# Slow-bolus infusion of r-tPA in the treatment of superior mesenteric artery embolism

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## SUMMARY

Thromboembolic occlusion of the SMA is an uncommon cause of acute intestinal ischemia that carries a high mortality. We report 2 cases of SMA embolism, treated with slow-bolus infusion of r-tPA. Angiography showed a partially occluded ileiocolic artery in the first patient and a total proximal occlusion of the SMA in the second patient. Thrombolytic drugs were selectively injected in both patients. The clot lysis was complete and the symptoms disappeared in the first patient. In the second patient clot lysis was incomplete and thus an extensive enterectomy was inevitable. Slow-bolus infusion of thrombolytic drugs is an effective method in carefully selected patients with SMA embolism.

Key words: Mesenteric ischemia, local fibrinolysis, mesenteric artery, embolism

### **INTRODUCTION**

Acute mesenteric ischemia is a complex disorder with varied clinical presentations, multiple causes and a high mortality rate.<sup>1-3</sup> It is frequently caused (40%-50%) by superior mesenteric artery (SMA) embolism.<sup>4</sup> Early diagnosis and reestablishment of mesenteric blood flow before the development of intestinal necrosis play the most important role in its prognosis. Although non invasive imaging modalities can provide useful information, selective angiography should be performed without any delay whenever SMA embolism is suspected.<sup>4-6</sup>

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Author for correspondence: Constantinos Giavroglou, 8 Pavlou Mela street, 546 22 Thessaloniki, Greece Operative revascularization and embolectomy are the traditional methods for the treatment of SMA embolism. However selective thrombolysis can also be used successfully in carefully selected cases.

We report two patients with SMA embolism who were treated with slow-bolus infusion of thrombolytic drugs.

## **CASE REPORTS**

Case 1: A 69-year-old woman with sudden onset of pain in her left leg was transmitted to our hospital from a Health Center with the diagnosis of left femoral embolism due to atrial fibrillation. On physical examination her left lower extremity was pulseless. Laboratory data showed: WBC:11.600/ml, Hb:12.1gr/dl, Hct:35.1%, PT:13/11, PTT:44/26, PLT:170.000µ/L. Thirteen hours after the onset of symptoms a surgical embolectomy was performed. During the operation she was given 30.000 U heparin systematically and after that Enoxaparine (low-molecular weight heparin-Clexane, Phone-Poulenc Rorer): 1mgr/kgr/12h. She was also given Cefuroxime sodium (Zinacef, Glaxo) in a dose of 750mgrX3 and Rantidine HCL Zantac, Glaxo): 50mgrX3 intravenously. Over the next two days the patient was twice taken to the operation room because of bleeding from the puncture site. New blood examination showed: WBC: 9.900/ml, Hb:8.8gr/dl, Hct: 25.9%, PT: 11/11, PTT: 25/25 and PLT: 134.000 µ/L.

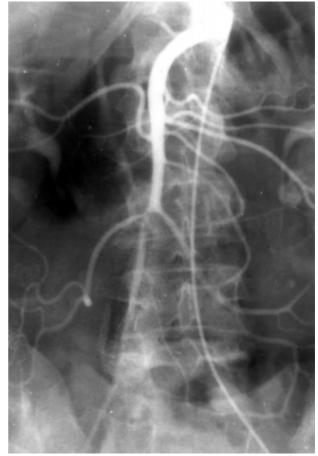
Three days after admission the patient complained of mild abdominal pain followed by diarrhea and a feeling of abdominal distention. On physical examination the abdomen was soft with normal bowel sounds. Plain film, ultrasonography and CT scan of the abdomen were normal. Eight days later the symptoms still existed and an abdominal angiography was performed because mesenteric ischemia was suspected. Selective angiography of SMA demonstrated a thrombus partially occluding the ileocolic artery (fig. 1a). There was no angiographic sign of vasoconstriction and the bowel perfusion distal to the clot was considerable. The patient's general condition and the recent operations were regarded as contraindications for surgery or low-dose selective thrombolysis and a slow-bolus of r-tPA (Actilyse, Boehringer, Ingelheim) was infused superselectively. With the tip of the catheter touching the clot, 10mgr of r-tPA was administered within 15 minutes. Control angiography showed complete clot lysis (fig. 1b). There was no complication or need for exploratory laparotomy. The patient was discharged 20 days after her admission free of symptoms. Three years later she remains asymptomatic, receiving long-term anticoagulation.

**Case 2:** A 67-year-old man with advanced atherosclerotic vascular disease was admitted to our hospital for bilateral embolism of tibial arteries. His clinical history included a coronary bypass operation and an embolectomy for left brachial artery embolism 18 months earlier. Four months

before admission he underwent sigmoidectomy and chemotherapy for a malignant neoplasm in the sigmoid. Clinical examination showed bilateral ischemia below the knee. Ultrasonography and ECG revealed an eneurysm of the left ventricle and thrombi within it. During hospitalization, 3 days after admission, he had an episode of severe acute midepigastric pain. The abdomen was soft and the bowel sounds normal. The abdominal x-ray was normal. Two hours later he started complaining of chest pain. Six hours after the onset of abdominal pain the abdomen was still soft but bowel sounds were absent. He had a regular pulse of 100/min and blood pressure was 110/80 mm Hg. He was a febrile and his hematocrit was 34%. There was no significant elevation of enzyme levels (SGOT, SGPR, CPK and serum amylase). The WBC count was 11.000/mm3, 17.000/mm3 and 23.000/ mm3 at 3 hour intervals. Cardiac infarction was excluded and the symptoms were confined to the epigastrium.

During this period the patient had 4 episodes of diarrhea.





**Figure 1.** (a) Selective SMA angiography shows a partially occluding thrombus in the ileocolic artery. (b) Fifteen minutes after the onset of r-tPA slow-bolus infusion. Clot lysis is complete.

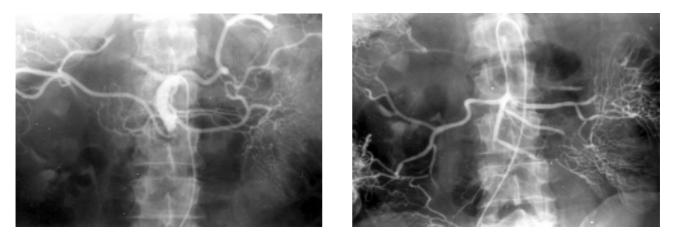
A second abdominal x-ray showed fluid in the small intestine, mild distension of a small bowel loop and moderate thickness of the mucosa. A SMA embolism was suspected and the patient, 7 hours after the onset of symptoms, was referred to the angio-suite for SMA angiography. Selective angiography revealed complete proximal (3cm from the ostium occlusion of SMA by a large thrombus (fig. 2a). The patient was considered as a poor surgical candidate and it was decided to perform slow-bolus selective thrombolysis. Actilyse (20 mgr) was selectively administered into the SMA within 1 hour. Follow-up arteriography showed partial lysis of the large thrombus and incomplete recanalization of many branches of the SMA with clots in most of them (fig. 2b). Because the symptoms from the abdomen didn't resolve and the thrombolytic result was not good, intestinal necrosis was considered as most probable. Thus, we decided to perform an exploratory laparotomy. The patient entered the operation room 8 hours after the onset of abdominal symptoms. He underwent SMA embolectomy and extensive small bowel resection. Fifteen days later the patient died from the syndrome of multiple organ dysfunction.

#### DISCUSSION

The most common source of emboli in SMA embolism is atrial fibrillation. Multiple synchronous embolisms or a history of embolism are not rare in such cases.<sup>6</sup> Clinical findings vary from mild to severe, depending on the occluded vessel and the bowel perfusion distal to the clot. In our first case the patient, although not having any history of embolism had two embolic episodes in 3-days. Our second patient had his first history of embolism (in brachial artery) 18 months before his admission and a second one (in tibial arteries) 3 days before SMA embolism. The left ventricle was the source of emboli in both patients.

Non-invasive imaging modalities can sometimes give useful information in SMA embolism. Dilatation of the loops and thickening of the small bowel mucosa are sometimes present in plain film of the abdomen, but these are not specific findings.<sup>7,8</sup> CT scan may sometimes show suspicious enhancement of the SMA lumen after contrast enhancement but duplex ultrasound is usually of little value.<sup>5,9,10</sup> Duplex sonography and CT scan were normal in the first patient. The dilatation of the loops of the small bowel and the thickening of the mucosa that were observed in our second patient impeded SMA examination with duplex sonography. CT examination was not performed in this patient for reasons, of time.

Delay in diagnosis is not uncommon in patients with SMA embolism because clinical signs and symptoms are no specific. In patients with partially occluded SMA or SMA branch occlusion, when the bowel perfusion distal to the clot is considerable and the symptoms are mild, diagnosis may be delayed. Since prognosis of SMA embolism is mainly dependent on early diagnosis, an immediate selective angiography is the method of choice whenever this is suspected.<sup>4,7,11</sup> Angiography was delayed in our first patient because the symptoms from the abdomen (pain, diarrhea and feeling of abdominal distension) were mild and the non-invasive modalities were normal. In the second patient, the symptoms from the abdomen were first attributed to his previous history and only 6 hours after the onset of symptoms did x-ray findings become suspicious for SMA embolism.



**Figure 2.** (a) Selective SMA angiography shows the proximal occlusion. (b) After the slow-bolus infusion of r-tPA there are still a lot of clots migrated in the SMA branches. There is a lack of peripheral blood flow.

Acute mesenteric ischemia is associated with a mortality rate as high as 43%.12 According to Hunter et  $al^3$  this is even higher (70%-90%). Traditional therapies for enteric ischemia due to SMA embolism have been laparotomy, embolectomy and resection of the infracted bowel. Surgical mortality in recent series varies from 27%-32%.<sup>12,13</sup> Systemic heparinization and vasodilator drugs have also been used.<sup>6,7</sup> Selective intraarterial infusion of papaverine proved to be successful in some cases.<sup>6,11,14</sup> Selective thrombolysis is another method of therapy with good results in carefully selected patients. Acute mesenteric occlusion can be either from emboli or thrombi. Selective thrombolysis has an equal success rate in both cases, although in thrombotic occlusion tramsluminal angioplasty (PTA) is usually needed.<sup>15</sup> In the literature there are reports of the effectiveness of streptokinase, urokinase and r-tPA in patients with acute thromboembolic occlusion of the SMA.5,16-18 In most of these patients there was a degree of peripheral blood flow either directly (because of partial occlusion) or due to collateral flow through the intestinal arcade.<sup>16-18</sup> The results of selective thrombolysis are good in SMA or SMA branch partial occlusion when the peripheral perfusion is considerable. Such patients may also be abdle to tolerate the period of ischemia during thrombolysis but in patients with total SMA occlusion and severe clinical symptoms the results are not so good and even if control angiography shows clot lysis, laparotomy and sometimes enterectomy are usually necessary. Rapid clot lysis is always necessary to avoid further ischemia or possible bowel infarction and thus enterectomy.<sup>16</sup> Beside the reported good results, catheter directed thrombolysis has been criticized because of the need for a prolonged infusion, during which ischemia may continue and necrosis of the bowel may occur.<sup>12,19</sup> For such cases the high speed and the minimal morbidity of mechanical thrombolysis (Angiojet aspiration device) is an attractive alternative to surgical embolectomy or pharmacological thrombolysis. This has been successfully used to remove the clot from SMA in highly selected cases of acute visceral artery thromboebolism.<sup>20</sup> Our first patient was considered a poor candidate because of her bad general condition. Recent operations were also a contraindication for systemic thrombolytic therapy. For these reasons, and because the symptoms from the abdomen were mild and there was no blood in the stools, a slow-bolus infusion of r-tPA was attempted. Since the occlusion of the ileocolic artery was partial with good peripheral bowel perfusion, and the symptoms disappeared totally after selective thrombolysis, there was no need for exploratory laparotomy.<sup>6,21</sup> In our second patient, the total proximal occlusion of the SMA, the lack of peripheral bowel perfusion and the non rapid clot lysis (presence of clots in most of the SMA branches in the follow-up angiography) were contraindications for the continuation of this conservative treatment. The possibility of intracerebral hemorrhage was also taken into consideration because of the age of the patient.<sup>22</sup> Furthermore, the patient's bad general condition and the continuation of symptoms made the need for exploratory laparotomy inevitable. In none of our patients were vasodilator drugs administered.

All the factors that may play a role in the decision for the SMA embolism treatment must be taken into consideration. Patients who are candidates for catheter directed thrombolysis must be carefully selected. Barakate et al, reported eight patients with SMA occlusion. Of these, one patient was managed successfully with catheter-directed lytic therapy and seven with open surgery. Four of them died.<sup>23</sup>

In conclusion, we may say that SMA embolism prognosis is closely related to three major factors: the site of occlusion, the bowel perfusion distal to the clot and the elapsed time between the onset of symptoms and definitive therapy. In SMA branch embolism, with good perfusion distal to the clot, the slow-bolus infusion of a thrombolytic drug must be the first treatment option. In patients with complete proximal SMA occlusion and lack of peripheral bowel perfusion, this method is associated with non-satisfactory thrombolytic result and thus exploratory laparotomy is considered necessary.

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