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A Rare Association of Congenital Asplenia with Jejun Arteriovenous Malformation

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: **Male, 21**
Final Diagnosis: **AVM intestinal bleeding**
Symptoms: **Melena**
Medication: **—**
Clinical Procedure: **EGD/colonoscopy/enteroscopy**
Specialty: **Gastroenterology and Hepatology**

Objective: **Congenital defects/diseases**

Background: Isolated congenital asplenia is a poorly understood and rare form of primary immunodeficiency, often associated with life-threatening infections.

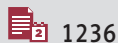
Case Report: We encountered a unique case of a 22-year-old asplenic male who presented with severe iron-deficiency anemia secondary to occult gastrointestinal bleeding since age 15. Our extensive work-up confirmed jejunal arteriovenous malformations as the source of the bleed. Six months after the treatment, the patient has reported no further episodes of gastrointestinal bleeding and his hemoglobin has remained stable.

Conclusions: A comprehensive literature review confirmed that this is the first reported case of adult congenital asplenia associated with arteriovenous malformation in the United States. The relationship of isolated congenital asplenia and arteriovenous malformation-associated bleeding remains unknown at this time; we postulate that this may be a congenital syndrome on its own.

Obscure bleeding in the presence of rare anomalies such as asplenia should be investigated as one of the important causes of unexplained intestinal arteriovenous malformations.

MeSH Keywords: **Arteriovenous Malformations • Congenital Abnormalities • Heterotaxy Syndrome • Spleen**

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/903741>



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Background

The absence of a spleen can be classified into 3 types: acquired asplenia following trauma or surgery, functional asplenia as seen in sickle cell disease, and congenital asplenia. Congenital asplenia is extremely rare and is of 2 distinct types: heterotaxy syndromes and isolated congenital asplenia (ICA) [1]. Ivemark syndrome is one of the heterotaxy syndromes characterized by asplenia, malformations of the heart, and malposition of internal organs in the chest and abdomen. ICA cases are also fatal in childhood, but there are reported living adult cases. Those affected are typically at increased risk for fulminant sepsis and can have a higher risk of noninfectious complications, such as thrombocytosis and mesenteric thrombosis. We report the first case in the United States of ICA with jejunal AVM responsible for multiple episodes of unexplained melena and severe iron deficiency over a 7-year period in a 22-year-old male.

Case Report

A 22-year-old, adopted, white male presented to our hospital with persistent microcytic anemia and recurrent melena. Medical history included congenital asplenia with frequent childhood infections. Congenital asplenia was diagnosed at 2 years old by ultrasound, which failed to demonstrate the spleen. Echocardiography revealed no detectable situs anomalies or cardiac defects at 19 years old. Melena was first detected at 15 years old. Colonoscopy and esophagogastroduodenoscopy along with extensive anemia workup did not reveal the cause of anemia at that time. The patient had intermittent melena 2–3 times per month since then, with a baseline hemoglobin of 12 mg/dL. He received multiple transfusions in the past for significant iron-deficiency anemia. On physical examination, he was hemodynamically stable, without evident cutaneous or mucosal telangiectasias, and had mild generalized abdominal tenderness. Pertinent abnormal laboratory results included hemoglobin 6.6 g/dl, hematocrit 22.3%, mean corpuscular volume $61.2 \mu^3$, and platelet count $504 \times 10^3/\mu\text{L}$. Contrast-enhanced CT abdomen and pelvis confirmed absence of the spleen (Figure 1). Esophagogastroduodenoscopy showed grade I erosive esophagitis with no active signs of bleeding. Intravenous iron infusion and capsule endoscopy were then initiated. The capsule study identified obscure gastrointestinal bleeding with a lesion proximal to the mid-jejunum and a possible second lesion in the lower jejunum. A subsequent enteroscopy with biopsy was consistent with AVMs, which were treated with 2 hemoclips and epinephrine injection, with successful hemostasis (Figure 2). Six months later, the patient has reported no further episodes of gastrointestinal bleeding and his hemoglobin has remained stable.

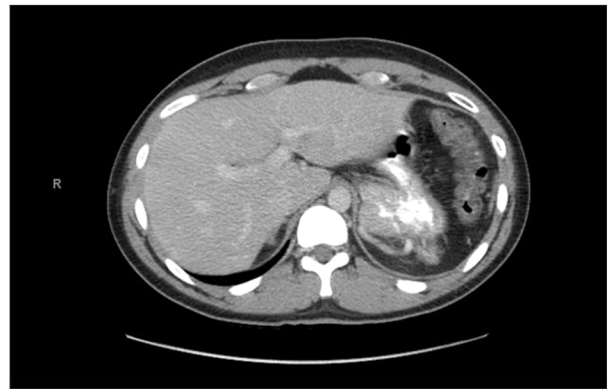


Figure 1. Contrast enhanced CT scan of the abdomen: the absence of a spleen is noted on the left.

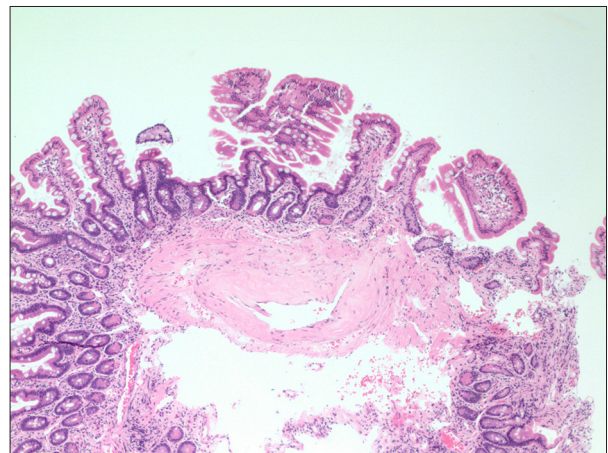


Figure 2. Jejunal biopsy.

Discussion

The spleen is a mesodermal derivative which first appears as a condensation of mesenchymal cells inside the dorsal mesogastrium at the end of the fourth embryonic week. It plays an essential role in generalized hematopoietic and lymphopoietic disorders, systemic infection, sepsis, and immunologic-inflammatory disorders. Some congenital anomalies of the spleen are common, such as splenic lobulation and accessory spleen, while other conditions are rare, especially isolated congenital asplenia [2].

Congenital asplenia, a poorly understood and rare form of primary immunodeficiency, is either associated with malformation syndromes such as heterotaxia, or it is an isolated finding, as was the case in our patient. Heterotaxia syndrome with situs abnormalities (Ivemark syndrome, OMIM # 208530) is a sporadic, autosomal recessive syndrome seen in cases of parental consanguinity. Patients with Ivemark syndrome generally die by the age of 6 months.

Table 1. Adult isolated congenital cases reported from 1956 till 2015.

Case No.	Familial or sporadic	Age at diagnosis/gender	Clinical presentation	Outcome	Reference
1	Sporadic	36 years/Male	Pneumococcal sepsis/Waterhouse-Friderichsen syndrome	Deceased	10
2	Sporadic	37 years/Male	Thrombocytosis	Alive	11
3	Sporadic	56 years/Female	Thrombocytosis/myocardial infarction	Alive	12
4	Sporadic	56 years/Male	Thrombocytosis	Alive	12
5	Sporadic	60 years/Female	Pneumococcal sepsis	Alive	13
6	Sporadic	77 years/Male	Mesenteric vein thrombosis	Alive	7
7	Sporadic	52 years/Female	Pneumococcal sepsis	Deceased	14
8	Sporadic	72 years/Male	Thrombocytosis	Alive	15
9	Familial	20 years/Female	Pneumococcal sepsis/2 children affected	Alive	3
10	Familial	35 years/Male	Asymptomatic/5 children affected	Alive	3
11	Familial	45 years/Male	Meningitis-pneumococcal/2 children affected	Alive	16
12	Familial	Unknown/Male	Asymptomatic/1 child affected	Alive	17
13	Familial	25 years/Male	Thrombocytosis/1 child affected	Alive	17
14	Familial	Unknown/Female	Asymptomatic/2 children affected	Alive	18
15	Familial	27 years/Male	Asymptomatic/sister affected with AVM	Alive	19
16	Adopted	22 years/Male	Small bowel AVM bleed, Mycoplasma pneumonia	Alive	Our case
17	Sporadic	28 years/Male	Streptococcal pneumonia/ulcerative colitis	Alive	20
18	Sporadic	44 years/Female	Thrombocytosis/Chronic thromboembolic pulmonary hypertension	Alive	21
19	Sporadic	67 years/Female	Waterhouse-Friderichsen syndrome/lung fibrosis	Deceased	22

AVM – arteriovenous malformation.

On the other hand, ICA (OMIM 271400), with the plausible autosomal dominant mode of inheritance, is often fatal in early childhood or complicated with life-threatening infections such as meningitis and purpura fulminans or noninfectious complications such as thrombocytosis and mesenteric thrombosis [3].

Bolze et al. studied 33 patients with isolated congenital asplenia from 23 kindreds, including 5 kindreds previously reported by Mahlaoui et al. and the family described by Ferlicot et al., suggested that heterozygous coding mutations in RPSA on chromosome 3p21 underlie most cases of isolated congenital asplenia, with apparently complete penetrance [3–5]. RPSA is not likely to have been identified through a candidate-gene approach, as RPSA is ubiquitously expressed and is not known to be involved in spleen development [4].

Furthermore, there are no large studies to confirm the relationship between asplenia (syndrome or isolated) and AVMs of the gastrointestinal tract. AVM is an acquired or congenital vascular ectasia that has a propensity to bleed spontaneously and can be found anywhere in the gastrointestinal tract. AVMs are typically divided into 3 types [6]. Type I are solitary and limited to the right colon, usually manifesting in patients over 55 years of age. Type II are larger, congenital, and tend to occur in the small bowel in patients less than 55 years of age. Type III are frequently associated with hereditary hemorrhagic telangiectasia [7]. Approximately 5% of obscure and overt GI bleed have a small bowel source not visible on EGD and colonoscopy [8]. Aortic stenosis, Von Willebrand disease, HHT, and end-stage renal disease can be associated with AVM gastrointestinal bleeding. Gastrointestinal bleeding has been

estimated to occur in 13–25% of HHT, formerly known as Osler-Weber-Rendu syndrome (OMIM # 187300). Inherited as autosomal dominant, HHT is characterized by epistaxis, cutaneous telangiectatic lesions, and a large AVM in the brain, liver, and lungs that can lead to catastrophic bleeding complications or shunting [9].

In our case, the AVMs were most likely congenital, considering age of onset and the additional inherited anomaly. We believe this is the first ICA case reported in the United States that is associated with jejunal AVM bleeding. These are clearly late microvascular complications without any other cardiovascular defects, which rules out Ivemark syndrome. HHT may be considered as a differential diagnosis for our case. However, our patient was adopted, with no other stigmata of HHT at this time, except for jejunal AVMs, which are typically not seen in HHT.

This prompted our comprehensive literature search of adult ICA cases that presented with complications other than those related to infection. Eighteen adult cases of ICA were identified and analyzed since the first report of Myerson and Koelle in 1956 (Table 1) [10].

Eleven of the 18 reported cases were sporadic and the remaining were familial. Familial cases are generally asymptomatic and usually diagnosed after a close family member/child suffers a life-threatening or fatal infection secondary to congenital asplenia. Associated findings included thrombocytosis, mesenteric vein thrombosis, chronic thromboembolic pulmonary hypertension, and pneumococcal sepsis (Table 1). Seven adult patients with ICA had invasive bacterial infections [3,10–15]. In addition, there were 5 adult cases of ICA with thrombocytosis but no infectious events were found [16–19]. Furthermore,

reflecting another risk associated with thrombocytosis in adults, Takahashi et al. also described the case of a 44-year-old female with ICA who had chronic thromboembolic pulmonary hypertension [20]. Our comprehensive literature review of 18 adult ICA cases revealed no isolated adult asplenia cases with AVM bleed. Consequently, we analyzed all reported cases of ICA since 1956, including all age probands, parents, and first-degree relatives [10–13,15–22]. One similar case of a 16-year-old girl with chronic iron-deficiency anemia due to recurrent bleeding from multiple angiodysplastic lesions of the stomach, duodenum, and jejunum had been reported in Europe [22].

Conclusions

This case clearly illustrates that patients with a coexisting congenital defect and obscure gastrointestinal bleeding require a prompt step-wise, multi-modality diagnostic approach to prevent delayed treatment. Further accumulation of cases with isolated congenital asplenia is required to elucidate the mechanisms linking AVM and isolated congenital asplenia. The medical community should be aware of the potential relationship of these 2 rare disorders.

Acknowledgements

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Conflicts of interest

None.

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