Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: informahealthcare.com/journals/irnf20

A Case of Progressive Hypertension Preceding Gemcitabine-Associated Thrombotic Microangiopathy Complicated by Acute Kidney Injury and Stroke

Paul J. Phelan, Aaron Liew & Colm Magee

To cite this article: Paul J. Phelan, Aaron Liew & Colm Magee (2009) A Case of Progressive Hypertension Preceding Gemcitabine-Associated Thrombotic Microangiopathy Complicated by Acute Kidney Injury and Stroke, Renal Failure, 31:8, 743-744, DOI: 10.3109/08860220903118582

To link to this article: https://doi.org/10.3109/08860220903118582

Published online: 09 Oct 2009.

Renal Failure, 31:743–744, 2009

ISSN: 0886-022X print / 1525-6049 online
DOI: 10.3109/08860220903118582

informa
healthcare

CASE REPORT

A Case of Progressive Hypertension Preceding Gemcitabine-Associated Thrombotic Microangiopathy Complicated by Acute Kidney Injury and Stroke

Paul J. Phelan
Department of Nephrology, Beaumont Hospital, Dublin, Ireland

Aaron Liew
Department of Medicine, Beaumont Hospital, Dublin, Ireland

Colm Magee
Department of Nephrology, Beaumont Hospital, Dublin, Ireland

Gemcitabine-associated thrombotic microangiopathy is being increasingly recognized as a serious complication of treatment. We report a normotensive patient who developed progressive hypertension after commencing gemcitabine therapy. She also developed subtle changes in her platelet count and serum creatinine months before her emergent presentation. Clinicians should be aware of new onset or worsening hypertension and 'mild' biochemical changes in gemcitabine-treated patients.

Keyword gemcitabine-associated thrombotic microangiopathy

INTRODUCTION

The spectrum of thrombotic microangiopathy (TMA) comprises the clinical syndromes of thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS). Clinically, patients develop microangiopathic hemolytic anemia and thrombocytopenia with acute kidney injury and neurological phenomena occurring to varying degrees. HUS classically occurs in children with a prodrome of infectious enterocolitis. TMA is often idiopathic in adults but has known associations with autoimmune conditions, pregnancy, HIV infection, malignancy, and certain medications including chemotherapeutic agents.[1,2] Mitomycin C is the agent most commonly associated with HUS/TTP,[3] but more recently, gemcitabine-associated TMA has been reported in 0.31% of cases, which was significantly higher than previously observed.[4] Gemcitabine is a nucleoside analog first approved for the treatment of pancreatic carcinoma in 1996. It has since been used in a variety of other cancers. Here, we report a patient with pancreatic cancer who develops a picture consistent with TMA after receiving gemcitabine treatment.

CASE

In August 2007, a 70-year-old Irish female presented with a three-day history of painless jaundice associated with pale stools. She had no past medical history and was taking no medications. Blood pressure at this time was 110/70 mmHg. Baseline renal function was normal with a serum creatinine of 73 μmol/L, which is an eGFR of 73 mls/min/1.73m^2 (creatinine can converted to mg/dL by multiplying result in μmol/L by 0.113). Full blood count also showed a normal Hb, WBC, and platelet count. She underwent magnetic resonance imaging of her biliary system and a CT scan of her pancreas. This revealed a mass in the head of the pancreas and a dilated biliary and pancreatic ductal system. Staging CT scans showed no evidence of metastatic disease.

In September, a Whipple's procedure was performed. Histology confirmed a well-differentiated adenocarcinoma of the pancreas, impinging on the ampulla of vater but with no local spread. She was assessed by the oncology service, which decided on adjuvant chemotherapy using gemcitabine. Six months of treatment was planned with weekly doses of gemcitabine for three out of every four weeks.

Received 9 April 2009; accepted 2 June 2009.
Address correspondence to Dr. Paul J. Phelan, Specialist Registrar in Nephrology, Beaumont Hospital, Dublin 9, Ireland; Tel.: 0035318092732; E-mail: paulphel@gmail.com

The dose of intravenous gemcitabine was 1000 mg/m^2. The patient tolerated chemotherapy well, although she was noted to have developed new onset hypertension. In January 2008, after three months of treatment, her BP was 190/85. She also developed some pedal edema and was treated with frusemide/amiloride. Mean BP during April was 170/86 mmHg. Her last cycle was completed in May 2008, and at this time her BP was 172/90 mmHg. Her platelets had fallen to 165×10^9/L from more than 600×10^9/L in April, and her creatinine was 96 μmol/L, which was in the normal reference range for the laboratory but equal to a drop in eGFR to 53 mls/min/1.73m^2.

In June, six weeks after her last dose of gemcitabine, she presented to the emergency department complaining of headache and general malaise. She was severely hypertensive, with a BP of 230/132 mmHg. Physical examination was otherwise unremarkable with a normal cardiovascular exam and no signs of hypertensive retinopathy on funduscopy. Laboratory tests showed acute kidney injury with a microangiopathic hemolytic anemia picture. Her serum creatinine had increased to 201 μmol/L, and her platelets dropped to 49×10^9/L and Hb to 10.0 g/dL. Further investigations revealed a normal fibrinogen and coagulation screen, a bilirubin of 33 μmol/L, an LDH of 2858 IU/L (reference range 0–500 IU/L), reticulocytes of 2.0%, high d-dimers, and undetectable haptoglobins. A blood film showed red cell poikilocytosis. A working diagnosis of hemolytic uremic syndrome was made and the patient was transferred to the nephrology service. Renal ultrasound was normal and treatment was directed at aggressive blood pressure control and supportive management. Labetalol was commenced, and rapid blood pressure control was achieved over the first 24–48 hours. Three days after presentation, she developed acute right hand and forearm weakness. MRI of her brain confirmed a small stroke, showing an acute lacunar infarct in left internal capsule. She was commenced on aspirin, atorvastatin, and folic acid. Fortunately, her deficit resolved over a number of days. Her hemoglobin dropped to 7.3 g/dL in late June before spontaneously improving. She was discharged home on labetalol and lisinopril.

In August, her laboratory findings continued to stabilize, but her blood pressure was 154/72 mmHg, so amlodipine was added. By September, her BP was down to 100/60 mmHg with a serum creatinine of 107 μmol/L, an LDH of 507 IU/L, and platelets of 267×10^9/L. Her amlodipine was stopped at this time. Microscopic hematuria remained, indicating ongoing glomerulonephritis. This gradually cleared over the coming months, and her serum creatinine normalized to 80 μmol/L, reflecting her premorbid level of kidney function.

DISCUSSION

Gemcitabine is commonly used to treat a variety cancers and reports of drug-induced TMA with this agent are increasing. This phenomenon was likely under-reported previously, with only the most severe cases being included. This is evidenced by the poor renal outcomes with earlier reports as opposed to less severe prognoses with later series.[4] Our patient was noteworthy in that the biochemical changes of TMA appeared to follow BP changes. Isolated new onset hypertension developed early in her treatment schedule, which was not treated. She then had subtle biochemical abnormalities with changes in her serum creatinine and platelet count, which remained in the reference range. By the time of her acute presentation, her hypertension was severe, and her biochemistry was consistent with a florid TMA picture. After improvements in BP with anti-hypertensive medication, her acute kidney injury stabilized and gradually resolved over the coming months. She did develop an ischemic stroke, however, which highlights additional dangers with this syndrome.

This case demonstrates the relationship between hypertension and TMA in a patient treated with gemcitabine. Clinicians should be aware of new onset or worsening hypertension and subtle changes in serum creatinine and platelet count in gemcitabine-treated patients.

DECLARATION OF INTEREST

The authors report no conflict of interest.

REFERENCES

1. Melnyk AM, Solez K, Kjellstrand CM. Adult hemolytic-uremic syndrome. A review of 37 cases. *Arch Intern Med.* 1995 Oct 23;155(19):2077–2084.
2. Milford DV, Goldstein A, Barrett M, Mann JR, Raafat F. Cancer associated haemolytic uraemic syndrome developing prior to treatment with cytotoxic agents. *Med Pediatr Oncol.* 1993;21(2):142–145.
3. D'Elia JA, Aslani M, Schermer S, Cloud L, Bothe A, Dzik W. Hemolyticuremic syndrome and acute renal failure in metastatic adenocarcinoma treated with mitomycin: Case report and literature review. *Ren Fail.* 1987;10(2):107–113.
4. Humphreys BD, Sharman JP, Henderson JM, Clark JW, Marks PW, Rennke HG, Zhu AX, Magee CC. Gemcitabine-associated thrombotic microangiopathy. *Cancer*. 2004 Jun 15;100(12):2664–2670.