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Surgical Treatment of Small Intestinal Bleeding Caused by Arterial Gastrointestinal Fistula: A 2-Case Report

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Abstract

Background: This study aims to better understand diagnosing and treating arterial gastrointestinal fistulas. **Methods:** The diagnosis and treatment of two patients with arterial gastrointestinal fistulas were reported, and the experience with diagnosis and treatment was summarized. **Results:** In these two cases, both patients were admitted with bleeding as the primary complaint, both underwent emergency laparotomies, and both patients were diagnosed with small intestinal bleeding before surgery. the first patient died as a result of an abdominal aortic aneurysm rupture caused by chronic vascular repair and postoperative implant infection; the second patient underwent vascular repair on time, we treated him with third-generation cephalosporin, and after he was stabilized, we performed left total iliac stent placement and left internal iliac artery embolization; he had no fever after surgery, his incision was healed, and he was successfully discharged from the hospital. **Conclusion:** Aortic gastrointestinal fistula is rare and has a high mortality rate, attention should be paid to distinguishing it from small intestinal bleeding. Timely diagnosis and rapid surgical treatment are keys to improving survival.

Keywords

Ileocecal Valve, Abdominal Aortic Aneurysms, Laparotomy Probe, Angiography, Primary Aortoenteric Fistula

1. Introduction

Small intestinal bleeding usually refers to the bleeding caused by intestinal lesions between the beginning of the Treitz ligament and the ileocecal valve, ac-

counting for 5% - 10% of the entire gastrointestinal bleeding, but the cause of the bleeding is an arterial gastrointestinal fistula, which is very rare. The incidence of this disease is low, the disease is dangerous, and the mortality rate is extremely high. Primary aortoenteric fistula (PAEF) is a rare but extremely serious complication of abdominal aortic aneurysms. Diagnosis and treatment are often delayed due to a poor understanding of the disease, resulting in extremely high mortality. Here we report 2 cases of small bowel bleeding due to rare causes admitted in February 2021 at our hospital.

2. Case 1: Abdominal Aortic-Duodenal Fistula

A 60-year-old male has been admitted to tacheng District hospital Complaining of Passing Intermittent blood in his stool for 8 days with one Attack of Bloody vomiting. The initial investigation in that hospital has shown erosive gastritis and bulbar duodenitis (gastroscopy), multiple colonic polyps, proctitis, and internal hemorrhoid (colonoscopy). The patient was referred to the emergency room of our hospital for further management, the patient was kept under observation but developed passing a large amount of blood in the stool and hematemesis. Emergency gastroscopy revealed evidence of a possible small gut bleeder, he was resuscitated with intravenous fluid and blood transfusion.

Diagnosis and Treatment

Vital signs revealed a body temperature of 37˚C, pulse rate of 85 beats per minute, respiratory rate of 20 breaths per minute, clear breath sounds in both lungs, and blood pressure of 110/76 mmHg (micro-pump norepinephrine). Physical examination showed mild abdominal tenderness, no rebound tenderness, and hyperactive bowel sound (7 times/minute). The results of hematological, and biochemical showed (hemoglobin 45.00 g/L; serum albumin 28.64 g/L) the abdominal pelvic contrast CT suggests local luminal dilation of the abdominal aorta (**Figure 1**). Gastroscopy showed active bleeding in the digestive tract, and small intestinal bleeding was more likely. Intervention and Outcome: Despite resuscitating the patient with fluid and blood transfusion, hematocrit progressively decreased, and the patient entered an impending shock state, so an emergency explorative laparotomy was decided. We did an intraoperative exploration of the anterior wall of the antrum and there was a palpable limited thickening of the tube wall, the opening of the gastrocolic ligament, and clearing of the duodenal surrounding tissues, then suddenly seeing a large amount of blood reflux in the antrum. We decreased the bleeding by applying pressure to the duodenal horizontal, and we asked the gastroenterologist to perform an intraoperative gastroscopy during the operation considered the abdominal aortic aneurysm-duodenal fistula, however, we use a titanium clip to locate it, and consult with a vascular surgeon. There were multiple atherosclerotic plaques in the abdominal aorta wall, tumor-like abdominal aorta, and abdominal aorta rupture into the duodenum, the bleeding site was clear, and gauze tamponade is

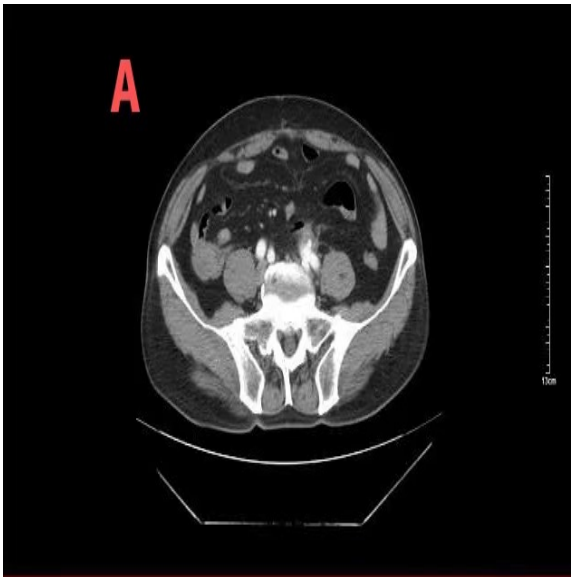

Figure 1. Abdominal pelvic CT showing the site of a left internal iliac artery-ileal fistula.

used to stop the bleeding in this case we should consider the abdominal aortic aneurysm resection and artificial vascular replacement surgery, Postoperative implant infection is likely, so abdominal aortic aneurysm stent endoluminal isolation was performed after the condition was stabilized, but the patient had sudden ventricular fibrillation and cardiac arrest during the operation, and was transferred to the intensive care unit after the rescue and died after the ineffective rescue.

3. Case 2: Left Internal Iliac Artery-Ileal Fistula

A 71-year-old male presented to our department with a history of 7 years of intermittent blood discomfort in the stool. Upon admission, the patient presented with abdominal pain (followed by syncope), a dark red stool (the specific amount is unknown), and no sign of fever, cough, vomiting, diarrhea, constipation, constipation seizures, asthma, dyspnea, or other discomforts. Following the admission, we performed the following treatment: colonoscopy prep. After colon polyp electrocoagulation, metal titanium clip closure, acid inhibition, hemostasis, and other symptomatic treatments, the patient has been improved and discharged, but despite the treatment, the patient appeared to have significant blood in the stool 3 - 4 times a day. The patient came back to the hospital for further treatment.

3.1. Diagnosis and Treatments

Vital signs revealed a body temperature of 37˚C, pulse rate of 76 beats/min, respiratory rate of 19 breaths/min(clear breath sounds in both lungs) arrhythmia, no murmur, and blood pressure of 108/52 mmHg. Physical examination showed normal bowel sounds, blood routine test showed (hemoglobin 51 g/L, biochemi-

stry: serum albumin 33.5 g/L) Patient has history of hypertension for 20 years, and 7 years ago, due to a "rectal malignant tumor", the patient underwent "rectal cancer radical resection".

3.2. Treatment and Outcomes

After admission, a CT of the abdomen and pelvis shows left ureteral disruption, iliac common artery bifurcation, level ureteral wall thickening, and a nodule (**Figure 2(A)**). *A colonoscopy* reveals ulceration of the small intestine with possible bleeding. At the same time as the laparotomy probe, the patient re-dissolves the blood three times, accompanied by syncope, an increased heart rate, a progressive decrease in blood pressure and hemoglobin, and shock manifestations, we actively stop the bleeding by giving a blood transfusion, and shock correction. As per intraoperative exploration, there was a lot of adhesion in the greater omentum, intestine, ileum, and posterior peritoneum, and the adhesion has been resolved. There was a large amount of blood gushing out of the adhesion site, and the amount of bleeding was uncontrollable, so we put pressure on the blood vessel with gauze, and the bleeding situation was better than expected. Furthermore, a vascular surgeon was asked to assist in the intraoperative resection of a portion of the ileum and to perform a lateral anastomosis after the operation, the patient was moved to the ICU, and after treatment, he was transferred to the vascular surgery department for left iliac vein stenting. He recovered smoothly after the operation and was cured and discharged from the hospital after one month. The patient did a CTA of the entire aorta 5 months after surgery, which revealed that the left common iliac artery stenting had changed, and the artificial blood vessels were still functional; the calcium plaque of the aorta, right common iliac artery, and bilateral internal and external iliac arteries were normal (**Figure 2(B)**).

Figure 2. Abdominal CTA shows (A) after the left internal iliac artery embolism, which also shows the site of the left common iliac artery stent implantation. (B) shows the site of vascular repair before the embolization of the left internal iliac artery.

4. Discussion

Aortic gastrointestinal fistula is a rare cause of gastrointestinal bleeding, with a low incidence and a very high mortality rate. It can be divided into primary and secondary. Secondary aortic gastrointestinal fistulas are common after an aneurysm or arterial occlusive disease after aortic reconstruction. Erosion, rupture of the arterial wall, and penetration of adjacent digestive tracts (esophagus, duodenum, jejunum, ileum, colon) cause primary aortoenteric fistula (PAEF). occurs mainly in the horizontal and ascending parts of the lower renal abdominal aorta and duodenum, accounting for about 83% of all cases; the rest can occur between the aorta and the small intestine, colon, and stomach. Foreign studies have reported that the most common cause of PAEF is abdominal aortic aneurysm, of which 85% originate from an atherosclerotic abdominal aortic aneurysm, 15% from infectious diseases, and a very small number from malignant tumors, duodenal ulcers, foreign bodies, or abdominal radiotherapy [1]. Traumatic or fungal aneurysms are the second most common cause, and other less common causes include radiation, infection, tumors, peptic ulcers, inflammatory bowel disease, and foreign body ingestion.

Literature reported 189 cases of PAEF, of which 147 (83%) had an aortic-duodenal fistula, mainly located in segments 3 and 4 of the duodenum. The autopsy detection rate was only 0.04% - 0.007%. PAEF was first reported and described by Sir Astley Cooper in 1829, and PAEF was first patched by Zenker in 1954. At present, there are few relevant studies, mostly seen in some case reports, and its onset population is mainly elderly patients over 60 years old. The main symptoms of PAFE include abdominal pain, abdominal mass, hematemesis, or melena. The triad of abdominal pain, abdominal fluctuating mass, and gastrointestinal bleeding is a typical symptom of PAEF, but the incidence of the triad is only 11% - 25% [2]. Sentinel bleeding, an intermittent mild to moderate bleeding that is a precursor to major bleeding, is a characteristic manifestation of an aortic gastrointestinal fistula. This is due to the temporary cessation of bleeding when the fistula is blocked by an organic thrombus during the first bleeding, followed by catastrophic hemorrhage due to increased arterial pressure after thrombus movement, shedding, or volume replacement [3].

This intermittent time window of bleeding is longer than 7 hours in more than 70 percent of patients, 50 percent over 24 hours, and 29 percent longer than one week, providing valuable timing for surgery [4]. The diagnosis of PAEF is difficult, and the preoperative diagnosis rate is only 0% - 36% [5]. In February 2021, our hospital admitted a patient with a left iliac ileal fistula. In this case, the patient was blood-based, and there was no obvious abnormality in the gastroscopy, and the colonoscopy showed that a small intestinal ulcer and bleeding may be possible because capsule endoscopy has certain limitations for patients with hemodynamic instability, previous surgical history, and possibly intestinal stenosis, so combined with the patient's symptoms and signs and gastrointestinal endoscopy results, the cause of small intestinal bleeding was unknown. The co-

lonoscopy showed that a small intestinal ulcer and bleeding may be possible because capsule endoscopy has certain limitations for patients with hemodynamic instability, previous surgical history, and possibly intestinal stenosis. The abdominal-pelvic CT and intraoperative exploration revealed that the cause of small bowel bleeding was the common iliac artery-ileal fistula. In patients who undergo radical rectal cancer resection for rectal malignancy, the intestinal tube may adhere and involve the iliac artery, eventually forming a left internal iliac artery-ileal fistula. The patient's abdominal-pelvic CT can only indicate the location of the lesion and suggests that there may be a lesion in the common iliac artery, which cannot be diagnosed, and colonoscopy shows that small bowel ulcers and bleeding may be possible, combined with the patient's abdominal-pelvic CT, colonoscopy, and intraoperative exploration results, to confirm the diagnosis of a left internal iliac artery-ileal fistula. In addition to clinical manifestations, the diagnosis of this disease mainly relies on abdominal and pelvic CT and colonoscopy, but both have their limitations. CT is often recommended as the test of choice, but a negative CT cannot be completely ruled out. In addition, colonoscopy is often normal when the bleeding stops, so this method should be performed whenever possible when bleeding is active. The key to the treatment of this disease lies in early diagnosis and timely surgery, and the mortality rate of non-surgical treatment can reach 100%. Patients with high suspicion of an aortic gastrointestinal fistula should be examined without hesitation to clarify the diagnosis. Rapid, noninvasive, contrast-enhanced CT is often used as a first-line diagnostic measure. Endoscopy may reveal active bleeding lesions and is important for differential diagnosis; however, it is difficult to detect distal duodenal PAEF because fistulas are often located in the distal duodenum to the jejunum, which most endoscopy cannot detect, and may cause massive bleeding by moving fresh thrombus at the fistula. Notably, endoscopy tends to entangle in diagnosing gastritis, ulcers, and other manifestations, resulting in delayed treatment and serious consequences. Although patients who had timely surgery had good treatment outcomes, stenting and surgical treatment may be safer in patients who are clinically rare, inexperienced in diagnosis, or unable to complete an angiography or abdominal CTA before surgery. In addition, sepsis and retroperitoneal infection are likely to occur in such patients due to arteries communicating with the intestine, eventually leading to surgical failure, so anti-infective therapy should be actively strengthened after surgery [6].

5. Conclusion

Fistulae formation between the intestinal tract and aorta or one of its branches remains an uncommon cause of intestinal bleeding with great mortality. Bidirectional endoscopic procedures may point to the small gut as the source of bleeding but usually fail to localize and diagnose the exact cause. In suspected hemodynamically stable cases, CT-Angiography of the abdomen and pelvis is the imaging modality of choice for the diagnosis. Hemodynamically unstable patients

with evidence of massive bleeding should immediately undergo either endovascular repair of the aorta (EVAR) or more invasive explorative laparotomy.

Patient Consent for Publication

Written informed consent for publication of the present report was obtained from the patient.

Author's Contribution

Maieryemu Sulaiman and Sakarie Mustafe Hidig conceived and designed this case report and wrote the initial draft of the report. All authors have read and approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Confirmed Envenomation by *Androctonus amoreuxi* (Egyptian Yellow Fat Tail Scorpion)

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Abstract

In the United States, envenomations by native scorpion species such as *Centruroides* are common and generally well-tolerated. On the contrary, *Androctonus* species envenomations are exceedingly rare outside the Middle East and North Africa but are particularly deadly. We report a case of envenomation by an Egyptian Yellow Fat Tail (*Androctonus amoreuxi*) scorpion and the subsequent clinical course. A hobbyist and dangerous scorpion collector was stung by his pet *Androctonus amoreuxi*, purchased online. Our patient rapidly developed severe localized pain followed by systemic effects, including tachycardia, hypertension, tachypnea, anxiety, GI symptoms, diplopia, dyspnea, profound myalgias, and intense paresthesias. Ultimately, he was diagnosed with a grade 2-to-3 scorpion envenomation based upon evidence of autonomic hyperactivity and cranial nerve dysfunction. He never progressed to cardiopulmonary compromise; neither dobutamine nor antivenom was administered, and he improved with supportive care alone. Case details were verified in person and via electronic medical record review.

Keywords

Androctonus amoreuxi, Fat Tail Scorpion, Envenomation

1. Introduction

Scorpion envenomations are common among scorpion collectors and hobbyists; however, the genus *Androctonus* is unusually deadly and a major cause of scorpion envenomation morbidity and mortality worldwide, particularly in the Middle East and North Africa. We report a case of envenomation by an Egyptian Yellow Fat Tail (*Androctonus amoreuxi*) scorpion and the subsequent clinical

course.

2. Case Report

A 47-year-old otherwise healthy male was stung once on his right middle finger while hand-feeding his pet *Androctonus amoreuxi* (Figure 1). He is a hobbyist and collector of dangerous scorpions he purchases online. Within 30 minutes of the envenomation, he developed localized pain and edema (Figure 2) in his right fingers and hand. He rapidly progressed to severe paresthesias of the right arm, crampy abdominal pain, nausea, and a throbbing headache. Fortunately, he was able to drive himself to a small local hospital.

Figure 1. *Androctonus amoreuxi*, the pet scorpion that the hobbyist purchased online.

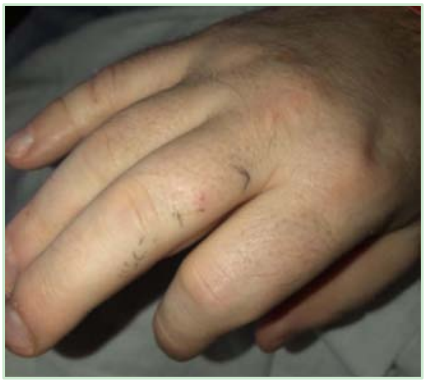

Figure 2. Right hand 15 minutes after envenomation.

He arrived in the Emergency Department (ED) 90 minutes after envenomation. His initial vitals were: temperature 38˚C, heart rate 120 beats per minute, blood pressure 180/90 mmHg, respiratory rate 24, and oxygen saturation 98% on room air. Laboratory testing was notable for a WBC 11.0 k/uL, bicarbonate 21 mEq/L, lactate 2.9 mEq/L, creatinine 1.35 mg/dL (baseline 1.0 mg/dL), pH 7.54, and pCO_2 27 mmHg. Serum sodium, potassium, transaminases, alkaline phosphatase, bilirubin, lipase, PT/INR, hemoglobin, and platelet count were within normal limits. He had no eosinophilia. EKG demonstrated sinus tachycardia with normal intervals, unchanged from his prior studies. The chest radiograph was clear without evidence of pulmonary edema, and the abdominal CT was unremarkable. Consequently, the Medical Toxicology team was consulted.

Over the next two hours, he developed progressive nausea, anxiety, and restlessness, followed by dyspnea, diffuse myalgias, and diplopia. The paresthesias intensified and spread to his face, left arm, and legs. He described his skin as "fire hot, embedded with shards of glass"; however, he was never hypoxemic or hypotensive. He received 2 liters of intravenous isotonic crystalloid for dehydration and fluid losses, IV ondansetron for nausea, acetaminophen and low-dose intravenous hydromorphone for analgesia, and intravenous midazolam for symptoms of anxiety, agitation, and neuroexcitation.

He was admitted to the Medical Intensive Care Unit (ICU) to monitor for cardiopulmonary decompensation, and his symptoms peaked at 12-to-18 hours post-envenomation. Notably, he never developed hemodynamic instability, hypoxemia, pulmonary edema, or coagulopathy and did not receive dobutamine, prazosin, or antivenom. Over the next 24 hours, his laboratory studies gradually normalized, and a transthoracic echocardiogram was normal. He was discharged on hospital day 3 with mild persistent abdominal pain and lingering paresthesias of his right hand and arm.

At a two-week follow-up visit, his symptoms had entirely resolved, and his wife had directed him to remove all scorpions and enclosures (**Figure 3**) from their home.

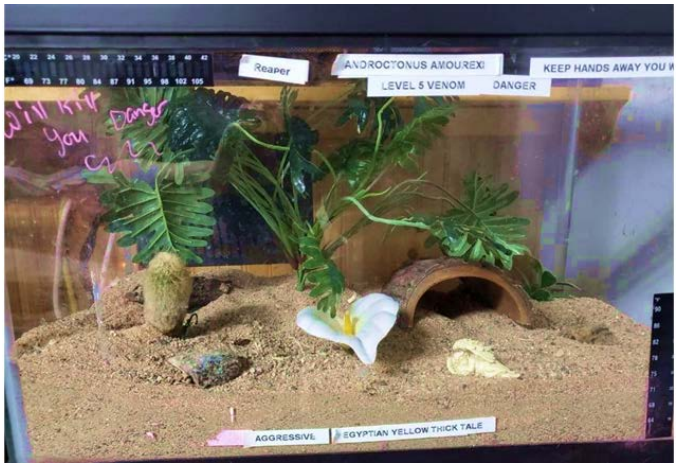

Figure 3. *Androctonus amoreuxi* enclosure.

3. Discussion

Androctonus amoreuxi is one of the multiple scorpions of the *Androctonus genus* found throughout North Africa and the Middle East. Scorpions from this area of the world account for 42% of the global sting burden and approximately half the fatalities. Case-fatality rates, which generally are imprecise measurements, are estimated at 0.42-0.52% [1].

Androctonus venom contains a complex milieu of neurotoxins, cardiotoxins, and immuno-inflammatory peptides. Alpha-toxins are the most clinically significant of these and are sodium channel openers that inhibit the fast inactivation of sodium channels, resulting in increased sodium influx and neuroexcitation [2]. Envenomation often causes localized symptoms that resolve with symptomatic and supportive care; however, a minority develop a nonspecific syndrome of life-threatening autonomic hyperactivity (including increased vagal tone) and massive catecholamine and cytokine release that can lead to a wide array of symptoms [3]. Mortality associated with *Androctonus* envenomation frequently results from cardiogenic shock and pulmonary edema (cardiogenic and noncardiogenic) and is often treated with a dobutamine infusion and vasodilators, respectively [4]. Antivenom is available in North Africa and the Middle East; however, it is challenging to obtain promptly, has questionable clinical efficacy, and has a high occurrence of adverse reactions. Local physicians argue against its administration as the standard of care [5].

In our case, the patient rapidly developed local and systemic toxicity consistent with a grade 2-to-3 scorpion envenomation based upon symptoms of autonomic hyperstimulation (adrenergic and cholinergic) and neuromuscular excitation. However, he never progressed to cardiopulmonary compromise and, accordingly, he did not receive dobutamine or antivenom and improved with symptomatic and supportive care alone.

4. Conclusion

Andoctronus envenomations are uncommon in the US but commonplace in scorpion collectors and hobbyists. Unfortunately, these envenomations have high morbidity and mortality.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Recurrence of Poorly Differenciated Cervical Cancer by Single Splenic Metastasis: Case Report and Literature Review

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Abstract

Background: The incidence of cervical cancer in Belgium is 11.1 per 100,000. With the introduction of cervical cytology screening and more recently anti-HPV vaccination, this rate has been decreasing for almost 20 years. Despite this, some patients are missed by the screening and prevention system and cervical cancer is still diagnosed at an advanced stage. Recurrences by splenic metastases are rare and are most often found at autopsy. Case Study: We describe the case of a 41-year-old caucasian patient with a single splenic recurrence after radiotherapy, chemotherapy, brachytherapy, and surgery for a poorly differentiated adenocarcinoma of the cervix grade 3 at an initial stage IIB according to FIGO. This recurrence happens 3 years after the initial treatment. After monitoring this asymptomatic lesion, the size increase results in laparoscopic splenectomy. Histology demonstrates a splenic metastasis recurrence of adenocarcinoma of endocervical origin. Conclusion: The spleen is a rare metastatic site in cervical cancer. Splenectomy followed by chemotherapy is the therapy most often found in the literature, which is however poor in this regard.

Keywords

Cervical Cancer, Recurrence, Splenic Metastasis, Human Papillomavirus

1. Introduction

Cervical cancer is the tenth most common cancer in the world of all ages and all sexes, according to the World Health Organization in 2018. In Europe, the incidence of cancer of the cervix is 13, 4 per 100,000, with a mortality rate of around

5%. In Belgium [1], there was an incidence of 11.1 per 100,000 (634 cases) in 2015, with 200 deaths, making cervical cancer the 12th most common cancer in women, while remaining a rare cause of death (1.7% of total cancer mortality). Almost entirely attributable to the HPV virus (99%) and its persistence, the incidence has been reduced from 60% to 90% and the mortality rate by 90% since screening with the PAP smear test. Thanks to HPV vaccination in Belgium from 2005 to 2015, the incidence decreased from 12.3% to 11.1%. The impact is still minimal to date but should be more significant in the years to come. In fact, the natural history of precancerous lesions towards invasive cancer is 15 years on average. Nevertheless, efforts are still to be made in the vaccination campaign, especially in the Wallonia-Brussels Federation. Indeed, vaccination coverage is 29% compared to 83% for Flanders [2]. In Belgium, the current coverage of cervical cytology screening, performed every 3 years, is 59%. Despite the almost systematic screening, some patients escape the system and we still see cervical cancer in advanced stages. In the case of invasive cancer [3], dissemination is preferably done by lymphatic route and hematogenous dissemination occurs often later. Typical preferred hematogenous metastatic sites are the lungs, liver and bone system.

Here we report the case of a recurrence by single splenic metastasis. These splenic metastases are rare and are more often found during autopsies. In the literature, 16 articles relate spleen metastases in the context of recurrent cervical cancer.

2. Case Report

A 41-year-old patient presents to the emergency room for smelly bleeding. The vaginal examination performed under narcosis objectifies a 5 cm cervical mass. The histological analysis of the mass pleads for a florid dedifferentiated epithelial neoplastic process, with a primitive glandular not excluded. The clinical stage according to FIGO is IB. The PET-scan shows a neoplasia of the cervix involving the cervix, the corpus uteri, the left parameter and associated with a bulky left external iliac adenopathy and right common iliac. Pelvic magnetic resonance imaging (MRI) confirms a large tumor lesion of the cervical region of 5cm with infiltration of the parameters and bilateral iliac adenopathies. The rest of the examination is strictly normal. The FIGO stage after imaging is IIB.

Initially, the patient receives 50.4 Gy radiation therapy combined with cisplatin-based chemotherapy on a weekly basis. A new vaginal examination under narcosis shows the persistence of a large friable tumor occupying the cervix and hanging in the vagina of 4 cm. The right parameter is dubious on the internal third. Following this, two brachytherapy sessions with a dose of 7 Gy per session are performed. After a new examination under narcosis, the tumor had shrunk in size and was 3 cm in diameter with a soft parameter. The initial treatment ended with an enlarged hysterectomy with bilateral iliac lymph node dissection for tumor residue. The anatomopathological result confirms a poorly differen-

tiated adenocarcinoma of the cervix of grade 3 of 2 × 1.1 cm with invasion of the right parameter. The surgical margins are clean. 3 out of 19 lymph nodes are invaded. The FIGO stage is IIB, TNM stage ypT2b ypN1. In multidisciplinary oncological consultation, simple monitoring is recommended.

Three years later, the patient presents a recurrence at the splenic level and at the pre-sacral level treated with chemotherapy (paclitaxel and carboplatin 8 cures). 8 months later, the metabolic response to treatment is complete in locoregional and almost complete in splenic location. Three months later, the patient presents a completely asymptomatic and isolated metabolic reactivation at the splenic level measuring 42 mm at MRI with expectant attitude. MRI 6 months later shows an increase in the lesion to 54 × 38 mm (**Figure 1**). 5 months later, a significant increase in size to 69 × 46 mm (**Figure 2**) will indicate the performing of a splenectomy.

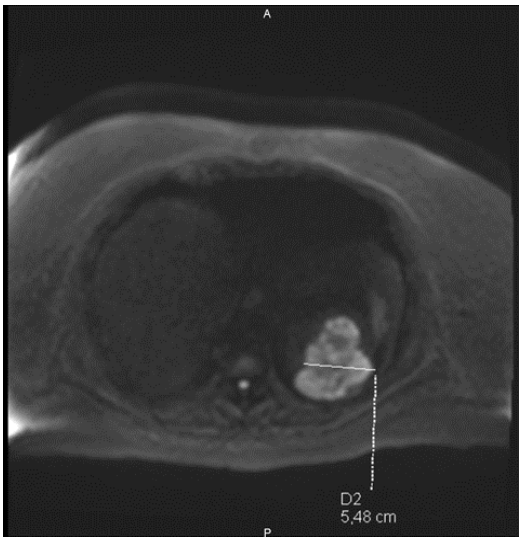

Figure 1. T2 weighted hyperintense lesion.

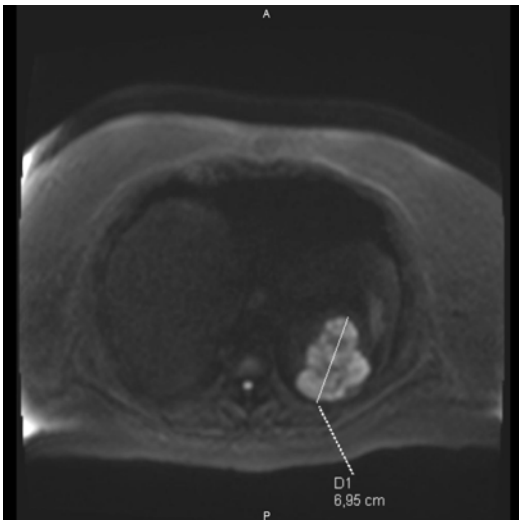

Figure 2. Size increase after 6 months.

The procedure is performed 18 months after the discovery of this unique lesion in the spleen (Figure 3).

On pathology analysis, it is indeed a recurrence of primary cervical neoplasia with a necrotized tumor metastasis of 5 cm corresponding to an adenocarcinoma of endocervical origin (Figure 4 and Figure 5).

The patient will remain without recurrence to the Pet-scanner performed at 4 and 8 months. But at 13 months, she will present an aggressive recurrence in the form of lung, peritoneal and left adrenal metastases. This recurrence will lead to the patient's death 14 months after the splenectomy was performed.

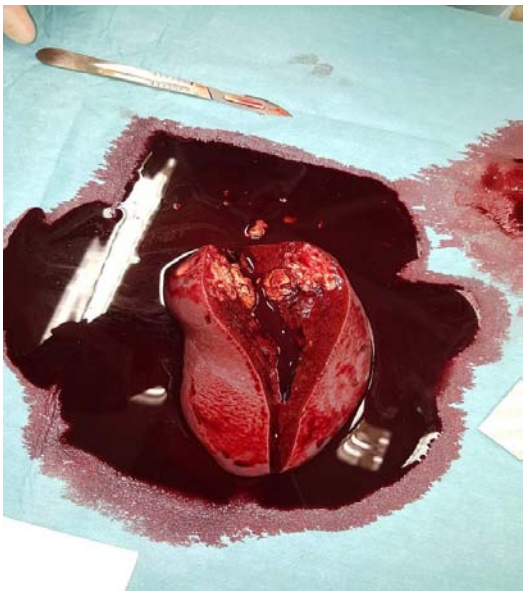

Figure 3. Metastasis in splenectomy specimen.

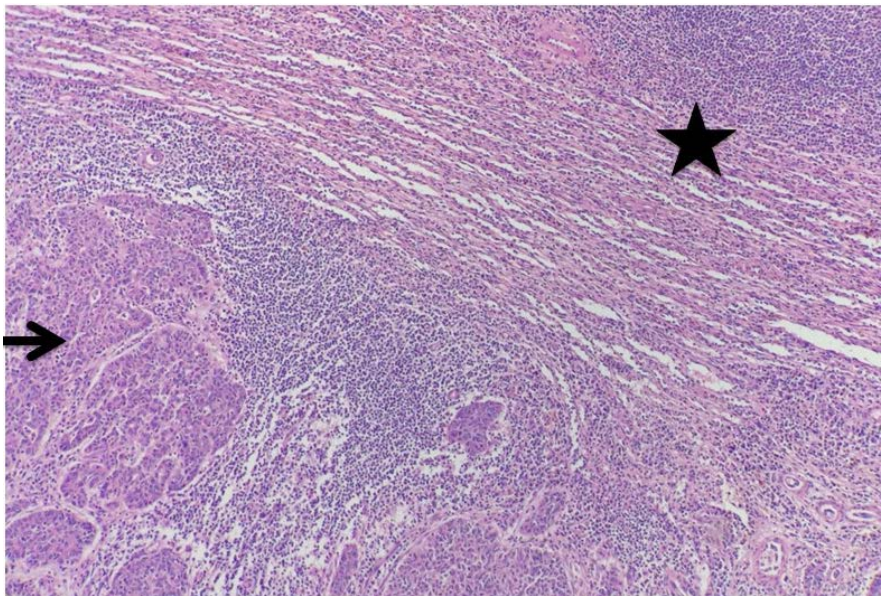

Figure 4. Splenic parenchyma infiltrated by the tumor. Arrow: tumor; Star: Splenic parenchyma. (HE; obj 10x).

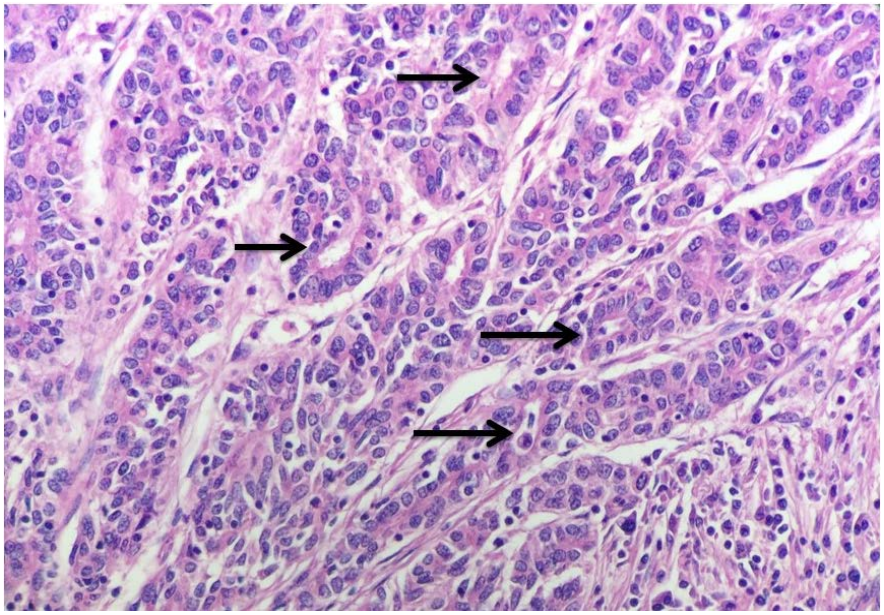

Figure 5. Histological image of adenocarcinoma. Arrows: formation of glandular lumen. (HE coloring; 40x lens).

3. Discussion

The follow-up of cervical cancer recommended by the European Society for medical oncology (ESMO) [4] includes, at least a clinical examination (vaginal examination and rectal examination) and an anamnesis with a cervico-vaginal smear (+HPV typing) 1x/3 - 6 months for 2 years then 1x/6 - 12 months for 3 years. After the 5-year period without recurrence, follow-up is done once a year. When two cervico-vaginal smears have a negative HPV typing, normal monitoring is resumed (smear 1x/3 years). If a recurrence is suspected following a clinical sign, a CT scan or PET-CT is performed.

Some authors [5] suggest the use of SCC antigen (squamous cell carcinoma antigen) [5] for epidermoid cancers, and CEA as a tool for monitoring the disease after primary treatment. Indeed, SCC antigen is a glycoprotein whose rate is influenced by tumor transformation. This biomarker is high in 28% - 88% of patients with epidermoid cancer. In the early stages, a high level of SCC-Ag is associated with a risk for recurrence (lymph node metastasis, stromal invasion, invasion of vascular spaces and big tumor size). We did not use SCC antigen but it probably have had little interest in the follow-up of adenocarcinoma.

In the case of splenic metastasis, the most common complaints are weight loss, pain in the left hypochondrium and nausea, which should therefore lead to an X-ray examination. However, in most cases, splenic metastasis is discovered during a follow-up examination in an asymptomatic patient (as in the case of our patient) or during imaging performed for a completely different reason. The risk of splenic metastasis is painful splenomegaly, thrombosis of the splenic vein and splenic rupture [6].

Splenic metastases are rare entities and are most often associated with lung,

breast or melanoma cancers. Their incidence varies between 2.9% and 9% for solid tumors [7]. They are found in more or less 1% of autopsies [8]. Fewer than 100 cases of single spleen metastases have been reported, 50% of which originate from the female genital tract [9].

To date, in the literature, 16 articles (Table 1 and Table 2) report cases of recurrence in the spleen after primary treatment for cervical cancer, 12 of which describe recurrence of cervical cancer by single splenic metastasis (Table 1). Most cases are published in the form of a case report with review of the literature. In the majority of the situations described, a splenectomy is performed, with anatomo-pathological examination of the nature of the lesion in order to confirm the recurrence [10]. The most frequent histological type is epidermoid cancer. The recurrence delay is between 8 months and 5 years.

Table 1. Single splenic metastasis (RT = Radiotherapy, BT = Brachytherapy, CT = Chimiotherapy).

Year	Author	Histological type	Initial treatment	Time to recurrence	Diagnostic/treatment	Age
1977	Brufman [11]	Epidermoid				
1987	Klein [12]	Epidermoid	RT + BT	4 years	Splenectomy	28
1992	Campagnutta [13]	Adenocarcinoma	Surgery + RT	5 years	Splenectomy	47
1997	Carvalho [14]	Epidermoid	RT	4 years	Splenectomy + CT	47
2004	Goktolga [15]	Epidermoid	Surgery + RT	3 years	Biopsy + Debulcking	45
2004	Pang [16]	Epidermoid	Surgery + RT	5 years	Splenectomye + CT	45
2008	Kim [17]	Epidermoid and Mucinous adenocarcinoma	RT, BT, CT RT, BT, CT	8 months 9 months	Splenectomy + CT for both of them	46 and 54
2010	Di Donato [18]	Epidermoid	Surgery	30 months	Splenectomy	/
2014	Taga [19]	Undifferentiated carcinoma	RT, CT	10 months	Splenectomy	49
2014	Shama [20]	Epidermoid		3 years	Biopsy	
2017	Bacalbasa [21]	Epidermoid		18 months	Splenectomy	31
2017	Applebaum [22]	Epidermoid	Surgery, BT			62

Table 2. Splenic metastasis and other concomitant lesion.

Year	Author	Histological type	Initial treatment	Time to recurrence	Diagnostic/ treatment	Location	Age
2006	Gupta [6]	Carcinoma	CT, RT	12 months	/	Spleen + Liver	41
2014	Villalon [7]	Adenocarcinoma	Surgery, RT, BT	2 years	Splenectomy + CT	2 splenic lesions	76
2014	Aitelhaj [23]	Epidermoid	Surgery, BT	8 months	Biopsy + CT	Spleen + Bresat	55
2016	Dixit [24]	Epidermoid	Surgery, RT, CT	17 months	Splenectomy +CT	Spleen + Mesentery	46

The spread of cervical cancer occurs more often either by local extension or by lymphatic route. The hematogenous pathway is rare. Therefore, the preferred hematogenous metastatic sites are the lungs, the bones, the mediastinum, the supraclavicular nodes and the liver. Furthermore, the pathophysiology of the mode of dissemination of cervical cancer within the spleen has not been clearly studied, but it seems that it is hematogenous [11]. The spleen is an unfavorable environment for the development of metastases. Several reasons have been put forward to explain this rarity of splenic metastases [22]:

1) Rare hematogenous pathway in cervical cancer; 2) the extension is most of the time local; 3) role of the splenic capsule; 4) poor afferent lymphatic vessels in the spleen; 5) tortuosity of the spleen vessels; 6) constant splenic blood flow with contractions in the spleen which force the blood from the sinusoids to go into the splenic veins; 7) anti-tumor antibodies present in the spleen; 8) concentration of phagocytes in the spleen.

Regarding therapeutic management, no consensus was found. Given that splenic recurrence is associated with a poor prognosis, excision of it by splenectomy seems to several authors to be an acceptable therapeutic option, more or less followed by chemotherapy according to certain publications, in order to improve survival [16]. Our patient had a 9 months disease-free survival, but an aggressive recurrence at 13 months.

4. Conclusion

In cervical cancers, splenic metastases are rare entities. The data in the literature is poor. No consensus is therefore determined for the monitoring and therapeutic management of these lesions. Splenectomy nevertheless seems to be the appropriate treatment to provide pathological confirmation of the recurrence and to avoid complications such as splenic rupture or thrombosis of the splenic vein. Monitoring by biomarkers like SCC antigen may be an approach for epidermoid types but this still requires studies. However, the key to this kind of neoplastic pathology is found upstream of the development of the disease through prevention; on the one hand, primary prevention with HPV vaccination and, on the other hand, secondary prevention with screening for precancerous lesions.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Right Post-Traumatic Diaphragmatic Hernia with Liver Dislocation

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Abstract

Diaphragmatic hernia is a rare consequence of thoraco-abdominal trauma. It may be associated with high morbidity and mortality, particularly if surgical intervention is delayed. We report a case of a right diaphragmatic hernia in a 75-year-old woman. The patient was referred to our hospital with mild dyspnea. Chest radiograph showed an overtly elevated right hemi-diaphragm. Thoracic and abdominal computed tomographic scan was requested and showed a defect of the right diaphragmatic muscle wall with intrathoracic ascension of the liver. During the postoperative course, the patient was still on mechanical ventilation, hemodynamically unstable. She developped urinary peritonitis and an extensive bowel ischemia worsening. We report this case to show that the prognosis is related to associated injuries and possible complications. The possibility of a diaphragmatic rupture should be kept in mind and surgery is mandatory in order to avoid complications.

Keywords

Thoraco-Abdominal Trauma, Right Diaphragmatic Hernia, Rare Complication, Liver Dislocation

1. Introduction

Post-traumatic diaphragmatic hernia is a particular and rare consequence of thoraco-abdominal trauma that may go unnoticed [1] [2]. The abdominal organ herniation through the right diaphragm is even rarer due to the liver protective function. Only half of cases are diagnosed early and this fact may lead to progressive herniation of intra-abdominal contents into the thorax [3] [4] [5]. The case reported concerns a patient suffering from right diaphragmatic hernia with liver dislocation complicated by bowel ischemia.

2. Observation

A 75 year old female patient, with no medical history, was admitted to the emergency department following a traffic accident. She was in a car that hit an electric pylon with the notion of a death on board. At admission, the patient was conscious and hemodynamically stable, with mild dyspnea. The clinical examination showed palpebral ecchymosis; no other external injuries were apparent. Thoracic examination revealed decreased breathing sound in the right lower hemithorax. The rest of the examination was unremarkable.

A chest X-ray showed an overtly elevated right hemi-diaphragm (**Figure 1**). Thoracic and abdominal computed tomographic scan (CT scan) was requested and showed a defect of the right diaphragmatic muscle wall measuring 84 mm in diameter with intrathoracic ascension of the liver and a small peritoneal effusion (**Figure 2**). The CT scan also showed the presence of a small leakage of iodinated contrast media under the bladder with emphysema of the perineal soft tissues due to a rupture of the bladder floor and a polyfractured pelvis.

She was then admitted to the surgery department for an exploration. They found a right diaphragmatic breach of 12 cm with the presence of the hepatic dome intra-thoracically and a breach in the anterior wall of the bladder of 2 cm. The procedure consisted of a repair of the diaphragmatic wound and the bladder breach by suture.

In the intensive care unit, on the second postoperative day, the patient was still on mechanical ventilation, hemodynamically unstable, put on 3 mg/h of norepinephrine with BP = 110/60 mmhg, HR = 112 bpm, Diuresis at 0.5 ml/kg/h. Blood test results showed an acute renal failure with urea = 1.14; creat = 28.3; cytolysis: ALAT = 224; ASAT = 374; hyperleukocytosis: WBC = 35.290/mm^3; CRP = 329; with abnormalitis of hemostasis PT = 46%; APTT = 38.4 seconds. On the fourth postoperative day, her hemodynamics got worse. There was also a largequantity of urine released from the redon drain. The patient was taken to the OR for surgery: there was serous effusion made of urine and extensive bowel ischemia (**Figure 3**). The prognosis was poor, the patient died on the 5th postoperative day.

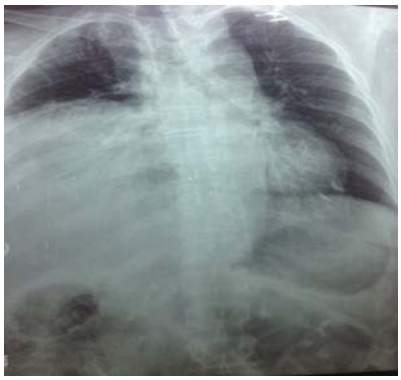

Figure 1. Chest X-ray showing elevated right hemi-diaphragm.

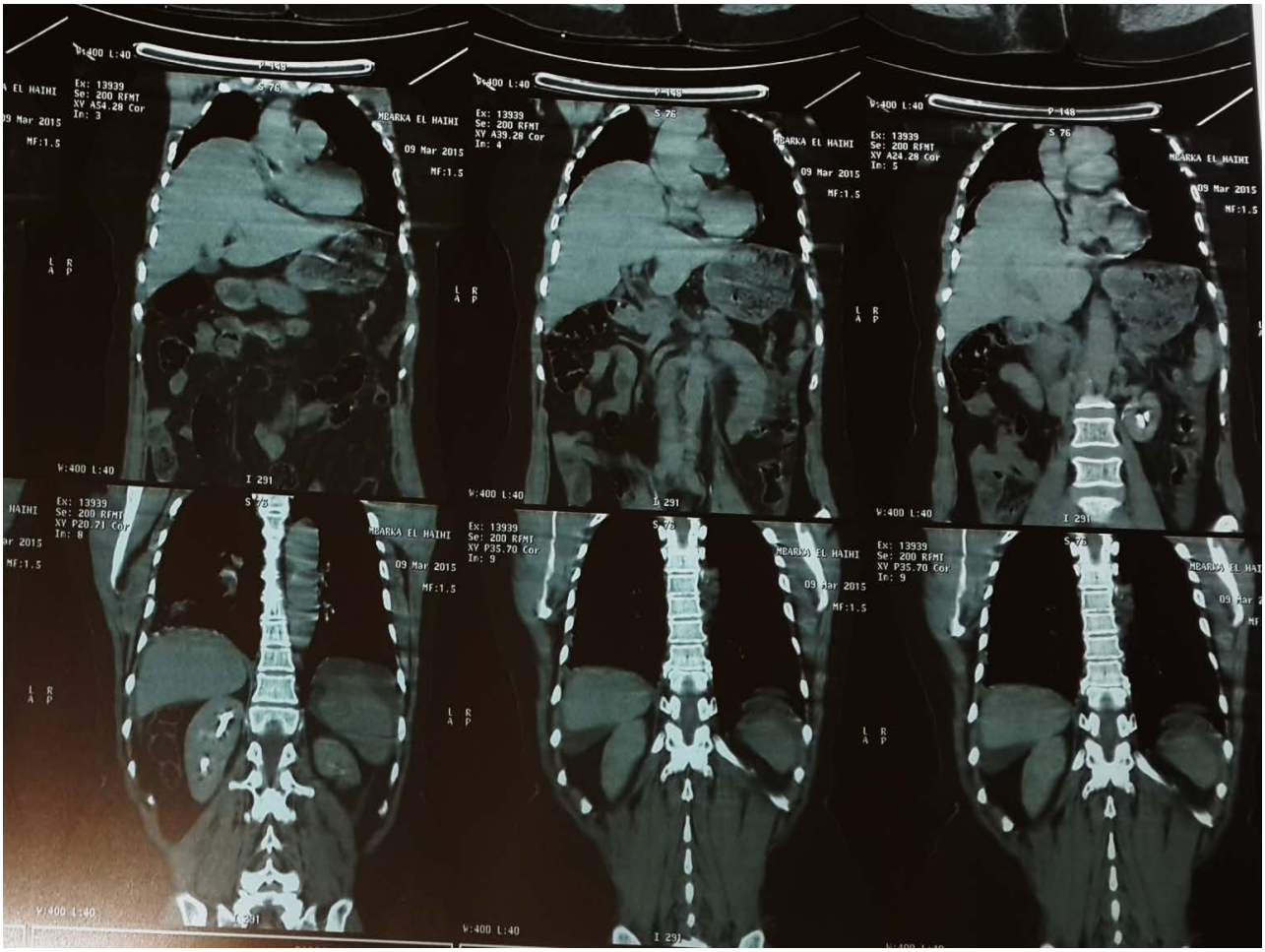

Figure 2. Thorax and abdominal CT showing the dislocation of the liver with compression of the right lung and shift of the mediastinum to the left.

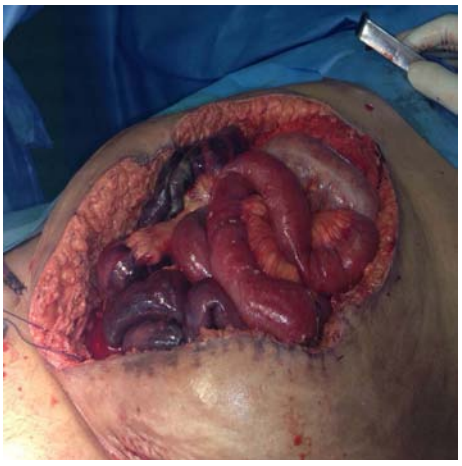

Figure 3. Intraoperative view showing acute bowel ischemia.

3. Discussion

The diaphragm is a dome-shaped and thin musculoaponeurotic barrier that plays

an important role in respiratory function. Traumatic diaphragmatic rupture is a rare clinicopathological entity. It occurs in 0.8%~7% of blunt trauma patients and 10%~15% of penetrating trauma patients [1] [2]. Left hemidiphragmatic hernia is more common because liver exerts a protective function against the herniation of the viscera. Petrone *et al.* reported a traumatic diaphragmatic hernia rate of 75% on the left versus only 25% on the right side [3]. Yet, many authors believe that the incidence of right diaphragmatic traumatic ruptures is underestimated. In fact, autopsy series demonstrated that there was an equal incidence between right and left lesions, leading some authors to wonder whether the left diaphragmatic hernias were more frequent or simply easier to diagnose [3] [4].

Clinical presentation is divided into three phases. The early phase is dominated by cardiorespiratory signs (dyspnea, orthopnea and chest pain). The intermediate period is characterized by clinical signs that may be absent or atypical such as epigastralgia, vomiting… Finally, the late phase is often noisy due intestinal obstruction [5].

X-ray and CT scan are most commonly used techniques for diaphragmatic rupture diagnosis. The chest X-ray could be normal or show marked elevation of one hemidiaphragm, especially on the right side, thus giving low sensitivity to this examination. It detects 27%~60% of left ruptures and 17% of right ruptures. On the other hand, chest CT scan detects 78% of left ruptures and 50% of right ruptures. CT scan has better sensitivity to diagnose right diaphragmatic rupture, by showing discontinuity of the hemidiaphragm, the dependent viscera sign, the collar sign, and intrathoracic herniation of abdominal contents [6] [7].

Once the diagnosis is made, surgery is mandatory in order to avoid complications. The approach could be laparotomic, thoracotomic or minimal invasive. Laparotomy is more appropriate in unstable patients when associated intra-abdominal injuries are suspected. Thoracotomy is necessary to handle late diaphragmatic hernia and isolated lesions of the right diaphragm and in case of expected chest injury [7] [8] [9].

Mortality is almost nil in isolated diaphramatic rupture. The morbidity in right diaphragmatic rupture are often due to associated intra-abdominal or intrathoracic injuries [4] [5] [6] [7] [8]. In our case, the prognosis was clouded by urinary peritonitis and the bowel ischemia.

The acute bowel ischemia observed in our patient is likely due to an abdominal compartment syndrom. The association between abdominal compartment syndrom and intestinal ischemia is further described in animal studies, showing a significant decrease in perfusion of intestinal mucosa and mesenteric arterial blood flow [10] [11]. If the abdominal compartment syndrome is not diagnosed or treatment is delayed, the outcome is almost always fatal. The reason for the high mortality is due to the early involvement of multiple organs. Also, the higher the abdominal pressure, the higher the mortality. Other factors associated with mortality include surgery lasting more than 2 hours, developing abdominal

compartment syndrome within 48 hours of admission, and an elevated lactic acid level despite treatment. Even those who survive have significant morbidity from residual deficits like renal failure, muscle wasting, respiratory distress, and liver dysfunction [12] [13].

4. Conclusion

Post-traumatic diaphragmatic hernia is not an uncommon sequel. But lack of awareness of this condition may delay in diagnosis and result in life-threatening complications. The diagnosis is difficult and often delayed. An awareness of the condition assisted by the radiological investigations will lead to an early diagnosis and treatment which ultimately helps in managing the patients better. The management is surgical. Prognosis is related to associated injuries. The possibility of a diaphragmatic rupture should be kept in mind and sought after any trauma of the thoracoabdominal junction.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Cholangiocarcinoma, Primary Sclerosing Cholangitis, or IgG4-Sclerosing Cholangitis: Similar Presentations with Different Managements

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Abstract

In our case, we present a case of an 80-year-old male who was referred to the gastroenterologist for evaluation of a suspicious mass. CT imaging at the time had shown intrahepatic and extrahepatic biliary dilations, and the patient was thought to have a pancreatic or a common bile duct mass. A mass biopsy showed no malignancy, and further evaluation was warranted. The patient was found to have elevated IgG4 levels and was diagnosed with IgG4-sclerosing cholangitis (IgG4-SC). IgG4 has been found to create a wide array of pathologies, including autoimmune pancreatitis, dacryoadenitis, and sialadenitis. These pathologies have been grouped under an IgG4-Related Disease (IgG4-RD) category. In some cases, this IgG4-RD can present as a subclass of primary sclerosing cholangitis due to immune depositions and swelling of the CBD. Due to the strictures caused by the sclerosing cholangitis, intrahepatic and extrahepatic dilations might be found on endoscopic ultrasound (EUS). It is imperative to differentiate this from a malignant mass as the early recognition and treatment of IgG4-SC can lead to complete resolution. In this case report, we present a case of a patient who was found to have IgG4-SC and responded well to steroid treatment.

Keywords

Cholangiocarcinoma, Sclerosing Cholangitis, IgG4 Related Disease, IgG4, IgGSclerosing Cholangitis, ERCP, CBD Dilation

1. Introduction

Sclerosing cholangitis is a diffuse inflammation and fibrosis that progressively

leads to stenosis and destruction of the bile ducts [1]. Further subclassification includes three types: primary sclerosing cholangitis (PSC), secondary cholangitis, and IgG4 sclerosing cholangitis (IgG4-SC) [2]. IgG4-SC is one of the forms in which IgG4-RD can present. IgG4-RD became recognized as a systemic disease in 2003 after patients with autoimmune pancreatitis were also found to have other manifestations [3]. IgG4 has been contrasted to IgG1, 2 and 3 due to the unstable disulfide bond between the heavy chains. This unstable bond leads to the dissociation of the heavy chains and the bonding of other heavy chains with different antigen-combining sites. This became known as the fragment antigen-binding (Fab)-arm exchange [3]. This altered immune complex can lead to dense lymphoplasmacytic infiltrates. In glandular organs, this can lead to a pathological aggregation and obstruction of the ductal structures leading to the destruction of the involved organs. Specifically, in the case of IgG4-SC, the presentation is similar to the other types of sclerosing cholangitis. They usually present with cholestatic symptoms like pruritus, abdominal pain, elevated ALP and GGT, and bilirubin. The obstruction and demolition of the CBD can lead to hepatic damage and subsequent failure. In contrast to the other types of sclerosing cholangitis, IgG4-SC has been shown to have better outcomes, treatment response to steroids, and less recurrence [4]. We hereby present a case of IgG4-SC presenting as cholangiocarcinoma.

2. Case Presentation

An 80-year-old male with a previous medical history of hypertension, diabetes, coronary artery disease, and bladder cancer was referred to the gastroenterology service for further workup after CT abdomen with IV contrast revealed intrahepatic and extrahepatic biliary dilations with an abrupt cutoff in the common bile duct (**Figure 1**). Mild streaky densities were also seen around the pancreatic head. Initial bloodwork was completed, which showed an ALT of 320 IU/L (Normal: 10 - 60 IU/L), AST of 297 IU/L (Normal: 1 - 40 IU/L), Bilirubin 1.4 mg/dL (Normal: <1 mg/dL), and GGT of 2032 IU/L (Normal: 5 - 40 IU/L), all steering the patient's differential diagnosis to a pancreatic or CBD mass. Endoscopic Ultrasound (EUS) was done, which showed an irregular mass in the CBD wall highly suspicious of cholangiocarcinoma. At that time, an endoscopic retrograde cholangiopancreatography (ERCP) was done, and malignant strictures were seen, consistent with the cholangiocarcinoma differential seen on EUS. These findings were suggestive of Bismuth-Corlette 2 and possibly 3A classification. The surgical service was then consulted, and the patient underwent an exploratory laparotomy with portal node biopsy. The biopsy results failed to show any signs of malignancy with completely benign margins leading to the reassessment by the gastroenterology service. A repeat ERCP with direct visualization cholangioscopy showed a diffusely dilated main bile duct with sludge and pus, a single diffuse stenosis in the right duct with nodularity and dilated vessels similarly seen in malignant mucosa (**Figure 1**), but the biopsy and cytology showed atypical glandular proliferation but no signs of dysplasia or neoplasia.

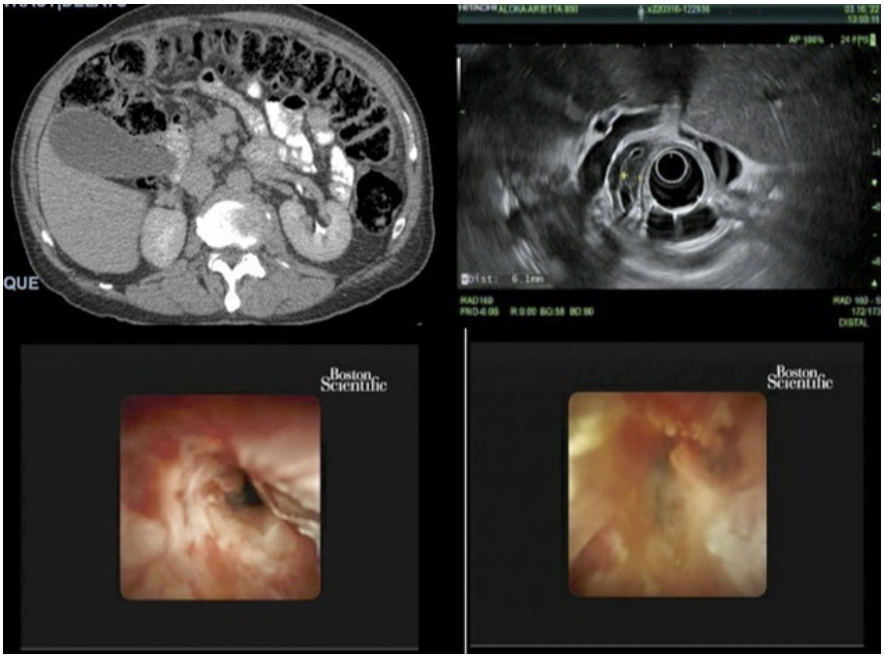

Figure 1. Top: CT of abdomen and ERCP. Bottom: Exploratory laparotomy.

Further evaluation later revealed that the patient had an IgG4 of 931 mg/dL. The combined picture of the dilated hepatic ducts, the nodularity seen on ERCP, and the IgG4 level led to the diagnosis of IgG4-SC. At this time, the patient was begun on a 20 mg prednisone daily regimen for one month, but his IgG4 levels continued to be elevated at 547 mg/dL, so the patient was asked to increase his dose of prednisone to 40 mg daily. At a follow-up two weeks later, the patient's IgG4 continued to trend down to 335 mg/dL.

3. Discussion

Sclerosing cholangitis (SC) can be categorized as primary sclerosing cholangitis (PSC), secondary cholangitis, and IgG4 sclerosing cholangitis. IgG4 related-diseases classification was proposed after autoimmune pancreatitis was found to haveextrapancreatic manifestations [3]. IgG4 immune complexes led to CD4+ and CD8+ depositions in various organs [1]. IgG4 related-diseases are subsequently the deposition of these IgG4 plasma cells and lymphocytes, leading to storiform fibrosis presenting as tumefactive lesions [3]. More specifically, the depositions of these IgG4 immune complexes in the bile duct wall have led to sclerosing of the CBD and hence the IgG4 sclerosing cholangitis subcategory of SC. IgG4 has been contrasted with IgG1, IgG2, and IgG3 as having weaker and unstable disulfide bonds between the heavy chains of the antibody [3]. This unstable bond led to the bonding of different heavy chains with different antigen-combining sites, known today as the fragment antigen-binding (Fab)-arm exchange. It is because of this immune antibody cross-matching that has led to the pathogenesis of IgG4-RD. The deposition of IgG4 plasma cells in ductal structures has led to the narrowing and strictures of these organs. IgG4-RD and, more specifically,

IgG4-SC can not be diagnosed simply by the elevation of IgG4 levels as the IgG4 concentrations can vary by a factor of more than 100 in different healthy people [3] [5] [6]. Because of that, it is the elevation of IgG4 from a known baseline of a specific patient with physical findings that one can be diagnosed with IgG4-SC.

IgG4-SC can present similarly to that of a cholangiocarcinoma or pancreatic mass; because of that, IgG4-SC can go unnoticed and undiagnosed. The strictures of these pathologies cause the narrowing of the intrahepatic and extrahepatic bile ducts may not be differentiated on imaging. In 2021, the Mendoza criteria were published to help differentiate malignant vs. benign causes of biliary strictures [7]. The criteria included visualization of the strictures and noted tortuous vessels, irregular nodulations, raised intraductal lesions, irregular surfaces, and tissue friability [7]. These signs have been associated with an increased likelihood of malignancy. The Mendoza criteria were found to have an overall diagnostic accuracy of 77% [7]. In our case, the patient did not meet any of the Mendoza criteria, which was in line with the benign nature of IgG4-SC.

IgG4-SC is distinctly different than that of primary sclerosing cholangitis. IgG4-SC is not associated with inflammatory bowel disease like PSC and is also found in older patients [1]. IgG4-SC is more commonly associated, but not always, with autoimmune pancreatitis, hence the reason that they were initially studied and understood to be of the same entity and pathology. The histological appearance of IgG4-SC is also different than that found in PSC. In PSC, mucosal erosion is seen, whereas, in IgG4-SC, dense lymphoplasmacytic infiltration of the bile duct wall and fibrosis of the periportal area of the liver is seen but with intact mucosa throughout [1]. Neutrophils, usually seen in PSC, are not a distinct feature of IgG4-SC. The distinction between these types of sclerosing cholangitis is essential due to the responsiveness to therapy. IgG4-SC is known to respond well to treatment with steroids such as prednisolone, whereas PSC has been managed supportively, and patients sometimes require liver transplants. In Japan, at the Teikyo University School of Medicine, a study was conducted to see the responsiveness of IgG4-SC to prednisolone [2]. It was noted that a total of 376 (90%) patients from a sample of 462 were found to have a reduction of ALP levels and alleviation of biliary strictures on imaging [2]. IgG4-RD can easily be mistaken for cholangiocarcinoma and can take a toll on the healthcare systems if initial testing is not initiated. Although it can be mistaken for a life-threatening pathology such as cholangiocarcinoma, this subtype of sclerosing cholangitis has significantly better outcomes and prognosis than the PSC subtype of sclerosing cholangitis.

4. Conclusion

Cholestatic symptoms such as jaundice, weight loss, and pruritis can be found in an array of gastrointestinal pathologies. When examining a patient and ordering investigative testing, a clinician should be aware of possible differentials. Pancreatic malignancies, cholangiocarcinoma, and sclerosing cholangitis should be

differentiated, and proper laboratory and procedural testing should be done. IgG4-sclerosing cholangitis can present very similarly to cholangiocarcinoma as it did with our patient, but further investigation will warrant a different prognosis and treatment. IgG4-SC is an IgG4-related disease presentation that may or may not present with autoimmune pancreatitis, dacryoadenitis, and sialadenitis. In all cases of suspected IgG4-SC, patients should be screened for the possibility of cholangiocarcinoma. If negative, IgG4-SC should be differentiated from other causes of sclerosing cholangitis, such as primary sclerosing cholangitis. IgG4-SC can be diagnosed with visualization of strictures, biopsy, and an elevation of IgG4 levels in a patient. In conclusion, although IgG4-SC can present similarly to cholangiocarcinoma or primary sclerosing cholangitis, it has significantly greater outcomes and can be managed with steroid therapy.

Consent

As this is a case report, consent was obtained for the purpose of this paper.

Conflicts of Interest

The authors report no conflict of interest. An ethical review is not necessary because this is a case report. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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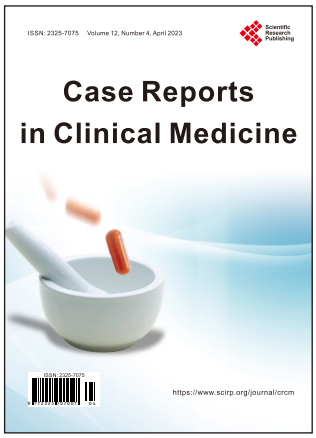

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