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Pylephlebitis after a duodenal ulcer in a patient with metastasised colon carcinoma treated with chemotherapy and bevacizumab: a case report

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ABSTRACT

Pylephlebitis or septic thrombophlebitis of the portal vein is a rare entity with a high mortality rate. It is often a complication of intra-abdominal infection most commonly caused by diverticulitis and appendicitis. Diagnosis is often delayed since clinical signs and symptoms are nonspecific. Pylephlebitis should be considered in patients with sepsis due to gut-associated organisms without a clear focus of infection.

We describe a patient with metastatic colon carcinoma treated with chemotherapy and bevacizumab who was diagnosed with pylephlebitis after a duodenal ulcer and responded well to antibiotic treatment.

KEYWORDS

Chemotherapy, colon carcinoma, duodenal ulcer, pylephlebitis

INTRODUCTION

Pylephlebitis or septic thrombophlebitis of the portal vein is a serious condition with significant morbidity and mortality. It is a rare complication of intra-abdominal infection that occurs in the region drained by the portal venous system.^{1,2} It has only been described once before in relation to a duodenal ulcer.³ The diagnosis of pylephlebitis requires the demonstration of a portal vein thrombosis usually accompanied by bacteraemia in a febrile patient.¹ Diagnosis is often difficult since no specific clinical signs, symptoms and laboratory parameters are involved. This may lead to a delay in treatment.²

We made a diagnosis of pylephlebitis in a patient treated for metastatic colon carcinoma, which occurred after a bleeding duodenal ulcer.

CASE REPORT

A 68-year-old male developed recurrence of liver metastases from colon carcinoma after hemicolectomy and a hemihepatectomy. Two months after systemic treatment was initiated with capecitabine, oxaliplatin and bevacizumab (CAIRO-2 Trial of the Dutch Colorectal Cancer Group, DCCG) he developed upper gastrointestinal bleeding due to a severe duodenal ulcer. There was no history of use of nonsteroidal anti-inflammatory drugs. Treatment with pantoprazol was started. Chemotherapy and bevacizumab were temporarily discontinued. One week later this patient presented with general malaise, fever, chills and abdominal pain in the upper right quadrant. There were no complaints of nausea or vomiting. At physical examination his blood pressure was 100/65 mmHg, heart rate was 110 beats/min. and his temperature was 39.4°C. His abdomen was tender upon palpation without signs of peritoneal involvement. Hepatomegaly was noted but appeared to be unchanged. Initial laboratory findings revealed a white blood cell count of $6.3 \times 10^9/l$ (normal 3.5 to $11.0 \times 10^9/l$), haemoglobin 6.6 mmol/l (8.1 to 10.7), platelet count $82 \times 10^9/l$ (120 to $350 \times 10^9/l$), CRP 118 mg/l (<5), total bilirubin 22 $\mu\text{mol/l}$ (<10), direct bilirubin 7 $\mu\text{mol/l}$ (<5), alkaline phosphatase 142 U/l (<120), aspartate aminotransferase 46 U/l (<40), alanine aminotransferase 28 U/l (<45), lactate dehydrogenase 378 U/l (<450) and gamma glutamyltransferase 76 U/l (<50).

An intra-abdominal focus of the infection was suspected and treatment with piperacilline and tazobactam was initiated. Blood cultures showed *Staphylococcus aureus*, *Lactobacillus* spp, anaerobe gram negative rods, viridans group *Streptococci* and *Fusobacterium nucleatum*. This suggested an origin of infection in the upper gastrointestinal tract. Urine cultures were negative. Serological tests for *H. pylori* taken before, appeared to be positive.

A CT scan still showed a deep duodenal ulcer with a close relation to the hepatic portal vein (figure 1A). The gas formation in the liver was at first interpreted as air in the biliary tract, which could be related to the hepatectomy. Signs of portal vein thrombosis were not seen. The patient recovered, his temperature normalised and after one week intravenous antimicrobial therapy was stopped. The patient continued oral antibiotic therapy with clarithromycin for *H. pylori* eradication and for treatment of *Staphylococcus aureus*, although for the last indication clarithromycin was not the first choice. However, within 24 hours the fever and chills recurred. Treatment with piperacilline/tazobactam was resumed.

A FDG-PET scan was performed and showed an increased FDG uptake at the liver hilus. Evaluation by CT scan was repeated, which now showed a thrombus in the portal vein (figure 1B). With this combination, the high FDG uptake at the liver hilus and the thrombus in the portal vein, the diagnosis of pylephlebitis was made. After six weeks of antimicrobial treatment (two weeks piperacilline/tazobactam intravenously and four weeks amoxicillin/clavulanic acid orally) the patient made a full recovery. Anticoagulant therapy was not administered due to the risk of fatal bleeding from his recent duodenal ulcer. After antimicrobial treatment chemotherapy was continued. Nevertheless, the patient developed progression of the metastatic colonic carcinoma and died a few months later.

Figure 1A. CT abdomen with duodenal ulcer (small arrow) closely related to the portal vein (large arrow) and gas formation in the portal veins (*)



Figure 1B. CT abdomen with portal vein thrombosis (arrow)



DISCUSSION

Pylephlebitis is a complication of intra-abdominal infection, most commonly caused by diverticulitis or appendicitis. Other causes have been described including cholangitis, pancreatitis and inflammatory bowel disease. In some of the patients, an underlying cause is not found.^{4,5} Portal vein thrombosis due to a duodenal ulcer has been reported once before.³ In our patient pylephlebitis may have been related to the duodenal ulcer, since the micro-organisms that were cultured indicated a source of infection in the upper gastrointestinal tract and no other underlying cause was found. There were no signs of local recurrence of the colon carcinoma neither on CT scan nor on FDG-PET that may cause this pylephlebitis.

Recently, it has been suggested that duodenal ulcers may be involved in the pathogenesis of bevacizumab-related bowel perforations,⁶ although in our patient *H. pylori* infection may also have contributed to the development of the duodenal ulcer.

The diagnosis of pylephlebitis is frequently delayed due to the nonspecific clinical signs. Symptoms with which patients can present are fever, chills and abdominal pain often without jaundice. Leucocytosis is a common finding and bacteraemia has been reported in most patients (50 to 80%).⁴ The infection is, as in our patient, usually polymicrobial.

The demonstration of portal vein thrombosis in a febrile patient with bacteraemia is indicative for the diagnosis pylephlebitis.^{1,2} Imaging techniques such as CT scan, ultrasonography, magnetic resonance imaging (MRI) and angiography are all considered appropriate to detect thrombosis of the portal vein. However, as demonstrated

in our patient, thrombosis may not always be visualised on CT scan³ and this may lead to a delay in diagnosis and treatment. The finding of gas formation in the portal vein has also been implicated in pylephlebitis, but the diagnosis of pylephlebitis is not proven by this.⁷ Another helpful imaging technique to diagnose pylephlebitis is the FDG-PET.⁸ Sensitivity and specificity of FDG-PET varies in different studies. A small study in diagnosing septic thrombophlebitis in patients with haematological malignancy showed a sensitivity and specificity of 100%. In a few cases diagnosis was made with FDG-PET even when thrombosis could not be visualised with duplex scan or venography.⁹ In other studies concerning FDG-PET investigation in patients with fever of unknown origin, sensitivity and specificity of FDG-PET are lower.^{10,11}

In our patient there was an increased FDG activity near the liver hilus. In combination with the CT scan results, both the gas formation in the beginning and the thrombus in the portal vein finally confirmed the diagnosis of pylephlebitis. Prolonged administration of broad-spectrum antibiotics and eradication of the underlying cause are the most important in treatment of pylephlebitis. The optimal duration of antibiotic therapy varies in the literature from four to six weeks.^{1,4} The role of anticoagulation therapy remains controversial. Limited data suggest a benefit for patients with hypercoagulable state or mesenteric vein involvement.⁵ Other studies have noted no benefit from anticoagulation.⁴ In a review Falagas *et al.* suggest that early administration of heparin in the management of septic thrombophlebitis might be useful and seems to be safe regarding the low complication rates, but the authors also stated that there are too few data to make a definite conclusion about the effectiveness and toxicity of heparin in patients with septic thrombophlebitis.¹² Treatment with thrombolytic therapy in pylephlebitis has been described in a few case reports but there is no conclusive evidence of efficacy.² Although in our patient a hypercoagulable state due to the advanced cancer may have contributed to the development of pylephlebitis, we did not apply anticoagulation therapy because of its dubious role in the treatment of pylephlebitis and the high risk of serious bleeding due to the duodenal ulcer. Although the incidence of pylephlebitis has decreased upon the availability of antibiotic drugs, it still carries a high mortality rate of 11 to 32%.^{4,5} Pylephlebitis may be complicated by severe therapy-resistant sepsis, which is responsible for the high

mortality rates.⁴ Other complications include hepatic abscess formation, and less commonly progression of the thrombus into the mesenteric vein and portal hypertension.^{3,5} In conclusion, pylephlebitis is a rare but serious condition, which may be difficult to diagnose even with imaging techniques such as CT scan. It should be considered in patients with sepsis due to gut-associated organisms without a clear source of infection. FDG-PET seems to be a useful additional method for diagnosing septic thrombophlebitis.

REFERENCES

- Wildi SM, Wallace MB, Hunter B, Noone TC, Hoffman BJ. EUS diagnosis of an unusual case of pylephlebitis mimicking metastatic pancreatic cancer. *Dig Dis Sci.* 2005;50:2255-8.
- Sherigar R, Amir KA, Bobba RK, Arsuru EL, Srinivas N. Abdominal pain secondary to pylephlebitis: an uncommon disease of the portal venous system, treated with local thrombolytic therapy. *Dig Dis Sci.* 2005;50:983-7.
- Ballantyne B. Portal vein thrombosis and portal hypertension as a possible complication of duodenal ulceration. *Am J Dig Dis.* 1969;14:748-52.
- Plemmons RM, Dooley DP, Longfield R. Septic thrombophlebitis of the portal vein (pylephlebitis): diagnosis and management in the modern era. *Clin Infect Dis.* 1995;21:1114-20.
- Baril N, Wren S, Radin R, Ralls Ph, Stain S. The role of anticoagulation in Pylephlebitis. *Am J Surg.* 1996;172:449-53.
- Tol J, Cats A, Mol L, et al. Gastrointestinal ulceration as a possible side effect of bevacizumab which may herald perforation. *Invest New Drugs.* 2008;26:393-7.
- Kluge S, Hahn KE, Lund CH, Gocht A, Kreymann G. Pylephlebitis with air in the portal vein system. An unusual focus in a patient with sepsis. *Dtsch Med Wochenschr.* 2003;128:1391-4.
- Bleeker-Rovers CP, Jager G., Tack CJ, van der Meer JWM, Oyen WJG. ¹⁸F-fluorodeoxyglucose positron emission tomography leading to a diagnosis of septic thrombophlebitis of the portal vein: description of a case history and a review of the literature. *J Int Med.* 2004;255:419-23.
- Miceli M, Atoui R, Walker R, et al. Diagnosis of deep septic thrombophlebitis in cancer by fluorine 18- fluorodeoxyglucose positron emission tomography scanning: a preliminary report. *J Clin Oncol.* 2004;22:1949-56.
- Meller J, Altenvoerde G, Munzel U, et al. Fever of unknown origin: prospective comparison of ¹⁸F-FDG imaging with a double head coincidence camera and gallium-67 citrate SPET. *Eur J Nucl Med.* 2000;27:1617-25.
- Kjaer A, Lebech A, Eigtved A, Højgaard L. Fever of unknown origin: prospective comparison of diagnostic value of ¹⁸F-FDG PET and ¹¹¹In-granulocyte scintigraphy. *Eur J Nucl Med Mol Imaging.* 2004;31:622-6.
- Falagas ME, Konstantinos ZV, Stavros A. Intravenous heparin in combination with antibiotics for the treatment of deep vein septic thrombophlebitis: a systematic review. *Eur J Pharmacol.* 2007;557:93-8.