Gastric Perforation Leading to The Diagnosis of Classic Ehlers Danlos syndrome: A Case Report of an Unusual Presentation.

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Case report

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Abstract

Background: Ehlers-Danlos syndromes (EDS) are a clinically and genetically heterogenous group of heritable connective tissue disorders caused by defective collagen synthesis or structure. Vascular subtype (EDS IV) is reported to be associated with higher incidence of gastrointestinal ruptures. The Most reported site of perforation was the colon particularly the sigmoid colon followed by small bowel. It is very rare to have stomach perforation. There were no reported cases among classic type I and II. In addition, this patient presented with Marfanoid habitus which may develop acute gastric volvulus in combined with pre-existing EDS, perforation can occur.

Case presentation: We are presenting a 14-year-old girl who attended our Emergency Department (ED) with abdominal pain and vomiting. Initially diagnosed with gastroenteritis and discharged once her condition improved. 24 hours later, she developed severe abdominal pain with recurrent vomiting with peritonitis evident on clinical examination. Initial KUB failed to show any free air, however enhanced Computed Tomography (CT) revealed free air and proximal gut contrast extravasation. During exploratory laparotomy, an ischemia anterior and posterior gastric wall with gastric perforation was encountered. A free-hand partial gastrectomy was done. Her post-operative period was complicated with wound infection that managed successfully with Vacuum assisted closure (VAC) dressing. She recovered well without gastrointestinal sequalae in 4 years follow up.

Conclusions: A high level of suspicion must be maintained for heritable systemic connective tissue diseases in any young patient with unusual spontaneous perforation. As these patients can develop life-threatening conditions, immediate intervention is required in addition to prepare for anticipated complications.

Background

Ehlers-Danlos syndromes (EDSs) comprise a wide spectrum of overlapping hereditary disorders of connective tissues. EDS results from defects in the synthesis of collagen synthesis, which may result in a wide-range of clinical presentations affecting the skin, ligaments, joints, blood vessels, and internal organs with a variable severity extent [(1)(2)(3)]. EDS is classified clinically by the 1997 Villefranche nosology into three major groups. They are classical, vascular, and hypermobility-type EDS; others, including kyphoscoliosis, dermato-sparaxis, and arthrochalasia, are extremely rare [(3) (4)]. Genetically, most classical EDS cases are caused by mutations in one of two genes encoding collagen type V (*COL5A1*, *COL5A2*); vascular EDS is caused largely by mutations in *COL3A1*, encoding collagen type III, and the genetics of hypermobility type EDS remains largely unresolved and is predicted to be heterogeneous [(3) (5)]. As EDS types have phenotypic heterogeneity and clinical overlap, clinical evaluation alone is often not definitive, and even after genetic testing the majority of EDS cases remain without a molecular diagnosis. Thus, some patients may show up late to clinical attention or present with complications [(3) (4)].

The clinical presentation among EDS patients varies depending on the sub type. Gastrointestinal(GI) symptoms were noticed in all the types of EDS. Mostly reported symptoms are abdominal pain, nausea, constipation, heartburn, irritable bowel syndrome (IBS)-like symptoms, vomiting, and diarrhea with a wide range of severity scale among the subtypes of EDS [6][7][8][9] . In a systematic review by El Masri and his group who reported 31 patients (27 case reports, 4 retrospective studies) showed that life-threatening digestive complications are mostly seen in the vascular type of Ehlers–Danlos syndrome (EDS IV). Spontaneous gastrointestinal perforation is the most common digestive complication, with colonic perforation as the predominant site in the majority of the cases particularly sigmoid as it contains high collagen volume followed by small bowel perforation, upper rectum, and limited cases reports regarding esophageal rupture, and to lesser extent gastric perforation [10] [11].Gastric symptoms in EDS patients were ranging from recurrent epigastric discomfort to severe bleeding [10] [11] .Peptic ulcers and its complications have been described mainly in patients with vascular-type EDS [10]. Gastric perforations is rarely documented, mostly were related to trauma [10].

Case Presentation

We are presenting a 14-year-old girl , with unremarkable past medical history, who presented to our Emergency Department with abdominal pain and vomiting, initially she was managed as case of gastroenteritis with symptomatic improvement then sent home. 24 hours later, she came back with picture of sepsis, worsening abdominal pain and repeated episodes of vomiting. On clinical examination, she was normotensive, with tachycardia up to 130 and no documented fever. Abdominal exam revealed diffuse tenderness. Radiological images included abdomen KUB x-ray supine, lateral decubitus displayed in **Figure 1 (A &B)**. Initial resuscitation management was carried out with good response. After stabilization, she was transferred to Computed Tomography CT for further characterization of underlying pathology, **Figure 1 (C &D)** for CT findings. However, the patient condition deteriorated upon returning from CT table, for that reason, she was taken emergently to Operating theatre.

Intraoperatively, Exploratory laparotomy was done, findings of ischemic anterior wall of the stomach with evidence of gastric perforation sized about 2x2 cm as displayed in **figure 2**. As well, Ischemic changes noted over the posterior wall mucosa. A Free-hand Partial gastrectomy was done. The necrotic edges were excised and left healthy bleeding edges, which were sutured together, see **figure 2**. A Jacson-Pratt (JP) drain placed, and the abdomen was closed temporarily with a plan of a second-look laparotomy within 48 hours joined with intra operative endoscopy to evaluate the posterior wall vascularity. The patient then was transferred to the Intensive Care Unit (ICU) intubated, with stable hemodynamics and off vasopressors.

Later in 48 hours, a planned Intra-operative endoscopy was performed. Finings of endoscopy was keeping with limited mucosal ischemic changes **(figure 3)**. Moreover, the stomach serosa remined healthy with no further ischemic changes and intact repair suture line. A Jejunostomy feeding tube was inserted followed by definite abdominal wall closure. Post operatively, patient remained in ICU for monitoring and

was successfully extubated. Jejunostomy Tube feeding started, and patient transferred to regular surgical floor. When we started oral diet, She was started gradually on 6 small meals per day owing to her small stomach.

Postoperative course was complicated with superficial surgical site infection which was managed with antibiotics and wound was managed using Vacuum Assisted Closure (VAC) device, figure 4 shows wound progression while on VAC dressing. Pathology report was of submitted specimen of the stomach is keeping with ischemic stomach wall.

Furthermore, as such presentation is worrisome for underlying systemic condition. A detailed clinical examination was done post operatively. Interestingly, examination was supporting marfanoid habitus with findings of long fingers, positive wrist, and thumb sign with mild hyperextensible skin. So, Marfan's syndrome and related disorders sequencing panel was requested, as well DNA sample was obtained. The result detected a heterogenous variant of uncertain clinical significance in exon 6 of COL5A1 gene, c.805G<A (p.Glu269Lys), that support the diagnosis of Classical EDS. In addition, rheumatological workups were ordered and were all within the normal range.

The patient remained in hospital for a couple of weeks post operatively for wound care management, nutritional support then discharged home after removed the JP and Jejunostomy feeding tube in a better condition. In clinic follow up patient was doing great from nutritional and surgical prospective, as well in her school performance.

Discussion

As the diagnosis and management of EDS is challenging sometimes, attention must be taken to estimate the possible complications to avoid further damage [12]. Patients with EDS have a wide range of presenting gastrointestinal GI symptoms. Frequently reported symptoms include nausea, vomiting, heartburn, constipation, abdominal pain and inflammatory bowel syndrome while ranging in severity between different subtypes [6] [8].However, GI complications more common in patients with the vascular form of EDS, and they are at high risk of spontaneous perforation [11] [13] [14]. Other major forms type I,II and III developed recurrent hernia as the most common complication which can be related to skin hyperextensibility [6] [10] [13].

Spontaneous bowel perforation is a well-documented and potentially life-threatening complication of EDS especially in vascular type. There are over two hundred reported cases in English literature. Mostly reported site of perforation is colonic perforation, specifically sigmoid colon followed by small bowel perforation in patients , that was noticeable the most among the vascular type of EDS [6] [11] [10] [12]. [15] [16] [17] [18] [19] [20]. Furthermore, Stomach perforation is not common and mostly related to traumatic injury [10] [21]. One of the important explained factors behind gastric perforation despite rich blood supply, and to a lesser extent in comparison to the vascular type IV, can be secondary to marfanoid habitus that can lead to gastric volvulus due to abnormality of gastric ligaments and diaphragm hernia

allowing for a higher chance of compromised blood supply and subsequent wall defects and perforation [22] [23] [24]. The rarity of such presentation implies a unique challenge in management.

As EDS patients with a hollow viscus perforation usually present acutely, they usually undergo an immediate surgical intervention. Surgical management of patients with vascular EDS who develop acute GI complications such as bleeding or perforation has been described in the literature. These approaches range from conservative non-surgical management of intestinal perforation to more conventional surgical management with resection of appropriate segments of the gut [20] [25] [26] [27]. Some cases underwent segmental bowel resection and primary repair with stoma creation with attempts of reversal afterward [18] [28].

Finally, a diagnosis of this hereditary condition has implications for the patient's family, and genetic testing needs to be offered to living relatives. As the patient has a one in two chance of having an affected child, reproductive counseling as well as predictive, diagnostic, and prenatal testing should be made available.

Conclusions

Gastrointestinal involvement in Ehlers Danlos Syndrome and Marfan's Syndrome are common, ranging from benign to life-threatening cases. Crucial management to prevent fatal complications, with the importance of identifying the subtype of EDS to predict the morbidity and mortality. Any young patient presented with bowel perforation at any site of GI tract or any vascular accident without a known etiology, EDS should be considered even if it in unusual site. The patient must be educated about the involvement of all the body organs, and the possible complications. As well family counseling and offering genetic tests are obligatory in these cases.

List Of Abbreviations

EDS: Ehlers Danlos syndrome

ED: Emergency Department

JP: Jacson-Pratt (JP) drain

CT: Computed Tomography

VAC: Vacuum assisted closure

IBS: Irritable bowel syndrome

KUB x-ray: Kidney, ureter, and bladder *X-ray*

ICU: Intensive Care Unit

GI: *Gastrointestinal*

Declarations

Consent:

Verbal informed consent was obtained from the patient and her father for publication of this case report and any accompanying images.

Ethics approval and consent to participate

Not applicable

Availability of data and materials.

Not applicable

Competing interests.

The authors declare that they have no competing interests

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Figures

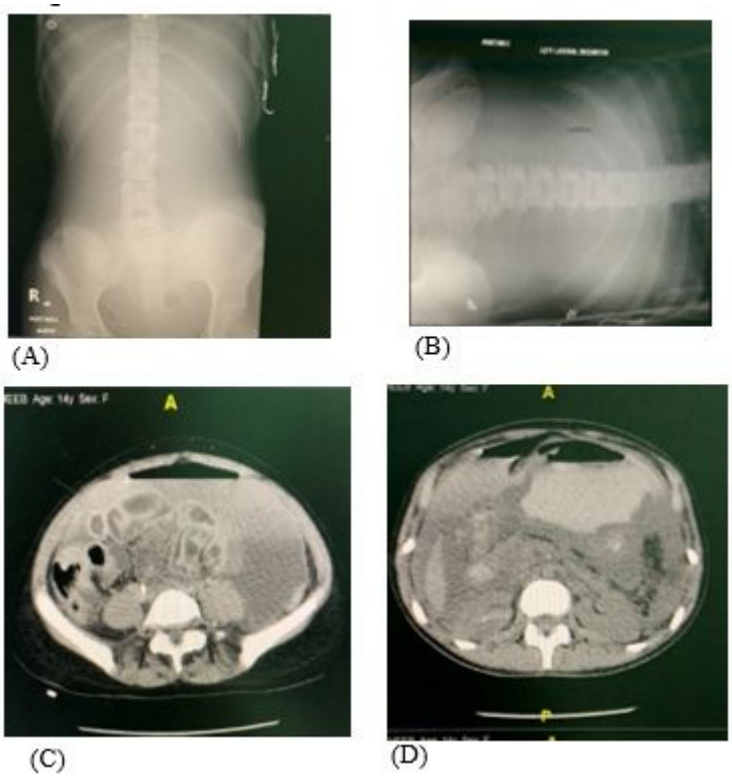

Figure 1

(A) abdomen KUB x-ray supine position , (B) lateral decubitus (C) and (D) Computed tomography image of the abdomen and pelvis with contrast with findings of contrast extravasation.

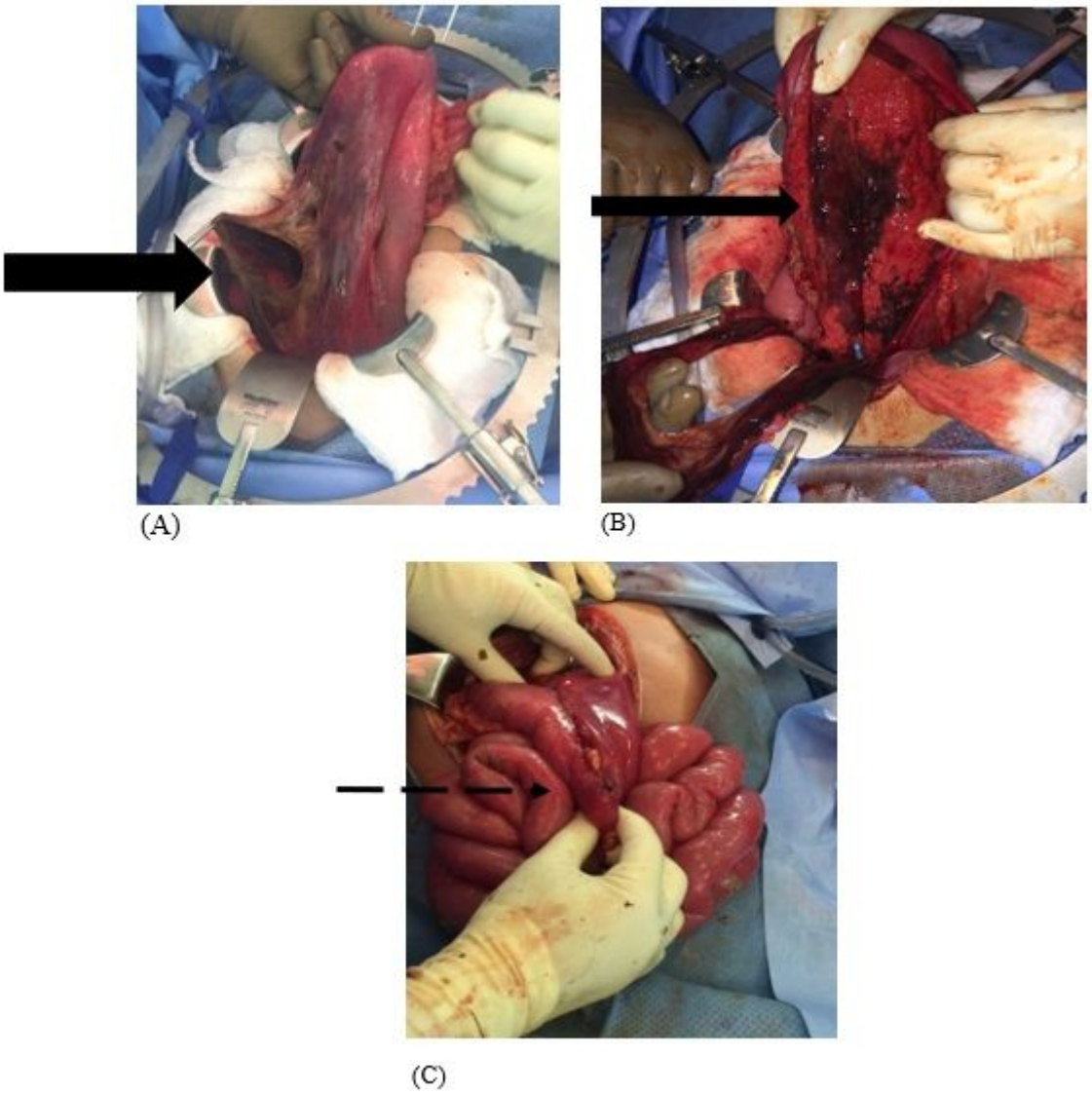

Figure 2

(A) and (B) intra-operative laparotomy showed completely ischemic anterior and posterior wall of the stomach with gastric perforation, 2x2 cm hole within the ischemic wall in A (bold arrow) and internal gastric wall in B (thin arrow). In (C) showed partial gastrectomy with gastrojejunostomy anastomosis (dotted arrow).

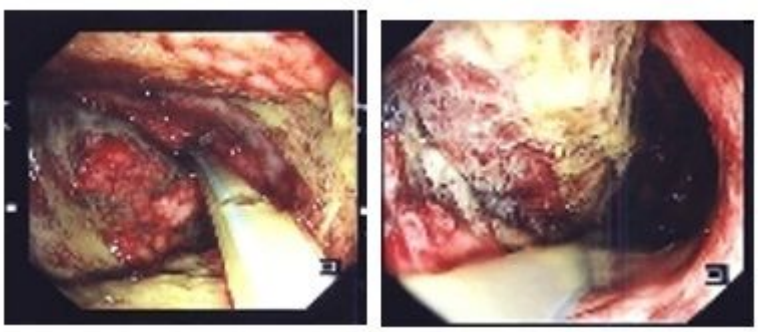

Figure 3

Intra Operative Endoscopy, with findings of necrotic mucosa.

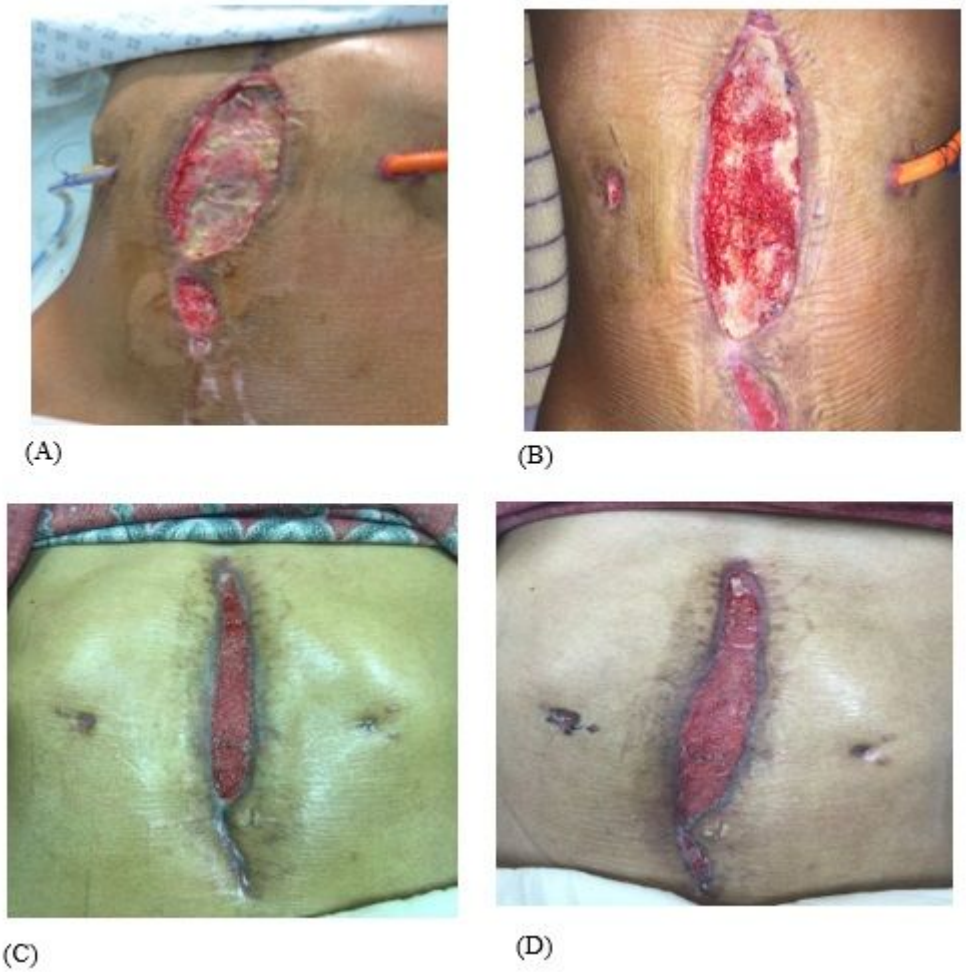

Figure 4

(A)and (B) showed jejunostomy feeding tube with superficial surgical site infection . (C) and (D) Interval removal of the feeding tube with wound progression Vacuum Assisted Closure (VAC).