

Livedo reticularis, rhabdomyolysis, massive intestinal infarction, and death after carbon dioxide arteriography

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In patients with renal insufficiency or hypersensitivity to iodinated contrast material, carbon dioxide gas (CO₂) is generally considered a safe alternative contrast media for digital subtraction angiography. However, we herein report a previously undescribed fatal complication of CO₂ angiography in a patient with acute renal dysfunction and congestive heart failure. The possible pathogenetic mechanisms of this complication are discussed. (J Vasc Surg 1997;26:337-40.)

Angiography is the diagnostic standard for patients in whom vascular disease is suspected. Although the use of iodinated contrast material is safe in the great majority of patients, serious contrast reactions are reported to occur in 1 or 2 per 1000 examinations.¹ In addition, the risk of contrast nephrotoxicity may limit the use of angiography in patients with underlying renal insufficiency. Digital subtraction angiography using intravascular injection of carbon dioxide gas (CO₂) has been described as a safe alternative for vascular imaging in such patients.²⁻⁸ CO₂ angiography can also be combined with conventional contrast angiography to reduce the amount of contrast material used. Minor and transient complications related to intravascular CO₂ injection include transient nausea and injection site discomfort. Major complications are extremely rare. In a review of 800 cases, Hawkins et al. found only one major complication related to CO₂ angiography, in which the patient had watery diarrhea related to transient ischemia of the left colon.⁵ Respiratory arrest and myocardial infarction have also been described.^{2,3}

We now report a case of livedo reticularis, rhabdomyolysis, intestinal infarction, and death after car-

bon dioxide angiography. To the best of our knowledge, no fatal systemic complications of CO₂ angiography have been previously reported.

CASE REPORT

A 67-year-old man was admitted to the hospital with hypertension, congestive heart failure (CHF), and progressive renal insufficiency. After initial treatment and stabilization, the patient was transferred to our institution for further evaluation of the cause of renal insufficiency before beginning hemodialysis. At admission, the serum blood urea nitrogen and creatinine levels were 83 mg/dl and 7.3 mg/dl, respectively. An ultrasound scan demonstrated that his right kidney measured 13 cm and that his left kidney measured 11.5 cm in length; duplex evaluation of the renal arteries was inconclusive. A transfemoral digital subtraction abdominal aortogram was obtained using 250 ml carbon dioxide gas and 10 ml nonionic contrast. CO₂ was drawn up slowly through a three-way stopcock into a 50 ml plastic syringe under a saline bath to prevent the inadvertent introduction of room air. After completely filling the syringe, the stopcock was opened to the saline bath to allow equilibration at a low pressure. A small amount of saline solution was then drawn into the syringe to provide a seal during transfer and connection of the syringe to the diagnostic catheter. Five separate boluses of gas were hand-injected over a 20-minute period through a pigtail catheter positioned in the upper abdominal aorta. Extensive atherosclerotic irregularity of the abdominal aorta was noted, and there were single patent renal arteries bilaterally.

Approximately 48 hours after the angiogram was completed, the patient complained of severe muscular pain in the buttocks, thighs, and legs. Physical examination revealed the skin over the lower abdomen, buttocks, and legs to have a mottled appearance consistent with livedo reticularis (Fig. 1). Pulse examination showed palpable bilateral femoral pulses and unchanged audible pedal pulses. No

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Fig. 1. Livedo reticularis on lower abdomen, thighs, and buttocks.

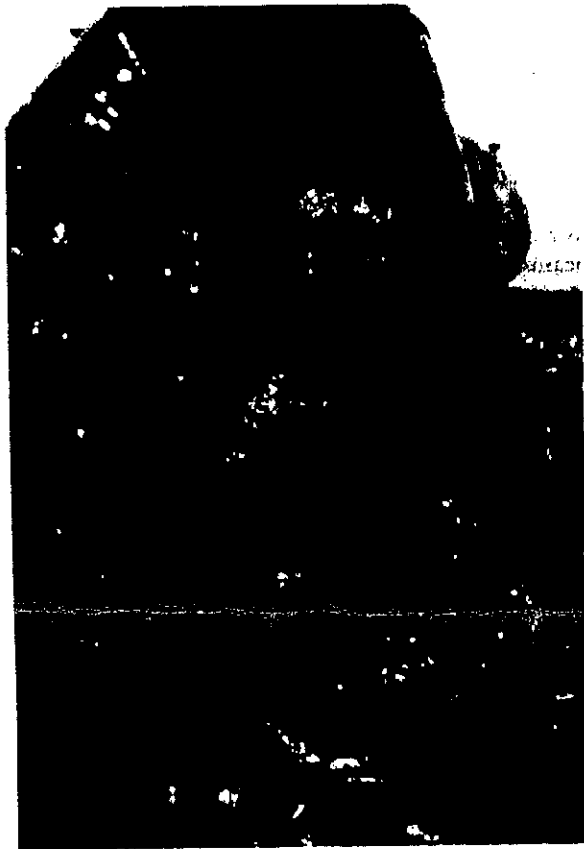


Fig. 2. Small intestine shows raised necrotic grey area over the antimesenteric border.

signs of compartment syndrome were evident. Laboratory analysis demonstrated markedly elevated serum creatinine phosphokinase (CPK) levels, and myoglobinuria was detected. The patient was suspected of having angiography-related peripheral atheroemboli and rhabdomyolysis, and he was given intravenous mannitol, hydration, and analgesics.

Over the next several days, the multiple areas of skin mottling coalesced and worsened, eventually resulting in skin necrosis and sloughing. Punch biopsy of the affected areas showed no evidence of atheroemboli, cholesterol clefts, or arterial thrombosis. Ten days after angiography, signs and symptoms of peritonitis developed, and an abrupt elevation in the patient's white blood cell count to 23,000/ml was noted. Surgical exploration revealed patchy areas of pale and ischemic small bowel, with multiple circular raised, grayish lesions over the antimesenteric border. A focal jejunal perforation was identified, and segmental jejunal resection was performed (Fig. 2). On palpation, the superior mesenteric artery was patent, and normal arterial pulsations were identified in the mesenteric intestinal arcade. Forty-eight hours later, abdominal reexploration showed the remaining small bowel to be ischemic, and complete resection of the small intestine was performed. Histopathologic examination of multiple sections of the small bowel and mesentery showed full-thickness necrosis of the antimesenteric wall, without evidence of thrombosis or atheroemboli.

The patient continued to deteriorate after the operation and died of multiorgan failure 31 days after angiography.

Table I. Reported experience with peripheral and visceral CO₂ angiography

	No. of patients	Studies	Additional iodine contrast	Complications (minor/major)*
Weaver et al. ²	33	40	11 (AVG 20 cc)	4/1
Secter et al. ⁴	115	128	61 (AVG 40 cc)	8/1
Takeda et al. ⁷	41	41	?	0
Collins et al. ⁹	29	29?	1	3/0
Personal Experience	13	24	11 (AVG 15 cc)	4/1
Total	231	262	84	19 (7.3%)/3(1.1%)

*Major complications include nonfatal myocardial infarction (n = 1), respiratory arrest (n = 1), and renal failure (n = 1, with use of additional iodine contrast).

DISCUSSION

Although arteriography remains the gold standard for the diagnosis of aortic, visceral, and peripheral vascular disease, its use may be restricted in patients who have renal insufficiency or contrast allergy. Carbon dioxide is a highly soluble, inexpensive, nonallergenic, and nonnephrotoxic gas and provides an alternative medium for arterial imaging in these patients. An injected bolus of CO₂ displaces flowing blood, providing sufficient differences in density and radiographic contrast to allow digital subtraction imaging.

Several potential problems exist with carbon dioxide angiography. Injections are made by hand using a large syringe, exposing the operator to ionizing radiation during image acquisition. CO₂ is invisible, and although it is heavier than air extreme caution must be practiced to avoid the inadvertent withdrawal of nonsoluble room air into the injection syringe. Furthermore, the use of a disposable CO₂ tank or microfiltration is necessary to prevent rust formation in the tank from contaminating withdrawn gas. Because CO₂ is compressible and buoyant, large volumes of gas must be injected in an "explosive"-type fashion for adequate arterial images. The explosive character of this injection raises the concern of disrupting plaque at the site of injection and causing peripheral microemboli. In addition, CO₂ may become transiently trapped in nondependent vessels such as the superior mesenteric artery resulting in a "vapor lock" phenomenon and causing transient ischemia.⁸ In a review of 262 CO₂ arteriographic examinations performed on 231 patients,^{3,4,6,9} minor and major complications occurred in 19 (7.3%) and three (1.1%) procedures, respectively (Table I). Ischemic colitis and worsening of peripheral arterial symptoms occurred in six cases and was transient in all instances.

Initially, our impression was that the patient had multiple atheroemboli resulting from the explosive

injection of carbon dioxide in a severely diseased aorta. Handel et al.¹⁰ have described the development of livedo reticularis and full-thickness bowel ischemia after coronary angiography. In both of their cases, typical biconvex needle-shaped clefts and cholesterol crystals were documented on biopsy in medium-sized arteries. However, despite a careful search, we failed in our case to document any peripheral atheroemboli or cholesterol emboli on multiple skin, intestinal, or mesenteric biopsies.

To our knowledge, there is no description of normal histopathologic findings in the affected tissues of patients with livedo reticularis as a result of cholesterol embolization syndrome. Therefore, it seems likely that the patient's syndrome was directly attributable to the intraarterial injection of CO₂. Although the delayed onset of livedo reticularis and abdominal symptoms is somewhat atypical, there are several possible explanations for this phenomenon. Although usually quickly absorbed, CO₂ may remain undissolved for a longer time if there is diminished arterial inflow or if the partial pressure of the intravascular CO₂ exceeds the kinetics of venous drainage in the vascular bed being studied.⁸ The presence of CHF in our patient may have resulted in both of these conditions, with consequent delayed clearing of CO₂ from the mesenteric and peripheral circulation. Furthermore, CO₂ itself may both indirectly and directly cause reductions in microvascular blood flow. Hawkins et al.¹¹ demonstrated a mean decrease of 12% in intrarenal blood flow for as long as 24 hours after intraarterial CO₂ injections. There are two possible explanations for this occurrence. First, prolonged intraarterial stasis of CO₂ may result in exchange at the capillary level with nonsoluble tissue nitrogen gas,^{4,12} thereby producing delayed and protracted tissue ischemia. Although in Hawkins dog model this was a result of direct injections into non-dependently positioned renal arteries, the presence of CHF was most likely responsible in our patient. Sec-

ond, static intraarterial CO₂ may produce vasoconstriction that directly results in intestinal ischemia. Kivilaakso and associates,¹³ in a model of hemorrhage-induced stress ulceration in pigs, showed increases in the tissue partial pressure of CO₂ to be associated with diminished microvascular gastric mucosal flow in a pattern suggestive of intense vasoconstriction. Interestingly, these microangiographic changes persisted after the tissue partial pressure of CO₂ was normalized.

In view of this pathogenetic mechanism, several considerations should be made before performing CO₂ angiography. ~~First, intraarterial CO₂ injections should be reduced or avoided in patients who have CHF or poor cardiac output, and all attempts should be made to improve the circulatory status of the patient before performing CO₂ angiography.~~ Second, unless direct examination of the mesenteric vessels is necessary, the catheter should be positioned at or below the level of the renal arteries for gas injection. Generally, the low viscosity of CO₂ will allow reflux and adequate visualization of the renal arteries while limiting or preventing filling of the nondependent superior mesenteric artery and celiac axis. Third, increasing the interval between recurrent injections should help to avoid the risk of tissue ischemic complications by allowing ample time for the absorption of transiently "trapped" CO₂. Finally, the application of a dedicated CO₂ gas injector, now in the investigation stages, should in the future allow safer CO₂ imaging by limiting the amount of gas injected.

CONCLUSION

CO₂ angiography is not nephrotoxic or allergenic, and generally allows safe vascular diagnosis. However, potential complications and technical difficulties mandate tremendous caution when using

this technique, particularly in patients who have impaired cardiac output.

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