Pathological physiology of the superior mesenteric artery syndrome.

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Abstract

Aim. To study the pathogenesis of the superior mesenteric artery syndrome (SMAS). **Material and methods.** We have analyzed 79 articles describing 227 cases of the SMAS from 1990 to 2015 and 8 our X-ray studies patients with functional dyspepsia. Based on the clinical data, all patients were divided into 3 groups. **Results.** The 1st group consisted of 101 patients aged 25.8 ± 3.4 years with obstruction of the duodenum which appeared 8.2 ± 1.9 days after severe stressful events. In 126 patients of the second group aged 36.7 ± 2.2 years, duodenal obstruction occurred after 17.2 ± 3.2 months of chronic peptic diseases. In more than 80% of patients with SMAS, the length of the duodenal obstruction zone was 3.30 ± 0.15 cm, and it was located significantly cranial from the aorta-mesenteric angle, and therefore cannot be explained by the compression between the aorta and superior mesentery artery. In 8 patients of the 3rd group we performed an X-ray examination of the stomach and duodenum with barium, to which vitamin C was added. This led to a clear visualization of the Ochsner's sphincter. Its location and length (3.20 ± 0.15 cm) were fully consistent with the length and position of the narrowed segment in SMAS. **Conclusion** In most cases of SMAS, the obstruction of the duodenum

occurs because of the sphincter Ochsner dyskinesia in response to hypersecretion of the hydrochloric acid. Conservative treatment should be directed to nasojejunal feeding and draining of the duodenum and its irrigation with an alkaline solution. In severe cases, it may be an effective balloon dilation of the Ochsner's sphincter.

Keywords: *duodenal obstruction; physiology; sphincter Ochsner; superior mesenteric artery syndrome; Wilkie's syndrome.*

Introduction. Superior mesenteric artery syndrome (SMAS) is a rare condition causing functional obstruction of the third portion of the duodenum [1]. This disease was first described by Professor Carl von Rokitansky in 1842. [2]. In 1861, he was the first to observe that superior mesenteric vessels may compress and obstruct the duodenum over the lumbar spine. In 1927 Wilkie published the first comprehensive series of 75 patients [3]. Since then, some authors have called this disease Wilkie's syndrome. This pathology is found in 0.2% to 0.78% of patients examined with barium [4]. It is believed that partial obstruction of the duodenum is the result of its compression in the angle between the aorta and the superior mesenteric artery (SMA). The aortomesenteric angle is normally 25–60° and the mean aortomesenteric distance is 10–28 mm. Subjects presenting with an angle <25° and aortomesenteric distance < 8-10 mm may be affected by the SMAS. According to this hypothesis, normally the retroperitoneal fat and lymphatic tissue push the mesenteric artery away from the aorta. It is believed that conditions reducing the distance and decreasing the angle between the SMA and aorta may contribute to the compression of the horizontal segment of the duodenum [5,6]. The typical symptoms of the SMAS are nausea, vomiting, abdominal pain, early satiety, postprandial fullness, and anorexia. Upper gastrointestinal studies show a dilated proximal duodenum with an abrupt

termination of the barium column in the third portion. Angiography has been suggested as the “gold standard” procedure for the assessment of the aortomesenteric angle and distance [7].

This syndrome can present itself as acute small bowel obstruction or intermittent compression with chronic symptomatology. The syndrome has been reported in association with pancreatitis, peptic ulcer, intra-abdominal inflammation, and cancer; against the background of abdominal muscle hypertrophy, prolonged immobilization, severe burns, anorexia nervosa, severe weight loss, tuberculosis, acute gastroenteritis, spinal cord injury, and scoliosis repair surgery [5]. Numerous predisposing conditions for SMAS can be summarized into three categories: severe weight loss in catabolic states, external and intra-abdominal compression, or mesenteric tension.[6]

Once radiologic studies have established a diagnosis, first-line treatment is usually conservative with jejunal or parenteral nutrition for the restoration of the aortomesenteric fatty tissue. If conservative management fails, surgical options include open or laparoscopic duodenojejunostomy or duodenal mobilization and division of the ligament of Treitz. The overall success rate of medical management in adults was 71.3% [8] and in pediatric patients to 86% [9].

An analysis of the literature revealed the following facts that contradict the accepted concept of the pathogenesis of the SMAS. 1) Low body weight is not a determining factor in the pathogenesis of the SMAS since 23.7% [8] to 50% [9] of the patients have a normal body mass index (BMI). 2) In third world countries, there are hundreds of millions of people with low BMI which does not increase the SMAS frequency. 3) Bhagirath Desai et al. produced a prospective study of 100 patients who had undergone a CT scan 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, which indicates that the

value of the aortomesenteric angle cannot serve as the gold standard [10]. The purpose of the present study was to investigate the pathogenesis of the SMAS.

Material and methods. We have analyzed 79 articles from PubMed describing 227 cases of SMAS from 1990 to 2015 and 8 patients with functional dyspepsia, who underwent an X-ray examination of the stomach and duodenum. All patients were divided into 3 groups. Based on clinical data, all 227 patients from selected articles were divided into 2 groups. The 1st group consisted of 101 patients aged 3 – 81 (25.8 ± 3.4) years with obstruction of the duodenum which appeared 1–53 (8.2±1.9) days after severe stressful events: complicated surgeries, burns, trauma, chemotherapy, etc. Of the 101 patients in the 1st group, there were 14 (14%) children and adolescents aged 3 to 17 years (mean 12 years). In 126 patients of the second group aged 17–86 (36.7±2.2) years, including 8 patients with anorexia nervosa, duodenal obstruction occurred after 3 -72 (17.2±3.2) months of the chronic diseases. Most of these patients had peptic disorders with hypersecretion of hydrochloric acid or other disorders corresponding to the concept of dyspepsia (**Table 1**). Among them were 3 teenagers aged 17-18 years.

Table 1. Distribution of the patients with SMAS depending on the duration of the disease.

Groups	Patient	Age (years)	M/F	Duration disease	Weight loss (kg)	BMI
1st	101	3 – 81 25.8±3.4	45/56	1 – 53 days 8.2 ±1.9	3 – 17 13.6±3.6	14 - 21 18.9±0.9
2nd	110	17 - 86 36.7±2.2	52/58	3 -72 months 17.2±3.2	3 - 29 18.0±4.3	15 - 28 16.0±3.6
Total	211	p <0.001	97/114	p<0.001	p >0.2	p >0.2

The third group included 8 cases, where a standard study of the upper digestive tract was carried out with an acidified barium suspension. The purpose of this

study was to determine the effect of acid on the duodenal function. For this purpose, we added 3 g of vitamin C to 200 ml of barium suspension.

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 superior mesenteric artery (SMA). On radiographs, all the values are greater than the real ones. We calculated the true value by multiplying the value measured on the roentgenogram by the projection increase factor. It is equal to the ratio of the true height of the third lumbar vertebra (2.5 cm) to the value of its image on the roentgenogram. 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. (Figure 1).

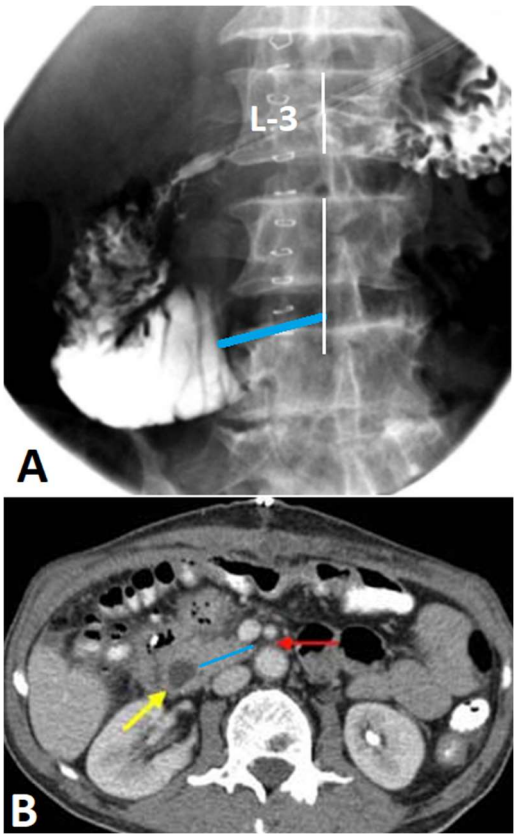

Figure 1. A 70-year-old man with a duodenal ulcer. On the 7th day after laparotomy and pyloroplasty, large residual volumes of stomach and vomiting appeared. Based on X-ray and CT studies, the SMAS was diagnosed. (From the article Chan DK. et al [11]. With the permission of the authors). Aortomesenteric distance (red arrow) is projected into the center of the vertebra. Duodenum - yellow arrow. A) The distance from the beginning of the narrowing

of the duodenum to the SMA projection is 3.5 cm (blue line). B) the same distance on the ST is 3.7 cm. (my measurements).

Statistical analysis was performed by the method of the Student's t-test. The level of significance was set as $P<0.05$.

Results. In 20 transverse sections of MRI and CT, we determined the location of the SMA relative to L-3. In 12 (60%) cases it was located on the midline of the vertebrae (see Figure 1, B). In 5 (25%) cases, SMA was to the left of the median line, and in 3 (15%) it was slightly to the right of the median line. The displacement from the median line was so insignificant that in all cases we calculated the length of the narrowed segment from the contraction line of the duodenum to the midline of the lumbar vertebra.

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. 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**).

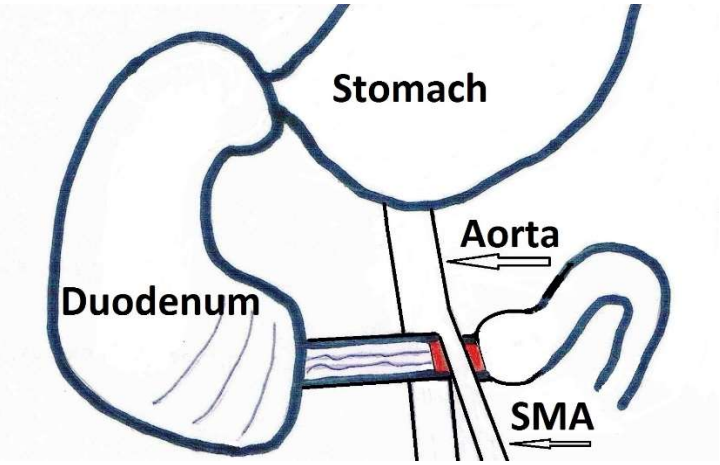

Figure 2. Scheme of anatomical relationships in patients with SMAS. A red area of narrowing is in the aortomesenteric angle.

Based on the clinical picture, all cases were clearly divided into 2 groups. The first group consisted of 101 patients in whom the SMAS developed acutely after a few days (an average of 8 days) against the background of severe catabolic process (after surgery on the spine - 16, other severe operations - 5, severe burns - 3, chemotherapy - 3, acute infectious diseases - 3, pancreatitis - 3, head injuries and heavy tetraparesis - 6, extreme physical loads - 2, etc. (see the Table). These were mainly young people with an asthenic physique, several days after the severe stress with significantly lost weight. In the 1st group, the conservative treatment was effective in 88.9% of cases. Non-operative treatment with gastric decompression was effective in most cases. In 6% of patients, the operation was performed without a preliminary attempt at conservative treatment, in 3% - after an unsuccessful attempt of the stomach decompression, and in 2% - after parenteral hyperalimentation only.

In 14 cases, SMAS was diagnosed in children aged 3-17 years (an average of 12 years). In 5 of them, the radiographs had a sharp widening of the stomach and duodenum, but there was no way to accurately measure the length of the narrowed segment. In 7 cases, only ST, MRI, or US results were presented in the articles. The diagnosis was based only on the narrowing of the aortomesenteric angle.

In patients of the 2nd group, the diagnosis of the SMAS was preceded by a long period of a disease (an average of 17.2 months). Among them were 10 patients with peptic ulcer disease, 12 patients with gastroesophageal reflux disease, 16 were taking medications that reduced the acidity of gastric juice, in 8 cases there was diagnosed dyspepsia, 4 patients had heart cachexia, 4 patients after the surgery for obesity, as well as patients having chronic pancreatitis, recurrent urinary tract inflammation and diabetes mellitus. Five patients categorically denied weight loss. In addition, 12 patients had BMI within normal limits and 4 patients after surgery for obesity. In patients of the 2nd group, the effect of the

conservative treatment was significantly less than in patients of the 1st group - 39% and 89.9%, respectively. The more time lasted the disease, the fewer chances the conservative treatment had. Unfortunately, there is no data on the time the conservative treatment lasted in the patients of the 2nd group for several reasons. Firstly, in most articles it is not indicated at all. Secondly, most surgeons consider the SMAS to be an indication for surgical treatment (47%). And thirdly, the conservative treatment in patients with a long-term disease isn't standardized neither in terms nor in methods. Some patients were sent home after a short period of intravenous parenteral nutrition with recommendations for postural treatment. In other cases, the surgical option was offered after 7-10 days of conservative treatment.

Third group. As a result of the application of barium with vitamin C, in all the patients of the third group clearly revealed two functional constrictions. These zones contraction created pendular barium movements between the narrowing in the 2nd and 3rd parts of the duodenum. They disappeared after the evacuation of barium into the jejunum (**Figures 3, 4**).

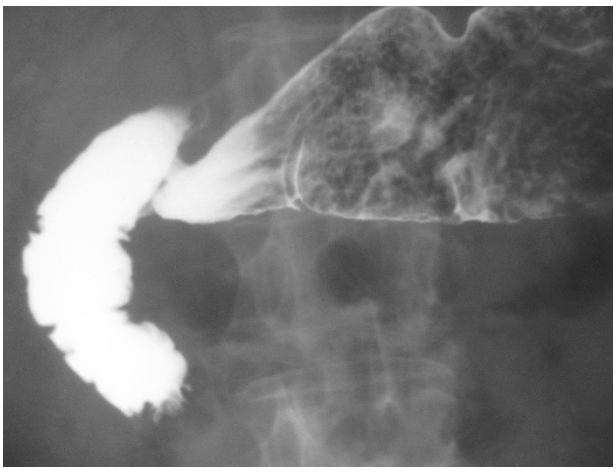

Figure 3. Radiograph of the gastroduodenal zone in a 68-year-old male with gastroesophageal reflux disease. The short-term sphincter Ochsner contraction without duodenal obstruction. This is a reaction of the duodenum to the acid to prevent the aggressive bolus from entering jejunum.

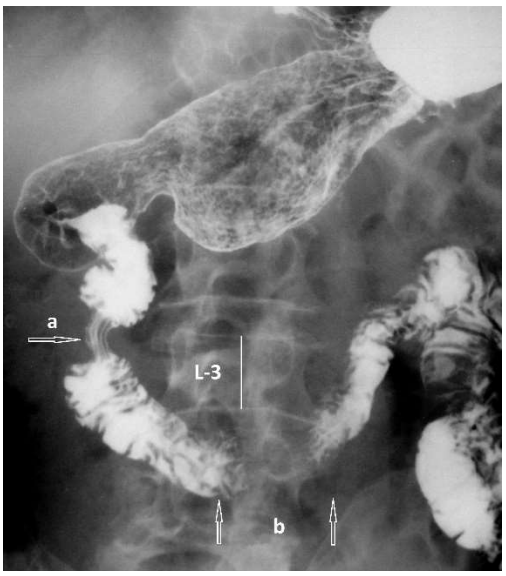

Figure 4. UGI study with Vitamin C in a woman aged 58 years. a) Sphincter Kapandji, b) sphincter Ochsner. Its length is 2.9 cm and it is located on the left of the median line of L-3.

Discussion. The length of the narrowing of the duodenum between the aorta (2 cm diameter) and the SMA (0.5 cm diameter) cannot be longer than 1 cm. However, the narrowing of such length was observed only in 6 (17%) of 35 cases. In 29 (83%) out of the 35 radiographs, the length of the compression zone was within 2.5-4.6 cm (3.30 ± 0.15 cm). This zone of the duodenal contraction was located to the right of the SMA and therefore in no way could be caused by these vessels. By length and location, it is the zone of the sphincter Ochsner functions, which normally contracts in response to the penetration of the acidic gastric contents into the duodenum. This sphincter prevents penetration of chyme with a low pH into the jejunum. During the contraction of the sphincter Ochsner, a chyme is discarded retrogradely to the sphincter of Kapandji, located between the bulb and the second part of the duodenum. The contraction of the sphincter of Kapandji prevents the penetration of the chyme into the bulb. The repetition of this process is described in the literature as a pendulum motion, leading to the mixing of the acidic gastric contents with the bile and pancreatic secretions. When the pH of the chyme between these sphincters increases, the

sphincter of Ochsner opens, allowing the bolus to enter the jejunum in a less aggressive state than originally [12]. The sphincter of Ochsner is rarely detected during upper gastrointestinal studies because acid, which provokes its contraction, is absent in the barium suspension. The use of Vitamin C greatly increased the detection of the sphincter of Ochsner and allowed us to calculate its length, which ranged from 2 to 4.2 cm (3.20±0.15 cm). Thus, the length and arrangement of the area constriction of the duodenum in 29 patients with SMAS fully coincides with the length and location of the sphincter Ochsner ($P > 0.2$). Vitebski showed that the narrowing of the duodenum in patients with SMAS completely disappears under the high pressure created proximal to the duodenal constriction as if it did not exist [13]. It is possible only as a result of the disclosure of the sphincter under the influence of the threshold pressure. Normally, the contraction of the sphincter Ochsner lasts only a few seconds. In the SMAS patients the sphincter may be in a contracted state for a long time, which indicates its dyskinesia. A short zone of constriction (≈ 1 cm) in 6 (17%) patients may be due to the fact that the caudal border of the sphincter of Ochsner, which we do not see, can be located to the left of the central line, as on the radiograph 4. In such cases, the true length of the sphincter is much larger than 1 cm.

Pathological physiology. The SMAS is an obstruction in the third part of the duodenum, resulting in the expansion of the duodenum and the stomach. The assumption that the SMAS arises because of weight loss, which leads to the disappearance of the fat pad in the aortomesenteric angle and, therefore, the decrease of this angle, is completely unreasonable. First, weight loss is not observed in all patients. Secondly, a strong positive correlation exists between BMI and the angle between the aorta and SMA in patients without SMAS]10]. This means that hundreds of millions of underweight people of the third world have a "pathologically small" aortomesenteric angle. However, there is no evidence that SMAS more prevailing in the third world than in developed

countries. Thirdly, it has obvious that the disappearance of symptoms after conservative treatment of 2-59 (13.4±2.9) days is not associated with the appearance of a fat pad in the aortomesenteric angle. It was shown that during the remission this angle does not change [14]. From the point of view of mechanics, the larger the volume of the fat pad in the interval between the aorta and SMA, the less space remains for the duodenum. This means that the pressure on the duodenum will increase. Hence it follows that neither the decrease in angle, nor the fat pad plays a role in the pathogenesis of SMAS. You can ask a question differently. If the soft fatty tissue can expand the vessels and increasing the angle between them, why the peristaltic duodenum cannot do it?

The zone of the duodenal constriction both in length and location corresponds to the contraction of the Ochsner sphincter. This sphincter normally reacts by a short-term contraction in response to irritation with hydrochloric acid. A prolonged and strong sphincter contraction, i.e., dyskinesia, is probably due to the excessive release of hydrochloric acid. Two different processes can lead to the appearance of duodenal obstruction. Sudden 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 [15,16]. 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 influence improving gastric pH [17].

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 the complete obstruction. Therefore, a moderate expansion of the duodenum without stagnation in the stomach and

presence of a short-term spasm of the sphincter Ochsner cannot serve as a diagnostic sign of the SMAS [18]. On the background of a long-term process occur changes in the wall of the duodenum. It becomes thick and rigid both in the region of the cranial segment and at the level of the sphincter Ochsner [19,20]. This may be the reason for the lower effectiveness of the conservative treatment in patients of the 2nd group.

Diagnosis. Analysis of the literature returns us to the previous diagnostic criteria: a combination of clinical symptoms of intestinal obstruction (vomiting, abdominal pain, bloating, weight loss, rapid saturation) with radiologic signs of obstruction in the third part of the duodenum (expansion of the stomach and duodenum with a long contraction of the sphincter Ochsner and very slow evacuation of barium to the jejunum). The study of the aortomesenteric angle and the distance between the aorta and the SMA does not make any sense, because it duplicates the BMI. This leads to erroneous conclusions. For example, in a study by Kawanishi with co-authors in 5 (11%) from 46 women with functional dyspepsia the aortomesenteric angle was ≤22° with a distance between the vessels was ≤8 mm. All 5 were women with a BMI significantly lower than the remaining 41 patients and they had neither the clinical nor radiological signs of SMAS [21].

Treatment. Based on our hypothesis, the dyskinesia of the sphincter Ochsner is caused by hypersecretion of hydrochloric acid and the pathogenetic treatment should be aimed at the reducing of the hydrochloric acid release and removing it from the duodenum. As the literature analysis has shown, the most effective are nasogastric decompression with nasojejunal feeding. Intravenous administration of the proton pump inhibitors may have a positive effect, especially in patients of the 2nd group. The duodenal irrigation with an alkaline solution is theoretically justified.

Conclusion.

The loss of the weight and the decrease of the aortomesenteric angle are the consequence and not the cause of the acute and chronic duodenal obstruction. In most cases the SMAS occurs due to dyskinesia of the sphincter Ochsner. The latter is due to hypersecretion of hydrochloric acid against the background of stress or chronic peptic disease. Conservative treatment should be directed to nasojejunal feeding and draining of the duodenum and its irrigation with an alkaline solution.

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