CLINICAL REPORT

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Volvulus and Bowel Obstruction in ATR-X Syndrome—Clinical Report and Review of Literature

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Alpha thalassemia-mental retardation, X-linked (ATR-X) syndrome is a rare genetic disorder with a variety of clinical manifestations. Gastrointestinal symptoms described in this syndrome include difficulties in feeding, regurgitation and vomiting which may lead to aspiration pneumonia, abdominal pain, distention, and constipation. We present a 19-year-old male diagnosed with ATR-X syndrome, who suffered from recurrent colonic volvulus that ultimately led to bowel necrosis with severe septic shock requiring emergent surgical intervention. During 1 year, the patient was readmitted four times due to poor oral intake, dehydration and abdominal distention. Investigation revealed partial small bowel volvulus which resolved with non-operative treatment. Small and large bowel volvulus are uncommon and life-threatening gastrointestinal manifestations of ATR-X patients, which may contribute to the common phenomenon of prolonged food refusal in these patients.

Key words: ATR-X syndrome; intestinal volvulus; emergency surgery

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INTRODUCTION

ATR-X syndrome is a rare X-linked recessive condition characterized in males by intellectual disability, facial dysmorphysm, ambiguous genitalia and alpha thalassemia. Females are usually asymptomatic [Gibbons et al., 1995a].

Gastrointestinal symptoms are common in ATR-X patients and include difficulties in feeding manifested often by abdominal pain and distention and the patient's refusal for food. Regurgitation and vomiting is commonly described and is attributed to gastric pseudo-volvulus or reflux which may lead to aspiration pneumonia and is a known cause of death in this syndrome. Constipation is described in about a third of the patients [Martucciello et al., 2006]. Bowel volvulus has been described previously as an uncommon gastrointestinal presentation in ATR-X patients but as a potentially fatal one [Martucciello et al., 2006].

We describe a 19-year-old patient diagnosed with ART-X syndrome who suffered from recurrent large bowel volvulus. After resection of his large bowel, he continued to have several small bowel volvulus episodes.

CLINICAL REPORT

We present the case of a 19-year-old male diagnosed at the age of 5 with ATR-X syndrome, after an established clinical suspicion due to distinctive clinical features was confirmed with sequence analysis. Genetic counseling confirmed a carrier status of the mother for ATR-X pathogenic variant. The patient suffered from severe intellectual disability, epilepsy, dysmorphic facies, and recurrent urinary tract infections related to previous ureteropelvic junction obstruction that required surgery. He also suffered from chronic constipation treated with laxatives on a regular basis.

Initially, the patient presented to our hospital with two separate episodes of large bowel obstruction due to volvulus and underwent successful decompression by colonoscopy. After the second episode, the patient's legal guardians declined our recommendation for elective sigmoidectomy as a permanent solution to the problem.

Several months later, the patient presented again with sigmoid volvulus, this time accompanied with clinical signs of sepsis and abdominal compartment syndrome due to the massively dilated

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colon. A chest and abdominal CT was performed which demonstrated aspiration pneumonia along with large bowel volvulus with massively dilated proximal large bowel (Fig. 1—Colonic Volvulos with a 14 cm dilated Sigmoid colon). Colonoscopic decompression attempt failed and the patient was taken to the operating room where volvulus of the proximal sigmoid colon was noticed along with necrosis of this area. Most of the large bowel proximal to the point of obstruction was severely dilated and ischemic and therefore a subtotal colectomy with end ileostomy was performed (Fig. 2—Massively dilated colon)

The patient recovered well and was discharged after 10 days, with a functioning stoma and with adequate oral intake.

Pathology analysis of the resected bowel specimen demonstrated colonic wall with ischemic changes in the mucosa and focally in the submucosa, and prominent vascular congestion. Specific staining for ganglions was found to be normal.

During the 1st year after the operation the patient was readmitted four times due to refusal for food intake, abdominal distention and dehydration. An abdominal CT scan showed small bowel obstruction at the distal ileum as a result of partial volvulus of the small bowel, with no mechanical obstructing transition zone (Fig. 3—Small Intestine Volvulos). In all occasions the patient recovered quickly after nasogastric tube for decompression.

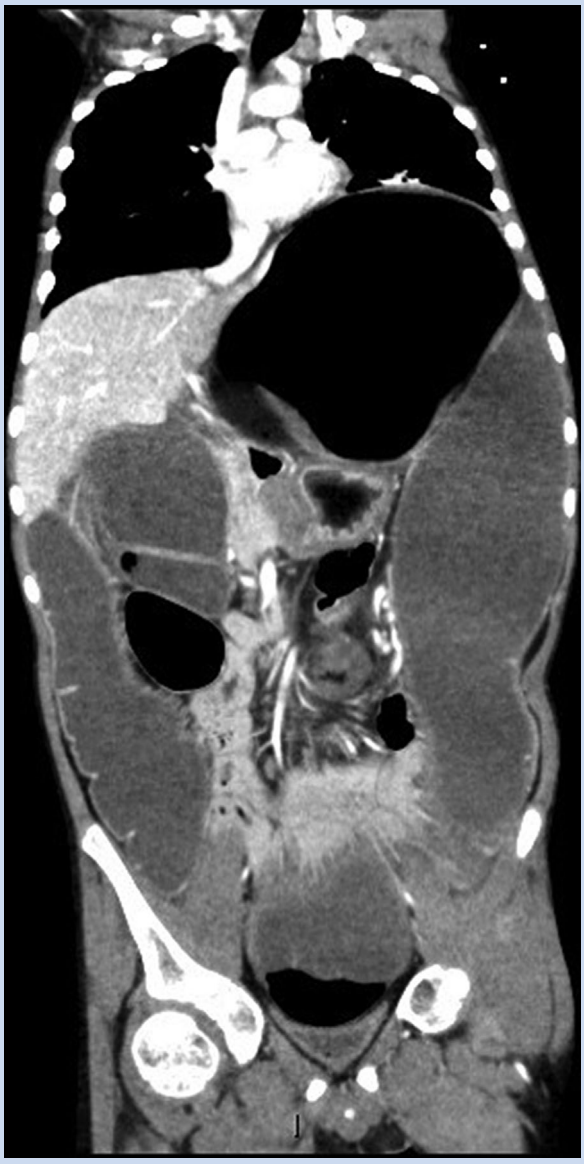

FIG. 1. Colonic Volvulos with a 14 cm dilated sigmoid colon.

DISCUSSION

ATR-X syndrome is a rare genetic condition, caused by a mutation to the ATR-X gene located on the Xq13.3 branch of chromosome X [Gibbons et al., 1995b]. The gene formulates a protein that seems to have an important role in normal development, though the function of the protein remains unclear.

Clinical manifestations of ATR-X syndrome include a variety of clinical presentations, most commonly developmental delay with intellectual disability [Gibbons et al., 1995a; Gibbons, 2006]. There is a wide spectrum of psychomotor retardation, most often speech is absent with low intellectual capabilities. Spasticity is developed in many occasions [Lossi et al., 1999], and seizures and epilepsy occur in one third of patients [Guerrini et al., 2000]. Another common clinical feature is a dysmorphic face, accompanied by facial hypotonia [Gibbons et al., 1995a].

Gastrointestinal manifestations are common findings in ATR-X syndrome such as feeding problems, vomiting, abdominal distention and chronic constipation (Gibbons and Higgs, 2000).

Martucciello et al. [2006] reviewed 128 cases of ATR-X syndrome patients with gastrointestinal manifestations, most commonly GE reflux, drooling and constipation.

Apparently, patient's refusal for food is relatively common among these patients and at times leads to dehydration necessitating hospitalization. This can be explained by reflux, regurgitation or even by gastric pseudo-volvulus. Another option would be intermittent volvulus of the small or large bowel as presented in our case.

Intestinal malrotation was a rare finding in Martucciello's review but was the cause of death in two out of four patients described [Martucciello et al., 2006]. No reports of emergency surgery for colonic volvulus have been described in the past. Also, the age of patients described is much younger than the patient in this report.

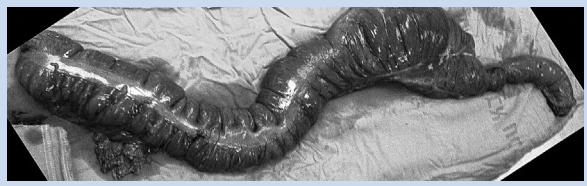

FIG. 2. Massively dilated colon with a transition zone at the distal sigmoid.

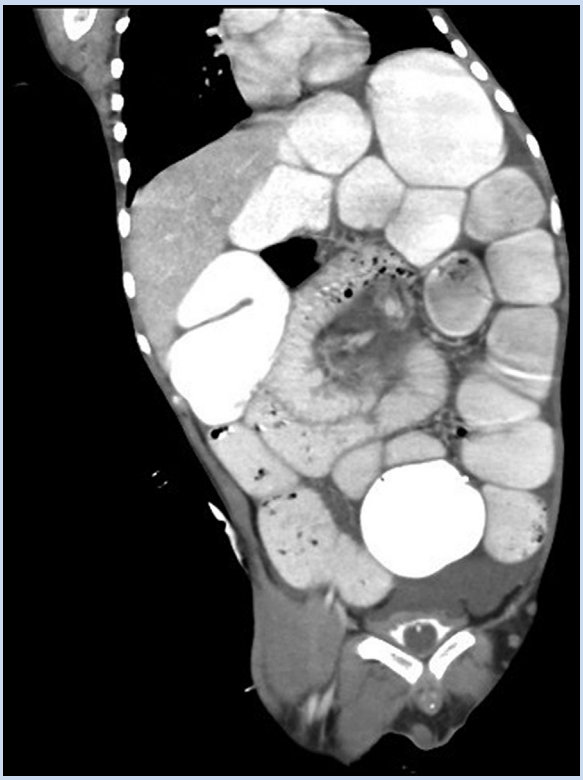

FIG. 3. Small intestine Volvulos.

It seems that ATR-X syndrome correlates with many gastrointestinal clinical problems, afflicting not only the feeding capabilities of the patients, but can also be a concerning medical problem, as aspiration pneumonia and bowel ischemia due to bowel obstruction can risk the patient's life.

We believe that large or small bowel volvulus should be suspected in ATR-X patients refusing oral intake and that imaging be performed accordingly. In the instance of large bowel volvulus, elective surgery should be considered.

CONCLUSION

ATRX syndrome is a rare genetic condition. Many of ATR-X patients present with gastrointestinal symptoms, including vomiting and chronic constipation. High level of suspicion for volvulus and bowel obstruction should be made since these may become a serious medical condition in these patients. We believe that patients with recurrent symptoms should be offered surgical treatment to prevent life threating complications.

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