMG+ intervals comprised only 9.1% of the scored intervals, 66% of the SS posturing episodes occurred during these intervals.

Case Follow-up. Because the study had indicated an association between reflux episodes and the head-tilt behaviors, and the persistence of considerable reflux during usual doses of PPI, the child was treated with more aggressive pharmacotherapy. However, a repeat EpHM, done 4 months later because of persistent head tilting, showed esophageal pH <4 for 6% of the total time and 7.5% of the fasting time, despite lansoprazole, 2.5 mg/kg, 15–30 min before breakfast and ranitidine, 6 mg/kg, at bedtime. Following an algorithm of management of PPI failure, the patient's medication administration and lifestyle details had been reviewed and optimized; his dose had been increased (and attempted twice daily without symptomatic benefit); EpHM on high-dose PPI had demonstrated incomplete control of acid reflux despite the high doses; and a bedtime dose of histamine-2 receptor antagonist had been added. (Use of other formulations of PPI including an intravenous formulation to assess absorption and addition of a prokinetic agent were not attempted but might have been useful steps.)

Because the study had also indicated a temporal relationship between voluntary somatic abdominal wall contraction and the patient's reflux episodes, he was treated with the addition of 4–6 months of EMG-guided biofeedback, to try to train him in relaxation of the abdominal wall musculature.

All of this therapy produced only partial benefit, and when the lansoprazole dose was decreased to 1.1 mg/kg in mid-2000, regurgitation into the mouth and head tilting worsened. In the autumn of 2000, the patient underwent a repeat endoscopy and an esophageal manometry study. Endoscopy and biopsies were completely normal, and the motility study was completely normal except for the somewhat low lower esophageal sphincter pressure of 8 mm Hg.

Because of concern about chronic high-dose medication and the failure of even these doses to relieve his head tilt, this child underwent laparoscopic Nissan fundoplication in September of 2001. Although his symptoms worsened during the immediate recovery from the surgery, within a few days his SS posturing improved dramatically for the first time in 4 years. His head tilt went away completely. His family noted the patient's new ability to stand completely still and upright and to be calm and more consistently happy and confident. Although the fundoplication does not prevent his belching, and he has vomited several times in the ensuing 2.5 years, the reflux symptoms have not returned, and he never feels regurgitation into his throat. He still avoids carbonated beverages, as he experienced terrible hiccups on the one occasion on which he tried to drink one.

DISCUSSION

Our extensive evaluation of this patient with SS has several implications for understanding the pathophysiology of reflux and its relationship to SS. First, this case study adds to the evidence concerning the role of somatic muscle contraction in the genesis of episodes of pH probe-documented reflux. Second, it provides additional insight into the pathophysiology, as well as the recognition, diagnosis, and management, of an uncommon entity, SS.

Regarding the relationship between abdominal wall motor contraction and reflux, "straining," leg lifting, coughing, and other activities that contract the abdominal wall clearly can induce reflux (15). Such strain-induced reflux occurs predominantly in the context of hiatal herniation, because in individuals without hiatal herniation the simultaneous contraction of the crural diaphragm during straining bolsters the lower esophageal sphincter in proportion to the increase in transmitted intragastric pressure, thus acting to prevent strain-induced reflux (19). However, transient lower esophageal sphincter relaxations (TLESRs), which occur both in normal individuals and in those with GERD, obliterate the crural diaphragm's protection against strain-induced reflux, because of the neurological coordination of crural hiatus relaxation and lower esophageal sphincter relaxation (20).

We have previously demonstrated that rectus abdominis contraction during reflux episodes in infants makes expulsion of the refluxate from the mouth (regurgitation) more likely (14). Now the data from the older child reported here suggest that such contraction also makes *non*regurgitant reflux more likely to occur. Because this child and the infants we studied earlier did not have evidence of hiatal herniation, their reflux episodes most likely occurred during TLESRs. We can thus merge the data from these two reports to conclude that when TLESRs occur, abdominal wall contraction makes reflux more likely to occur, and also makes any reflux that occurs likely to rise higher in the esophagus, even to the point of being regurgitated from the mouth. This potential role of abdominal wall muscle contraction in reflux is coherent with the literature on the role of "straining" in the genesis of reflux episodes and suggests that reflux has more in common with rumination than has usually been appreciated (16).

The literature includes between 40 and 65 cases of SS (1–12). These reports document a preponderance of males, common onset during the early school years (rarely in infants or adults), and neurodevelopmental normalcy in a large proportion of the children. Reported children often presented with marked hiatal herniation, erosive esophagitis, malnutrition, and chronic anemia. Cases with subtler esophageal involvement may be more challenging to diagnose with certainty, as in our patient. When GERD is less evident, one must consider multiple other etiologic categories, including neurologic (e.g., seizure disorder, vestibular disease, brain tumor), musculoskeletal (e.g., congenital or acquired abnormality of the neck musculature or cervical spine), ophthalmologic (e.g., palsy or imbalance of ocular musculature), otolaryngologic (e.g., otitis, mastoiditis), and psychological (e.g., habit tics or hysterical conversion). Two studies of gastric emptying in children with SS found delayed gastric emptying in one child but normal gastric emptying in another (21, 22). Matching our experience, fundoplication surgery was required for adequate management of about half of the SS cases, a considerably higher frequency than for management of most other GERD manifestations (23–25). Our patient's posturing failed to remit even with several years of aggressive PPI therapy, supplemented by histamine-2 receptor blockade and rigorous lifestyle modifications, although fundoplication relieved the symptoms in a matter of days.

Regarding the pathophysiology of SS, our patient's failure to exhibit any posturing when the distal esophageal pH was persistently >5 adds further support to the accepted existence of a pathophysiologic relationship between acid reflux and SS posturing.

Some descriptions in the literature imply that the posturing might induce reflux episodes (4). However, it is challenging to align this suggestion with the near-universal abrupt resolution of the behaviors after fundoplication.

The second possibility is that the SS head tilting is a tic behavior: that is, something else induces both the head tilt and the reflux. In this scenario, a psychobehavioral habit could cause both the neck muscles and the abdominal muscles to contract, the latter contractions producing reflux episodes. In our patient, we demonstrated concordance of the head tilting and "voluntary" abdominal wall muscle activity (EMG+) and we also documented the association of the abdominal wall contractions and reflux episodes. The possibility that a tic might consist of simultaneous head tilt and reflux-inducing abdominal contraction could be consistent with our patient's evaluation, were it not for the abrupt resolution of the tilting by fundoplication, after failure of behavioral interventions. In our patient's case, the incompletely effective behavioral interventions even included interventions directed at relaxation of the abdominal musculature.

The third possible pathophysiologic relationship is that that the reflux episodes produce the posturing. This is the most likely relationship, as supported by resolution of the behaviors after surgical treatment of the reflux in our case and many in the literature. Reflux might cause SS behaviors via learning of the behaviors to aid in clearance of reflux, for example, as suggested in one case by improvement in esophageal motility during head tilting: increase in esophageal contraction pressure—from 47 to 74 mm Hg—and propagation speed—from 2.5 to 4 cm/sec (7, 8).

Alternatively, reflux might cause SS behaviors reflexively, based on shared embryologic neural connections in the brain stem and cranial nerves that could allow stimuli at the gastroesophageal junction to cause neck muscle contractions (11). Thus afferents from the distal esophagus might link to efferents in the neck musculature in anatomically or physiologically susceptible individuals. Like many reflexes, sleep may suppress this pathway. Surgical manipulation via fundoplication, even if loose, may interrupt the afferent limb of this reflex by anatomic mechanisms not completely dependent on elimination of acid reflux.

Our patient's detailed evaluation extends our information about the role of abdominal wall contractions in inducing the onset of reflux episodes, even when they are not regurgitant. It also provides important information about SS, which may occur initially in the absence of hiatal hernia, macroscopic esophagitis, or reflux symptoms. It supports other reports that implicate reflex interactions between events in the lower esophagus and dystonic movements of the neck in certain individuals, who may be susceptible to SS due to variants of neural anatomy or physiology.

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