Hypersecretion of hydrochloric acid as a cause of superior mesenteric artery syndrome

Michael D Levin

Currently, all authors of articles adhere to the hypothesis that explains the presence of clinical and radiological symptoms of obstruction in the 3rd part of the duodenum, by its compression in the aortomesenteric angle (AMA). Therefore, this syndrome has received the name "Superior mesenteric artery syndrome" (SMAS). There are many contradictory statements in this hypothesis, which will be discussed below. To understand the pathological physiology of SMAS, it is necessary to focus on the normal physiology of the duodenum [1].

I. Duodenal motility.

In the duodenum, from the pyloric sphincter (PS) of the stomach to the duodenojejunal junction, four sphincters function, which protects the small intestine from the aggressive effects of hydrochloric acid. If the bolus would pass through the duodenum as quickly as through the esophagus, then an extremely low pH bolus would cause irritation of the jejunum or, at best, a dumping syndrome [2].

1) **The postbulbar sphincter (PBS)**, together with the pyloric sphincter (PS), provides evacuation of the chyme from the stomach as portions of a certain volume **(Figure 1).**

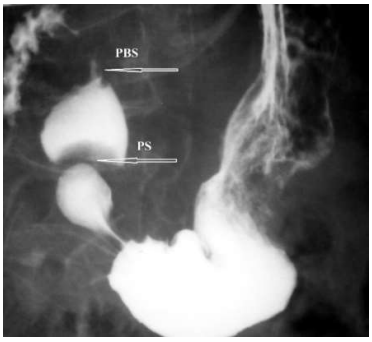

Figure 1. During antral systole, the duodenal bulb filled to the limit, because of which the pyloric sphincter (PS) contracted, stopping the flow of barium from the stomach into the bulb. Then, during the peristaltic contraction of the bulb between

the PS and PBS, the pressure rises, which causes the PBS to relax, and the bolus penetrates the 2nd part of the duodenum.

2) **Ochsner's Sphincter.** When the acid bolus reaches the Ochsner's sphincter, which is in the 3rd part of the duodenum, it causes it to contract, preventing aggressive chyme from entering the jejunum (**Figure 2**).

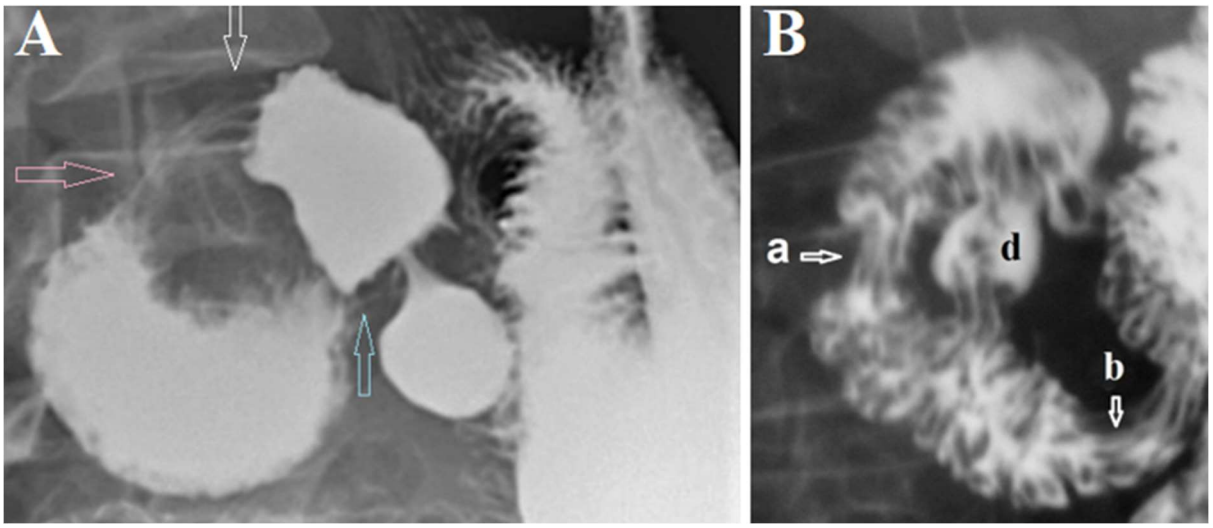

Figure 2. Radiographs of elderly patients with duodenitis and duodenal dyskinesia. **(A)** The white arrow shows PBS location. An expansion of the duodenum is determined between the Kapanji's sphincter (pink arrow) and the Ochsner's sphincter (blue arrow). **(B)** The duodenum was emptied, but the barium remained in deep folds because the barium-filled bowel was very wide. Two zones of contraction with longitudinal folds are visible: **(a)** the Kapanji's sphincter, and **(b)** the Ochsner's sphincter. The juxtapupillary diverticulum **(d)** is located between them. These diverticula result from the extrusion of the mucosa between the muscular fibers. Thus, this diverticulum is evidence of high pressure that occurs during contraction between Kapanji's sphincter and Ochsner's sphincter.

Repeated movement of the bolus between the Kapanji and Ochsner sphincters back and forth is described as a pendulum movement. At this time, the chyme of the bolus is mixed with bile and pancreatic juice, which have an alkaline ph. When the bolus pH rises to an acceptable value, the Ochsner sphincter opens and allows the bolus to pass into the jejunum. The motility of the Ochsner's sphincter is a periodic change of contraction and relaxation, depending on the pH of the bolus. Normally, radiologists cannot see a contraction of the Ochsner Sphincter

works because they use an acid-free contrast agent. I have done research adding 3g Vitamin C to 200 ml of barium. This made it possible to determine and measure the length of Ochsner's sphincter. It turned out that in length (3.2 ± 0.15 cm) and location it corresponds to the length (3.30 ± 0.15 cm) ($P > 0.2$) and location of the narrowing of the duodenum in the so-called SMAS [3].

Ochsner described in detail the functional sphincter in the 3rd part of the duodenum in 1906. During gallbladder and stomach operations he found "in many cases, the duodenum is distended with gas to a point just below the entrance of the common duct, while below this it is contracted, and upon raising the transverse colon and finding the origin of the jejunum, this portion of the intestine will also be found in a contracted condition. In all these specimens, there is also a marked thickening of the intestinal wall at a point 2 to 4 centimeters below the entrance of the common duct, and a careful study of this thickening demonstrated the presence of a marked increase in the circular muscle fibers. These facts pointed towards the presence of a sphincter at this point whose physiological function would consist in providing for a means of retaining the chyme in the upper portion of the duodenum sufficiently long to provide for thorough mixing with bile and pancreatic fluid". Ochsner believed that "under certain forms of irritation or inflammation of the gallbladder or ducts, this duodenal sphincter had taken up an action"[4]. The 12 out of 14 patients described by Ochsner were diagnosed with gastric ulcer (4), duodenal ulcer (2), cholecystitis (7), chronic appendicitis (5), pancreatitis (7). All patients had a dilated duodenum, and 6 of them had a gastric dilatation.

3) Kapanji's sphincter. It is widely known in the scientific literature in French and Russian [5].

4) Oddi's sphincter. This is the only sphincter of the duodenum, which is described in the English-language literature. The pathology of this sphincter is closely related to the pathology of the bile and pancreatic ducts.

II. Analysis of the vascular hypothesis of the pathogenesis of SMAS

1. It is believed that obstruction of the 3rd part of the duodenum is caused by intestinal compression in the aortomesenteric angle (AMA).

The abdominal aorta is located near the middle of the vertebra (Figure 2.b) Its width is approximately 2 cm, and the width of the superior mesenteric artery (SMA) is 0.5 cm. Logically speaking, the length of the constriction that these vessels can create cannot exceed 1 cm. On radiographs, CT, and MRI from 35 articles we measured the distance from the sharp contraction in the 3rd part of the duodenum to the location of the SMA, i.e. up to the middle of the 3rd lumbar vertebra (L-3). On radiographs, all the values are greater than the real ones. We calculated the true value by multiplying the value measured on the radiograph by the projection increase factor. It is equal to the ratio of the true height of the first lumbar vertebra (2.2 cm) to the value of its image on the radiograph. When analyzing CT and MRI, the coefficient is equal to the ratio of the true diameter of the abdominal aorta (2 cm) to the value of its image on the scan.

In 29 (83%) cases on X-ray examination or on CT and MRI, the length of the narrowed segment of the duodenum ranged from 2.5 to 4.6 cm (3.30 ± 0.15 cm) and always started far to the right of the median line (Figure 2 a, b, c, d). Only in 6 (17%) of 35 cases where the length of the narrowed segment of the could be measured, it looked short, since the place of obstruction was near the midline of the vertebra and its length was within 1 cm. However, as seen in Figure 2 e, the narrowed segment of the duodenum can be located to the left of the midline of the vertebra, which is confirmed by Ochsner's observations during surgery.

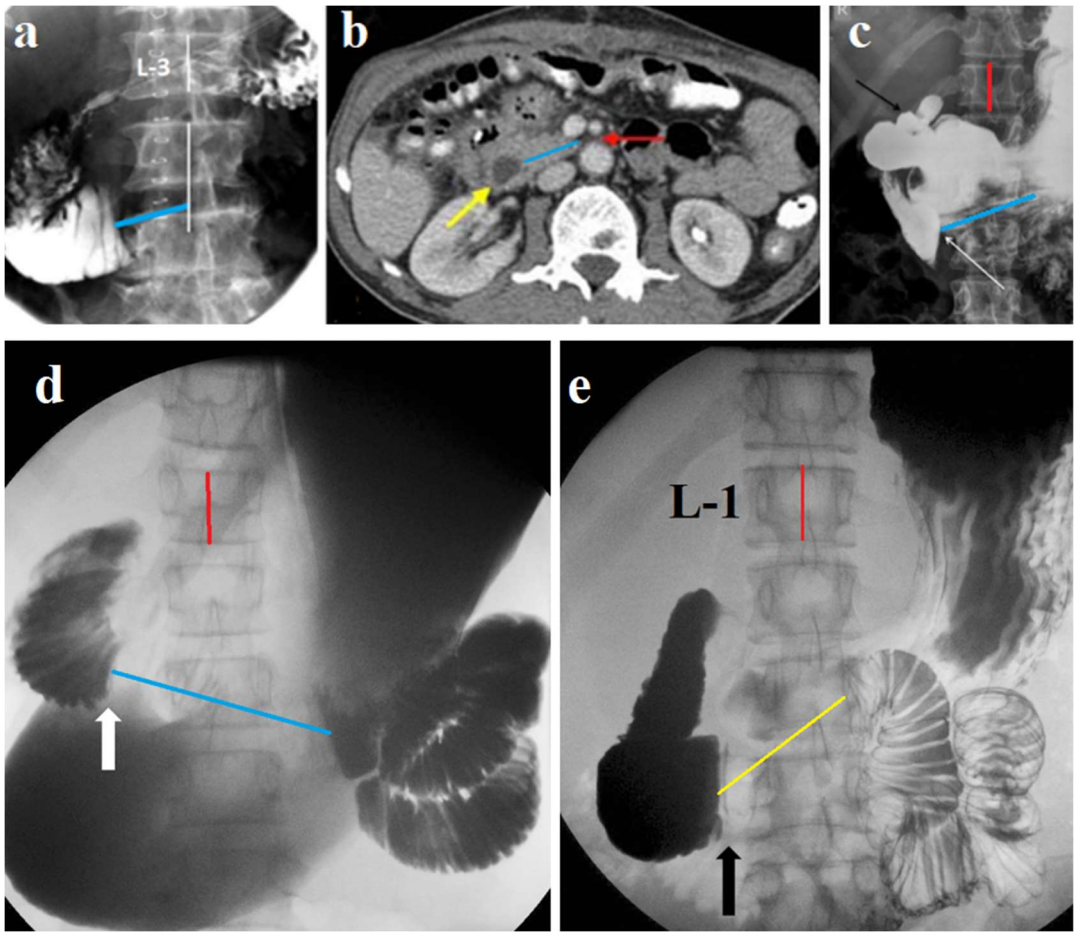

Figure 2. X-ray examinations of patients with a "diagnosis" of SMAS. **(a)** A patient after laparotomy. The beginning of the narrowed segment of the duodenum (blue line) is located 3.2 cm from the midline L-3. His CT **(b)** shows that the narrowed segment is located far from the AMA (red line). **(c)** In a patient with a bulb ulcer (black arrow), the narrowed segment of the duodenum begins to the right of L-3 (white arrow) and ends to the left of L-3. Its length is 4.6 cm. **(d)** The distance from the duodenum to the jejunum is 6.5 cm. **(e)** In a patient the narrowed segment of the duodenum начинается справа от L-4 и заканчивается слева от срединной линии L-3. Its length is 4.9 cm.

It follows from this that in all cases, the contraction of the Ochsner sphincter, and not the compression of the duodenum in the AMA, is the cause of the so-called SMAS.

2. It is argued that the cause of the compression of the duodenum in the AMA is rapid weight loss and the disappearance of adipose tissue, which normally supposedly push the SMA away from the aorta.

A) In a significant percentage of patients with SMAS, the mean body mass index (BMI) was within normal limits. So, for example, in a series of 14 children, it was 21.3 kg/m² (range 13.3-30.4 kg/m²). The mean weight loss before diagnosis was 3.8 kg (range 0-20 kg). No weight loss was found in 50% of the patients [6].

B) Among patients with acute development of the disease, i.e., within 1 - 53 (8.2 ± 1.9) days, conservative treatment was successful after 2-59 (13.4 ± 2.9) days in 88.9% of patients. First, it is obvious that during this time the volume of adipose tissue in the AMA could not change significantly. Second, repeated CT after resolution of clinical symptoms did not reveal any changes in AMA [7].

C) If soft adipose tissue appears between the aorta and the SMA, then how does it push forward the tense vessel and does not push back and squeeze more compliant duodenum?

3. What does the AMA value indicate?

A) All authors, referring to the article by Neri et al [8], believe that the AMA value less than 25 ° is an important diagnostic feature of SMAS. However, the study was carried out with numerous violations that do not allow us to consider its results reliable, that is, scientific. Studies with the presence of reduced AMA (<25 °) were initially selected. No justification for the choice of this figure is provided. There are no characteristics of 50 healthy subjects (control group). The authors did not change AMA for persons with different BMIs. Therefore, they had no reason to report normal boundaries at all. The US detected reduced angles <25 ° in 29 of the 950 subjects (3.05%). X-ray with barium (Figure 3a) revealed compression on the third segment of the duodenum in 28 of 29 patients during the symptomatic period and in nine of 29 during the symptom-free interval.

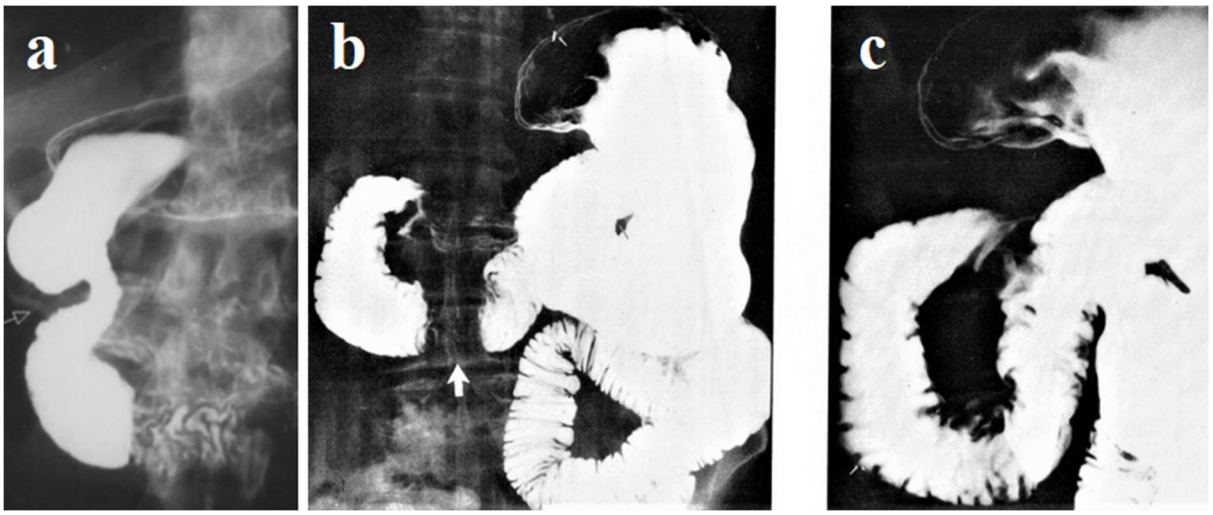

Figure 3. (a) Radiograph from the article Neri et al [8]. There is no enlargement of the stomach and duodenum. An obstacle to the advancement of barium arose to the right of the spine. There are no longitudinal folds in the mucosa. (b, c) Radiographs from the textbook. Signed: "Normal patient with transient proximal duodenal dilatation (b) Radiograph shows apparent obstruction third portion of the duodenum (arrow) suggesting the SMAS. (c) The view obtained slightly later shows the duodenal sweep to be entirely normal" [9].

On the radiograph (Figure 3a) presented in the article by Neri et al, firstly, there are no signs of obstruction, and secondly, the narrowing that begins to the right of the vertebra has nothing to do with AMA. This radiograph does not correspond to the concept of SMAS and all the conclusions of the article by Neri et al are a falsification of the facts for the invented limit of the AMA norm - 25°.

The article by Neri et al says: "The aortomesenteric angle is normally 25–60 ° [2, 3, 6, 7, 10-12] and the mean aortomesenteric distance of 10–28 mm [1-3, 6, 7, 10-12]. Subjects presenting an angle <25° and aortomesenteric distance <8-10 mm may be affected by SMA syndrome" [8]. However, none of these references, show AMA studies in healthy patients with different BMIs, like the article by Neri et al. Moreover, most of the links are descriptions of isolated cases. This is false information, an indicator of the quality of the article. This lie had to confirm the reliability of the proposed parameters of the norm.

I disagree with Eisenberg that Figure 3 (b-c) X-ray picture of a healthy person. I am sure that Eisenberg was examining a suffering patient and not a healthy one. In addition, since the Ochsner sphincter contracts when examined with barium without acid, this indicates duodenal dyskinesia.

It is noteworthy that in cases of mild clinical forms of Ochsner sphincter dyskinesia (Figure 2B, 3b) its length does not exceed 2 cm, while in case of obvious duodenal obstruction (Figures 2d, e) its length reaches 6 cm. This can be explained by the fact, that in contrast to the anatomical sphincters (lower esophageal, anal, etc.), which have anatomical limitations, functional sphincters contract depending on the strength of irritation.

B) Bhagirath Desai et al. did a prospective study of 100 patients who had undergone CT scans for various other complaints. A strong positive correlation was found between BMI and the angle between the aorta and SMA. With BMI increase, the angle also increases. In 25% of patients, these rates were less than the norm.

In third world countries, there are hundreds of millions of people with low BMI which does not increase the SMAS frequency. This suggests that AMA <25 is a concomitant (parallel) symptom since most patients with so-called SMAS are of low weight.

C) How AMA increases.

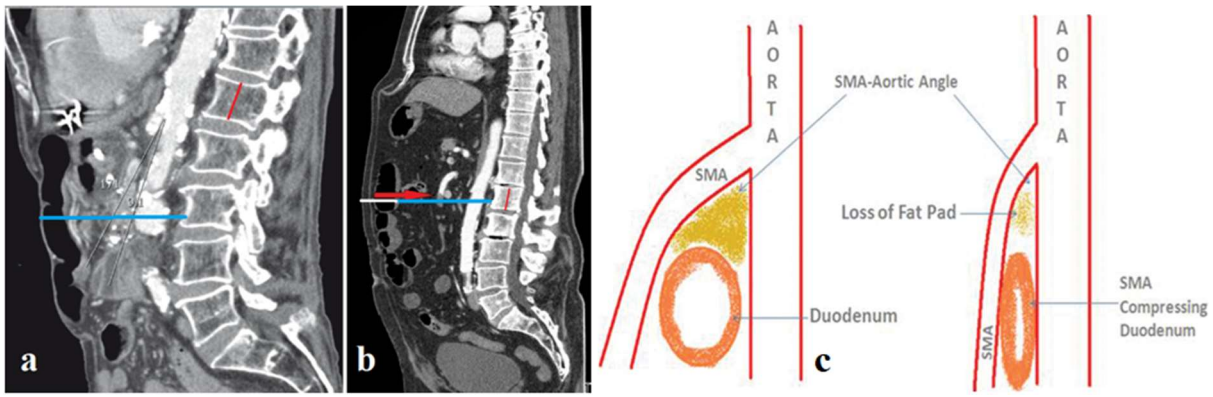

Figure 4. Central sagittal scans (CT). The true height of the 1st lumbar vertebra (red line) is 2.2 cm. (a) In a patient with SMAS, the greatest distance from the anterior abdominal wall to the spine is 8 cm. (b) A patient with SMA thrombosis (red arrow) has a large volume of adipose tissue pushed the anterior wall and colon forward to a distance of 5 cm (the white part of the total distance of 13.2 cm from the anterior abdominal wall to the vertebra). The SMA that supplies blood to the colon together with the colon is pushed forward, which leads to an increase in AMA. (c) Scheme of the generally accepted hypothesis of the pathogenesis of SMAS, which contradicts physical laws.

Conclusion. 1) No one has determined AMA in healthy people of different ages and weights. 2) Amount of AMA is proportional to BMI. 3) The statement that AMA is less than the normal border (25°) when supposedly should be suspected of SMA, is the result of not conscientious research.

4. Diagnosis

We have analyzed 79 articles from PubMed and PMC describing 227 cases of SMAS from 1990 to 2015. Based on clinical data, all patients were divided into 2 groups. The 1st group consisted of 101 patients aged 3 – 81 (25.8 ± 3.4) years. The obstruction of the duodenum appeared in them 1–53 (8.2±1.9) days after severe stressful events: complicated surgeries, burns, trauma, chemotherapy, etc. In 126 patients of the second group aged 17–86 (36.7±2.2) years, including 8 patients with anorexia nervosa, the duodenal obstruction occurred after 3 -72 (17.2±3.2) months of the chronic diseases. Most of these patients had acid-related upper gastrointestinal tract diseases. It became apparent that two different processes can lead to the appearance of duodenal obstruction.

(1) Acute development of symptoms is typical for the stressful conditions (group 1), which in the catabolic stage are accompanied by significant weight loss (severe injuries, burns, malignant formations, and after severe operations). This is especially often observed in adolescents after surgery on the spine [1]. It is known that stress states are accompanied by a decrease in the pH of gastric

contents. In such cases, even high doses of proton pump inhibitors do not have an effect in improving gastric pH [11].

(2) In patients of the 2nd group with functional dyspepsia, postprandial syndrome, and peptic diseases the hypersecretions of hydrochloric acid are also present. They, in contrast to the patients in the 1st group, have a long history of the disease. Disturbance of the duodenal patency increases gradually: from slight disruption without duodenal dilatation to complete obstruction. In these patients, as Ochsner showed, hypertrophy of the circular muscle layer occurs. This may be the reason for the lower effectiveness of the short-term conservative treatment in patients of the 2nd group.

5. Etiology. Hypersecretion of hydrochloric acid provokes by the food ingredients. These provocateurs or stimuli includes delayed-onset diseases, that can be mediated by intestinal mucosal mechanisms involving not only IgE but also T cells, mast cells and eosinophils that produce proinflammatory mediators. Belong of this kind of disease: atopic dermatitis, celiac disease or eosinophilic GI diseases, such as esophagitis, gastritis, gastroenteritis, enterocolitis and proctitis" [12]. It turned out that under stress "mast cells (MC) are important effectors of brain-gut axis that translate the stress signals into the release of a wide range of neurotransmitters and proinflammatory cytokines, which may profoundly affect the gastrointestinal physiology" [13]. In both cases, one of the end products is hydrochloric acid hypersecretion. The lactose is the most common provocateur of hydrochloric acid hypersecretion [14]. It causes the release of histamine from mast cells, which, through a chain of mediators, leads to the hypersecretion of hydrochloric acid. There are patients with histamine intolerance [15] and others.

Thus, the hypersecretion of hydrochloric acid is the cause of all acid-dependent diseases (esophagitis, GERD, stomach ulcer and gastritis, duodenal ulcer and duodenitis, sphincter of Oddi dyskinesia and cholecystitis, as well as SVBA). As a rule, each of these problems, to a greater or lesser extent, are present in every

patient. Historically, doctors are used to diagnosing by the most obvious manifestation.

6. Pathogenesis SMAS

It is known that the Ochsner sphincter contracts in response to irritation with hydrochloric acid. With hypersecretion of hydrochloric acid, the duration and force of contraction of the sphincter increase, which leads to a violation of the evacuation of the bolus into the jejunum. In patients with a long history, there is hypertrophy of the circular muscle layer and rigidity of the Ochsner sphincter **(Figure 5).** The authors signed this figure as follows: - Axial post intravenous contrast enhancement CT image demonstrating distention of the stomach and proximal duodenum leading to compression of the third part of the duodenum (small arrows) between the abdominal aorta (large black arrow) and the SMA (small black arrow).

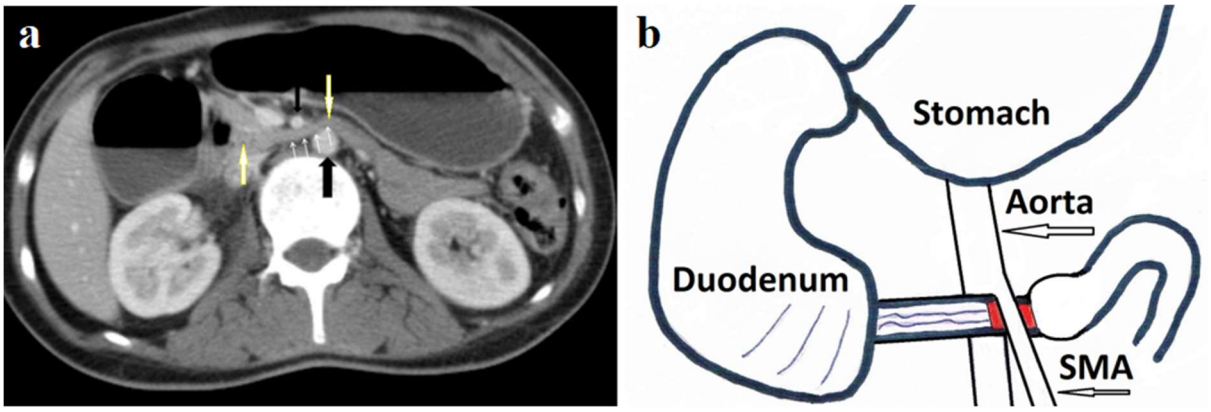

Figure 5. (a) The narrowed segment of the duodenum is located between the two yellow arrows. Its true length is 5.6 cm. (b) Diagram of the pathological physiology of SMAS. The narrowing of the 3rd part of the duodenum is caused by dyskinesia of the Ochsner sphincter. The red color shows a duodenal site that could be compressed in the AMA.

Why, in 227 cases of SMAS, the authors describe not what they see, but what they should see, based on textbooks? Unfortunately, this is not only a medical problem.

7. Treatment (Suggested based on literature analysis)

1. Drainage of the stomach with periodic irrigation with antacids for alkalinization of gastro-duodenal contents.

2. Nasojejunal feeding, completely excluding the introduction of provocateurs of hydrochloric acid release (lactose, histamine, citrus fruits, honey, and allergens of this patient).

3. We recommend using PPI therapy via intravenous loading dose followed by continuous intravenous infusion as in the treatment of upper gastrointestinal bleeding [16].

4. Treatment should continue for at least 2 weeks with a gradual decrease in the PPI dose.

5. The transition to oral food intake is possible only after a contrast study, which has proven a sufficient rate of evacuation of barium into the jejunum.

respectfully

M.D. Levin, MD, PhD, DSc. Radiologist,
nivel70@hotmail.com;
http://www.anorectalmalformations.com

References

1. Levin MD, Korshun Z, Mendelson G. [Duodenal motility in norm and in some diseases. Hypothesis]. Ter Arkh. 2016;88(4):68-74. doi: 10.17116/terarkh201688468-74.[Article in Russian] (PubMed).
2. van Beek AP, Emous M, Laville M, J Tack J. Dumping syndrome after esophageal, gastric or bariatric surgery: pathophysiology, diagnosis, and management. Obes Rev. 2017 Jan;18(1):68-85. doi: 10.1111/obr.12467.
3. Levin MD. Ochsner's Sphincter Dyskinesia Is the Cause of Superior Mesenteric Artery Syndrome. J Gastrointest Surg. 2019 Aug;23(8):1714-1716. doi: 10.1007/s11605-019-04246-5.
4. Ochsner AJ. VIII. Construction of the Duodenum Below the Entrance of the Common Duct and Its Relation to Disease. Ann Surg. 1906 Jan;43(1):80-7. doi: 10.1097/00000658-190601000-00009. (Open access).
5. Aldot G, Kapandji M, Ringendach J. Physiology of timed duodenal intubation. II. Role of Ochsner's sphincter in the mechanism of normal duodenal intubation and in that of certain prolongations of so-called

Oddi's closed time. (1956) Arch Mal Appar Dig Mal Nutr. 1956 Dec;45(12):449-57.
6. Biank V, Werlin S. Superior mesenteric artery syndrome in children: a 20-year experience. J Pediatr Gastroenterol Nutr. 2006 May;42(5):522-5. doi: 10.1097/01.mpg.0000221888.36501.f2.
7. Santer R, C Young C, Rossi T, Riddlesberger MM. Computed tomography in superior mesenteric artery syndrome.Pediatr Radiol. 1991;21(2):154-5. doi: 10.1007/BF02015638.
8. Neri S, Signorelli SS, Mondati E, et al. Ultrasound imaging in diagnosis of superior mesenteric artery syndrome. J Intern Med. 2005 Apr;257(4):346-51. doi: 10.1111/j.1365-2796.2005.01456.x.
9. Diagnostic imaging in internal medicine. By R.L. Eisenberg. Copyright © 1985 by McGraw-Hill, Inc. p.694.
10. Bhagirath Desai A[1], Sandeep Shah D[2], Jagat Bhatt C[2], et al. Measurement of the Distance and Angle Between the Aorta and Superior Mesenteric Artery on CTScan: Values in Indian Population in Different B MI Categories. (2015) Indian J Surg. Dec;77(Suppl 2):614-7. doi: 10.1007/s12262-013-0941-1.
11. Lenz K[1], Buder R, Firlinger F, Lohr G, Voglmayr M. Effect of proton pump inhibitors on gastric pH in patients exposed to severe stress. (2014) Wien Klin Wochenschr. Jan;127(1-2):51-6. doi: 10.1007/s00508-014-0637-y.
12. Cuomo R, Andreozzi P, Zito FP, et al. Irritable bowel syndrome and food interaction. World J Gastroenterol. 2014 Jul 21;20(27):8837-45. doi: 10.3748/wjg.v20.i27.8837.
13. Konturek PC, Brzozowski T, Konturek SJ. Stress and the gut: pathophysiology, clinical consequences, diagnostic approach and treatment options. J Physiol Pharmacol. 2011 Dec;62(6):591-9.
14. Minenna MF, Palieri A, Panella C, Ierardi E. Gastro-oesophageal reflux disease and lactose malabsorption: Casual comorbidity or neglected association? Dig Liver Dis. 2006 Jun;38(6):437-8. doi: 10.1016/j.dld.2006.01.013. Epub 2006 Mar 29.
15. Comas-Basté O, Sánchez-Pérez S, Veciana-Nogués MT, et al. Histamine Intolerance: The Current State of the Art. Biomolecules. 2020 Aug 14;10(8):1181. doi:10.3390/biom10081181.
16. Barkun AN, Almadi M, Kuipers EJ, et al. Management of Nonvariceal Upper Gastrointestinal Bleeding: Guideline Recommendations From the International Consensus Group. Ann Intern Med. 2019 Dec 3;171(11):805-822. doi: 10.7326/M19-1795. Epub 2019 Oct 22.