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Angiographic Complications Caused by Vasopressin Infusion of Gastrointestinal Bleeders

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消化管出血症における経動脈的 Vasopressin infusion の合併症について

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もともと血管造影には何らかの危険性を伴うものであるが、消化管出血にはその危険性は更に高い。経動脈的に Vasopressin infusion をした41例の消化管出血症のうち、有意な合併症を伴ったものは12%であつた。これに対して消化管出血

症以外の一般診断（腹部及び末梢血管）のために血管造影をしたものの合併症は1.6%にすぎなかつた。

しかし、これら合併症のうち、生命に関係するような重症例はなかつた。

Abstract

Risk of complications is unavoidable in any angiographic procedure but is greatly increased for patients with gastrointestinal bleeding. In a series of 41 patients with gastrointestinal bleeding who received vasopressin infusion, 12% experienced major complications; whereas in a series of 432 patients who underwent diagnostic angiography, 1.6% had unfavorable side effects. Although the incidence of complications is high for patients receiving vasopressin for gastrointestinal bleeding, the number of patients who suffer serious consequences is low.

Introduction

Angiography is a complicated invasive procedure, and risk of complications is unavoidable, especially to patients with gastrointestinal bleeding. Despite the number of papers already written about angiography of gastrointestinal bleeders, little has been said about complications, particularly those resulting from drug infusion. After evaluating a series of patients who received vasopressin to control hemorrhage,

I want to report some unexpected findings in five representative cases.

Material and Result

Between April, 1974 and April, 1976, visceral and peripheral angiography were performed on 473 patients at the Veterans Administration Hospital, Wood, Wisconsin. The Seldinger technique was used to insert the catheter via the femoral artery. Of the 473 patients, 12 developed complications, some requiring medical treatment. In 9 patients, complications resulted from catheterization technique and in the remaining 3, from contrast media. Local hematomas, bleeding or minor reactions to contrast media were not considered serious complications (Table 1).

Table. Angiographic complications

Case	Diagnosis	Study	Complication	Followup
1	Variceal bleeding	*SMA with vasopressin	Thrombosis in SMA in four days	Clot resolved in 10 days
2	Variceal bleeding	*SMA with vasopressin	Thrombosis in SMA in six days	Clot resolved within 2 months. Unrelated death
3	Gastritis	Left gastric A. with vasopressin	Thrombosis in left gastric A. in one day	Unrelated death
4	Variceal bleeding	*SMA with vasopressin	Gangrene of small bowel	Death related to vasopressin infusion
5	Variceal bleeding	*SMA with vasopressin	False aneurysm of SMA	Unrelated death
6	Mallory Weiss Syndrome	Left gastric A.	Subintimal injection	Bleeding stopped immediately
7	Variceal bleeding	*SMA	Subintimal injection	Bleeding slowed down and stopped. Unrelated death
8	Renal tumor	Renal A.	Dissection of renal A.	Resolved in 48 hours
9	Pancreatitis	Celiac, SMA*	Infected groin	Occlusion of femoral artery
10	Cirrhosis (hep. precoma)	*SMA, hep. venogram	Renal failure	Death related to angiography
11	Claudication of lower extremities	Abdominal aorta Femoral A.	Hypotension	Heart block (2 degree)
12	Pulmonary emboli, rule out	Pulmonary A.	Severe hypotension	No consequence

*Superior mesenteric artery.

Of the 473 angiographic procedures, 41 were therapeutic and 432 were diagnostic. We used vasopressin for the 41 therapeutic procedures to control gastrointestinal bleeding, and there were 5 complications in this group. Among the remaining 432 diagnostic examinations, 7 showed complications, 4 related to catheterization techniques and 3 related to contrast media.

The incidence of complications among patients receiving vasopressin infusion for therapeutic purposes is 12% (5 of 41); whereas the incidence of complications among the patients who underwent diagnostic examinations is 1.6% (7 of 432), or if the cases with side effects induced by contrast media are disregarded, 0.9% (4 of 432).

There were two deaths related to complications. The first death resulted from gangrene of the bowel, due to pre-existing hypotension or the effect of vasopressin or a combination of the two. The

other death was caused by renal failure following administration of 120 ml of meglumine diatrizoate (66%) and sodium diatrizoate (10%) (Renografin 76). This patient did not receive any vasopressin infusion.

Case report

Case 1

On March 31, 1976, a 53 year old male developed variceal bleeding. Vasopressin was infused (0.2 u/min) to the superior mesenteric artery, and because of intermittent hemorrhage, infusion was continued for three days. At that time high resistance through the catheter prevented further therapy. A new catheter was inserted from the other femoral artery, and angiographic examination demonstrated an incompletely obstructing thrombus involving the main trunk of the superior mesenteric artery (Fig. 1-A). Because of brisk bleeding, vasopressin infusion was resumed. Bleeding was successfully controlled



Fig. 1-A (Case 1). A superior mesenteric arteriogram taken after vasopressin infusion (3 days) for variceal bleeding, shows incomplete obstruction by thrombus at the proximal portion of the superior mesenteric artery.

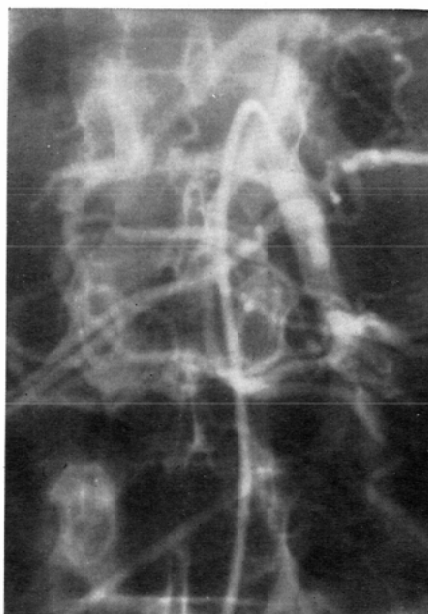


Fig. 1-B (Case 1). A followup superior mesenteric arteriogram taken 18 days later, shows complete resolution of thrombus. Throughout the course, the patient was asymptomatic.

within three days. When the catheter was removed on April 8th, angiograms showed the thrombus unchanged in size and a small saddle type thrombus a few centimeters distal. The patient did well until April 22nd when variceal bleeding recurred. An angiogram however, demonstrated complete resolution of thrombus (Fig. 1-B). Bleeding was successfully controlled by vasopressin infusion, and the patient is now awaiting elective shunt surgery.

Case 3

A 59 year old male developed melena from gastric erosions. He had been placed on a regimen of aspirin and Butazolidine for the treatment of rheumatoid arthritis. A left gastric arteriography was done

using a previously described technique³⁰ of advancing the catheter tip well into the left gastric artery. Trial infusion of vasopressin ($0.2 \text{ u/min} \times 15 \text{ min}$) restricted the peripheral flow of the left gastric artery (Fig. 2-A) therefore, therapeutic infusion was maintained at the rate of 0.1 u/min . The bleeding was controlled within two hours, and 12 hours later, the catheter was removed. The patient, however, died ten days later of congestive heart failure. An autopsy revealed complete thrombosis of the left gastric artery and submucosal hemorrhage of the stomach corresponding to the left gastric artery distribution (Fig. 2-B).

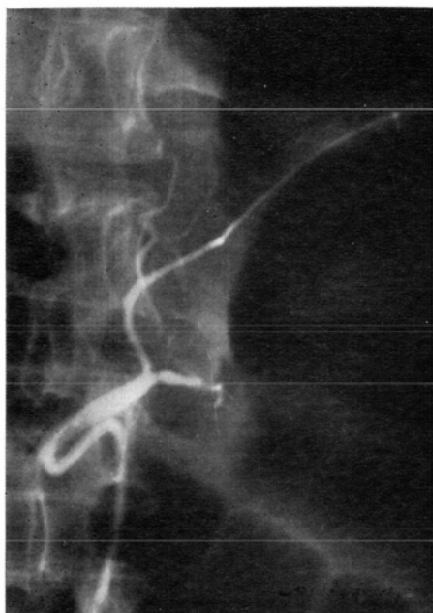


Fig. 2-A (Case 3). A super-selective left gastric arteriogram obtained after 15 minutes of trial infusion of vasopressin infusion (0.2 u/min) shows no flow through the distal branches of left gastric artery.

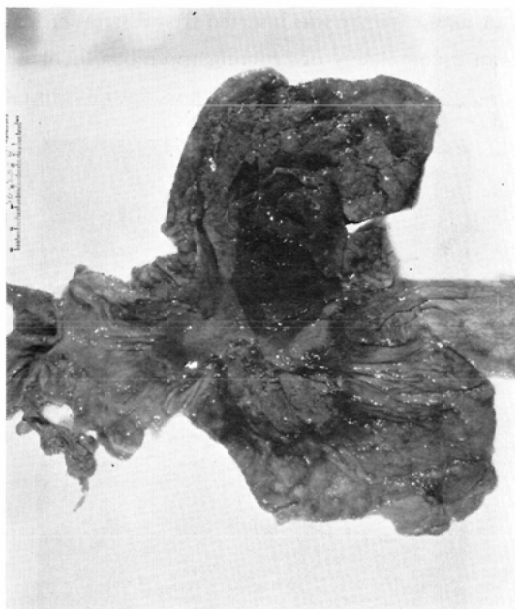


Fig. 2-B (Case 3). Autopsy specimen of stomach demonstrates submucosal hemorrhage of lesser-curvature of the stomach corresponding to the left gastric artery distribution. Note large clot adherent to gastric wall (arrow).

Case 4

A 51 year old male suffering from variceal bleeding and he was admitted to the hospital. His pulse was 96/min and systolic blood pressure 60 mmHg. His hematocrit was 19%. After his condition stabilized, a superior mesenteric arteriogram showed spasm of the mesenteric artery branches (Fig. 3). Vasopressin infusion (0.3 u/min) controlled the bleeding for the next twelve hours. Bleeding resumed, so the dosage was increased to 0.38 u/min and finally to 0.45 u/min . Bleeding persisted, however, and on the third hospital day, a laparotomy was done to control bleeding. The surgeons were surprised to discover early gangrenous changes of the entire small bowel. The incision was closed, and the patient died in the recovery room. Throughout his hospital stay, the patient's blood pressure stayed below 100 mmHg. At autopsy gangrenous changes of the small bowel, and to a lesser degree of the ascending colon, were noted. The descending colon and sigmoid colon were normal.

Case 5

A 58 year old male with variceal bleeding was given vasopressin infusion on June 6th and June 23rd of 1975. Bleeding was successfully controlled and a meso-caval shunt was created. The patient died on July 10 of hepatic encephalopathy. A postoperative mesenteric arteriogram taken on July 7th showed a pseudoaneurysm in the main trunk of the superior mesenteric artery (Fig. 4). On re-evaluation, the angiogram from June 23rd shows a small defect possibly an intimal elevation at the site of the pseudoaneurysm. Evaluation of the mesenteric artery at autopsy showed no evidence of mycotic aneurysm. We believe that pseudoaneurysm was caused either by a jet of contrast media, the guide wire or catheter, or a combination of these.



Fig. 3 (Case 4). A superior mesenteric arteriogram prior to vasopressin infusion demonstrates constriction of main trunk as well as entire peripheral branches of superior mesenteric artery. The small bowel is dilated by gas, probably the result of air introduced at the time of esophago-gastrosocopy.



Fig. 4 (Case 5). Followup superior mesenteric arteriogram taken 2 weeks after the last angiogram and followed by 2 days of vasopressin infusion. Followup film shows pseudo-aneurysm near the origin of the mesenteric artery. Pseudo-aneurysm later proved to be mechanically induced aneurysm.

Case 6

A 46 year old male developed acute bleeding in the upper gastrointestinal tract as a result of a Mallory-Weiss tear. The celiac arteriogram demonstrated the anomalous common origin of the left gastric artery and left hepatic artery (Fig. 5-A). No extravasation of contrast material was evident. Subintimal injection forced us to abandon catheterization of the left gastric artery. An angiogram showed significant narrowing of the proximal portion of the left gastric artery (Fig. 5-B) but, interestingly, the left gastric artery was not visualized. The bleeding stopped immediately and did not resume for 48 hours. At surgery a Mallory-Weiss tear was confirmed and successfully ligated. Bleeding stopped, probably as a

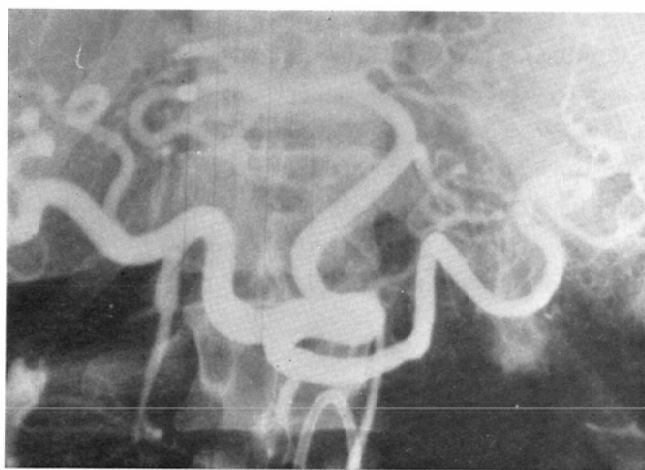


Fig. 5-A (Case 6). A celiac arteriogram performed for Mallory-Weiss tear shows common origin of left gastric artery and left hepatic artery.



Fig. 5-B (Case 6). A selective arteriogram shows evidence of subintimal injection. Note: because of decreased perfusion pressure, left gastric artery is not filled (arrow). Bleeding immediately stopped without drug infusion.

result of a temporary drop of perfusion pressure in the left gastric artery.

Discussion

Angiographic complications are likely to develop in gastrointestinal bleeders because of hemocoagulopathy secondary to blood loss; and in cirrhotic patients, because of abnormal liver function. In addition, some patients receiving vasopressin have a catheter in place for several days, thus increasing the risk of thrombosis.

My experience has shown that incidence of complications for therapeutic angiography is higher than for diagnostic angiography. 12% of the 41 patients receiving vasopressin, experienced major complica-

tions. Among patients who underwent diagnostic angiography at other institutions, the incidence was 0.48–1.75%⁵⁾. Among patients I saw, incidence was 1.6%.

Complications of vasopressin infusion can include thrombosis of the infused artery¹⁾⁸⁾, mesenteric vein thrombosis⁷⁾, ischemic necrosis of the stomach⁶⁾, and mycotic aneurysm as well as local complications.

In the 41 cases studied, there were three instances of thrombosis near the catheter tip. None of the patients suffered serious consequences. Two of these patients had variceal bleeding, and one had gastritis. Of the patients with variceal bleeding, one (Case 1) developed thrombosis of the mesenteric artery four days after the catheter was inserted; and the other (Case 2) six days after insertion. In the first case, a repeat angiogram ten days after placement of the catheter showed spontaneous resolution of the thrombus. The second patient showed no thrombus at the time of autopsy two months later. The patient with gastritis underwent vasopressin infusion of the left gastric artery (Case 3) and developed thrombosis in all the branches of the left gastric artery. As a result, the lesser curvature of the stomach corresponding to the left gastric artery distribution became ischemic with subsequent submucosal hemorrhage. Although there were no serious consequences, complications such as gastric necrosis⁶⁾ would have been life threatening. However, because several vessels supply the stomach, gastric necrosis is highly unusual. It is possible in this case that peripheral vessels are so well constricted by the drug that no collateral flow could develop. Consequently, gastric necrosis resulted. If so, prolonged superselective vasopressin infusion may offer more risk than therapeutic embolization.

Thrombosis of the superior mesenteric artery can result in more serious consequences such as ischemic or gangrenous bowel⁸⁾. On the other hand, two cases in the present series were asymptomatic throughout the course of treatment. It appears if enough time elapses, the thrombus will resolve spontaneously.

Case 4 is a good example of non-occlusive ischemia of bowel. The exact role of vasopressin in this case is difficult to determine because the patient was in shock before angiography was started, and hypotension persisted even after vasopressin infusion was begun. An angiogram taken before the administration of vasopressin demonstrated significant constriction of the branches of small bowel. Even if small vessels are shown to some degree in patients with hypotension, blood flow will bypass the serosa of the bowel without perfusing the mucosa²⁾. Based on these facts, it can be assumed that hypotension does contribute to the development of ischemia of the bowel. Nevertheless, the role of vasopressin cannot be ignored, particularly since autopsy findings revealed selective gangrene of the superior mesenteric artery distribution. It seems wise to conclude that when an angiogram shows severe vasoconstriction, vasopressin infusion should not be used to control hemorrhage.

Autopsy revealed that one case (Case 5), thought to be mycotic aneurysm secondary to prolonged catheterization, was actually a simple dissection without any evidence of infection. A jet of contrast media probably was responsible for the damage.

Two additional complications in gastrointestinal bleeders included subintimal dissection of the left gastric artery (Case 6) and of the superior mesenteric artery (Case 7). Interestingly, in one patient (Case 6) bleeding stopped, and in another (Case 7) it slowed down when perfusion pressure dropped distal to the site of subintimal dissection.

The remaining five complications occur commonly in diagnostic angiography: (as shown on the table) dissection of the renal artery, infection of the groin with subsequent thrombosis of the femoral artery,

renal failure due to contrast media, and hypotension.

Conclusion

Reviewing the complications associated with vasopressin infusion, some unexpected results were obtained. In two patients thrombosis of the superior mesenteric artery, a potentially life threatening condition, resolved spontaneously, indicating that patients with thrombus formation due to vasopressin infusion need not undergo endarterectomy. If asymptomatic, these patients have a chance for spontaneous resolution. On the other hand, a patient who was hypotensive before and during vasopressin infusion unexpectedly developed gangrene of the small bowel. Incidence of ischemic complications following vasopressin infusion is usually low. However, nonocclusive mesenteric ischemia secondary to decreased cardiac output is well known and care should be taken with this type of the patient. Vasopressin infusion should be avoided when the patient shows signs of vasoconstriction of the mesenteric artery.

In conclusion, even if overall incidence of complication due to vasopressin infusion appears high (12%), serious consequences are low indicating that the benefits of the procedure may outweigh the adverse effects.

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