Visceral artery embolization after endoscopic injection of Enteryx for gastroesophageal reflux disease

Naseem Helo[1*], Alex Wu[2], Eunice Moon[2], Weiping Wang[2]

1. Department of Radiology, Loma Linda University Medical Center, Loma Linda, CA, USA

2. Section of Interventional Radiology, Imaging Institute Cleveland Clinic Foundation, Cleveland, OH, USA

* **Correspondence:** Naseem Helo, Department of Radiology, Loma Linda University Medical Center, 11234 Anderson St, Loma Linda, CA 92354, USA
(*nhelo@llu.edu*)

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ABSTRACT

Gastroesophageal reflux disease (GERD) can be difficult to manage medically and may require endoscopic or surgical interventions. The Enteryx procedure was designed to enhance the gastroesophageal barrier function by endoscopic injection of a copolymer into the lower esophageal sphincter. We present a rare case of a patient who was found to have migration of the copolymer into the celiac trunk and bilateral renal arteries during a work-up for persistent intermittent hematuria, which began shortly after Enteryx therapy for GERD.

CASE REPORT

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A 22-year-old man presented with lower back pain and intermittent painless hematuria. He denied fever, chills, urinary frequency, or other constitutional symptoms. Past medical history was significant for severe gastroesophageal reflux disease (GERD) since age 15, for which he received Enteryx therapy at an outside hospital 6 months before presenting at our hospital. His vital signs and blood tests were within normal limits, and results from a cystoscopy were also normal. A plain radiograph of the abdomen obtained as part of the intravenous pyelogram revealed a curvilinear high-density material at the expected location of the gastroesophageal junction (GEJ), the site of the Enteryx injection. There were additional irregular linear radiopaque densities lateral to L1 to the right and left of the spine, at the region of the renal arteries (Figure 1). In addition, a small filling defect was seen within the upper pole calyx of the right renal collecting system after IV contrast injection, which the interpreting uroradiologist suggested was focal extrinsic compression (Figure 2). Magnetic resonance angiogram of the kidneys did not demonstrate any abnormalities in the renal arteries, and subsequently, renal arteriography was performed for further evaluation. The flush aortogram demonstrated linear filling defects along the main celiac trunk and both renal arteries (Figure 3A). Right renal arteriogram demonstrated a tubular filling defect at the superior aspect of the main right renal artery (1 cm from the origin) extending into the bifurcations and causing partial occlusion of two segmental arteries (Figure 3B). Similarly, left renal arteriogram demonstrated a linear filling defect along the superior aspect of the proximal vessel (Figure 3C). There were no perfusion defects, arteriovenous malformations, or venous anomalies in either kidney. These findings were most consistent with embolization of Enteryx copolymer into the celiac trunk and renal arteries.

Since the initial presentation, the patient has been followed for 7 years. His renal functions and blood pressure values have remained within normal range. However, the patient continues to suffer from intermittent hematuria.

DISCUSSION

Treatment strategies for GERD include lifestyle modifications, medical therapy, surgical procedures, and minimally invasive endoscopic therapies that boost the function of the esophageal sphincter. Surgical treatment for GERD is considered in patients with Barrett's esophagus or high volume reflux, those for whom medical management has failed, and patients who are noncompliant with medical therapy. Minimally invasive procedures include thermal ablation, endoscopic suturing, and implantable or injectable agents [1]. Injection of Enteryx (Boston Scientific, Natick, MA, USA) into the lower esophageal sphincter (LES) at the GEJ was one such technique. Early randomized, placebo-controlled studies showed that Enteryx treatment was effective in providing symptomatic relief from GERD [2,3]. However, after reports of multiple serious complications, including death and unintended injection into pleura, mediastinum, and aorta, Boston Scientific Corporation issued a recall of Enteryx on September 23, 2005 [4]. The U.S. Food and Drug Administration (FDA) issued a preliminary public health notification on October 14, 2005, and Enteryx was permanently removed from the market [4]. Although Enteryx was withdrawn from the market, the FDA continues to update information regarding complications associated with Enteryx injections.

Enteryx is a biocompatible polymer (8% weight/volume [W/V] ethylene-vinyl alcohol copolymer) mixed with a radiopaque contrast agent (30% [W/V] tantalum powder) and dissolved in an organic liquid carrier (dimethyl sulfoxide [DMSO]) [3]. Upon injection, DMSO rapidly diffuses into the tissue and precipitates into a spongy polymer. Enteryx injection was performed under both endoscopic and fluoroscopic guidance to ensure intramuscular injection [3]. However, accidental injections into the mediastinum, pleural space, and aorta have occurred. Migration of Enteryx into the celiac artery and bilateral renal arteries associated with persistent hematuria has never been reported in the literature. Because Enteryx is unlikely to be absorbed intravascularly once the material polymerizes in the soft tissue of the LES, we believe that direct injection into the aorta is likely the underlying cause of visceral arterial embolizations of Enteryx.

Inadvertent intra-aortic injection of Enteryx can occur for several reasons. First, the distal esophagus descends along the right side of the descending aorta in the posterior mediastinum and then runs anteriorly and slightly left to the aorta in close proximity. Therefore, there is a potential risk of direct aortic puncture. Second, because Enteryx is injected with a 1-mL syringe, an inadvertent injection may not be readily apparent under fluoroscopy because of the small volume and the rapid vascular dilution and dissipation of the polymer [2].

While chest pain, cough, shortness of breath, dysphagia, and significant weight loss are known complications of Enteryx treatment, gross painless hematuria has never been reported as the initial presenting symptom in patients who underwent Enteryx therapy [4].

There are many possible causes of hematuria, including medications, interstitial nephritis, papillary necrosis, hemorrhagic cystitis, urolithiasis, and glomerular or nonglomerular causes. The patient's original hematuria may be incidental. However, Enteryx embolization to the renal arteries cannot be excluded as the cause of the patient's hematuria in light of the close temporal relationship, with the procedure occurring only 6 months before presentation. Potential long-term complications could occur as a result of embolization into the renal arteries, such as hypertension and renal function compromise, although these symptoms were not present in this patient. In addition, other Enteryx-like solutions such as Onyx 18 (EV3 Neurovascular, Irvine, CA, USA) have been successfully used to treat arteriovenous fistulas, showing the possibility of Enteryx as an embolic material [2,5].

TEACHING POINT

Endoscopic injection of Enteryx into the lower esophageal sphincter carries the risk of inadvertent intravascular injection and migration of the polymer into visceral arteries. Although the product has been withdrawn from the market, similar products may be developed in the future and operators need to be aware of the potential complications of such injection and the risks of intravascular embolization. A test in which contrast is injected before the polymer mixture can help ascertain the location of injection and improve the safety of the procedure.

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FIGURES

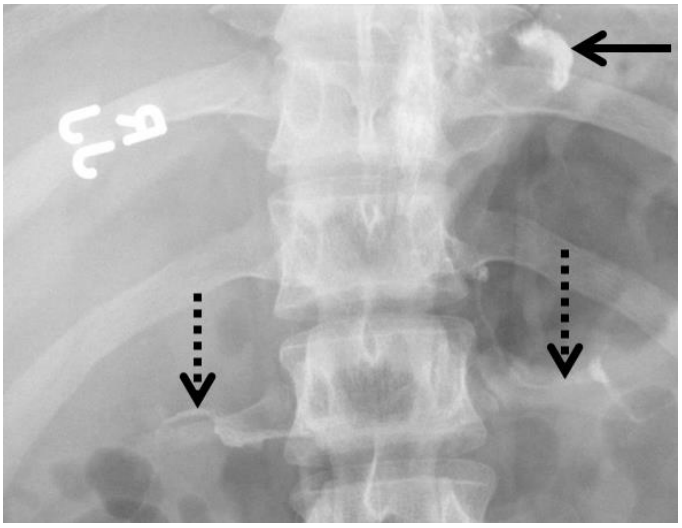

Figure 1: A 22-year-old man who presented with intermittent hematuria was found to have visceral artery embolization of injected Enteryx. A plain radiograph of the abdomen showed a cashew nut-shaped radiopaque density at the gastroesophageal junction (solid arrow), suggesting the site of injection of Enteryx. The dotted arrows indicate linear densities in the expected regions of the renal arteries.

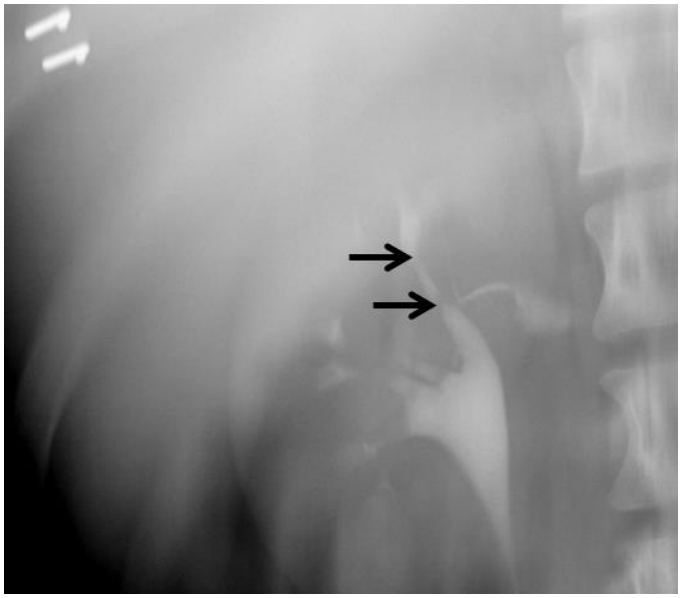

Figure 2: A 22-year-old man who presented with intermittent hematuria was found to have visceral artery embolization of injected Enteryx. A plain radiograph of the abdomen taken 11 minutes after intravenous injection of contrast showed a small filling defect within the upper pole calyx of the right renal collecting system (arrows).

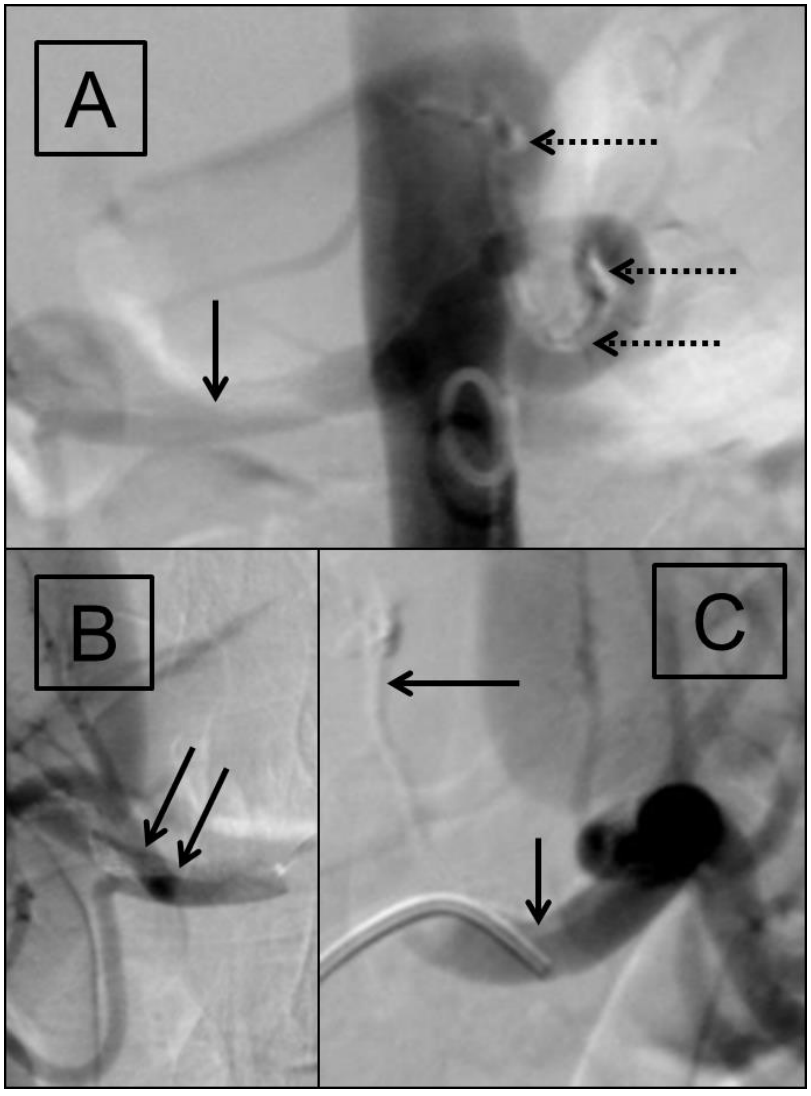

Figure 3 (left): A 22-year-old man who presented with intermittent hematuria was found to have visceral artery embolization of injected Enteryx. (A) Abdominal aorta-renal arteriography demonstrated filling defects at the celiac trunk (long dashed arrow), left (solid arrow) and right (short dashed arrows) renal arteries, indicating migration of Enteryx to those areas. (B) Selective right renal arteriography confirmed the presence of filling defects at the superior aspect of the right main renal artery extending into the bifurcation(solid arrows) (C) Selective left renal arteriography also showed filling defects at the superior aspect of the left proximal main renal artery (arrows), suggestive of Enteryx migration.

Etiology	Likely transmural injection of Enteryx through the esophagus into the aorta
Incidence	Unknown; this is the first case report
Sex ratio	No specific sex predilection
Age predilection	No specific age predilection
Risk factors	Esophagus abutting the aorta
Treatment	None
Prognosis	Unknown
Imaging findings	Filling defects of the visceral arteries on angiogram.

Table 1: Characteristics of visceral artery embolization after Enteryx injection

Differential diagnosis	Intravenous pyelogram	MRI	Angiogram
Medication-induced hematuria	No specific findings	No specific findings	No specific findings
Interstitial nephritis-induced hematuria	Persistent patchy nephrogram	No specific findings	Persistent patchy nephrogram
Papillary necrosis-induced hematuria	Subtle streak of contrast extending from fornix parallel to long axis of papilla; triangular or bulbous cavitation of papilla	Triangular or bulbous cavitation of papilla	Excretory phase: subtle streak of contrast extending from fornix parallel to long axis of papilla; triangular or bulbous cavitation of papilla
Hemorrhagic cystitis-induced hematuria	Thickened, coarse mucosal folds with cobblestone appearance	Thick-walled bladder, pericystic inflammatory changes	No specific findings
Urolithiasis-induced hematuria	Ureteral calculi; enlarged kidney on obstructed side; hydronephrosis	No signal; large, detectible signal voids	Ureteral calculi; excretory phase: enlarged kidney on obstructed side; hydronephrosis

Table 2: Differential diagnosis table for hematuria after Enteryx injection

ABBREVIATIONS

GEJ: gastroesophageal junction
GERD: gastroesophageal reflux disease
FDA: Food and Drug Administration
LES: lower esophageal sphincter

KEYWORDS

GERD; embolization; GEJ; Enteryx; hematuria

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