Bevacizumab-associated Gastrointestinal Perforation Reported to the Adverse Drug Reaction Reporting System in Taiwan

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Objective

To study the bevacizumab-associated gastrointestinal perforation (GIP) and its associated clinical outcomes in cancer patients.

Methods

This study collects reports from electronic database of National Adverse Drug Reaction Reporting System in Taiwan from January 2005 to December 2010. Cases with bevacizumab-associated gastrointestinal perforation were included in the study. GIP was defined by both free air on the plain X-ray or computed tomography and acute clinical presentation of acute peritonitis stated by reporters. The perforation sites were identified in the cases receiving surgical intervention. The clinical demography, clinical management, surgical findings, and outcomes of the GIP events were analyzed.

Results

11 bevacizumab-associated GIP cases during the six-year period were identified. There were 5 males and 6 females. The mean age was 55.7 years (range, 24-82 years). Bevacizumab was prescribed for 7 patients with colorectal cancer, 1 patient with gastric cancer, 1 patient with non-small cell lung cancer, 1 patient with pancreatic cancer and 1 patient with renal cell carcinoma. Among the 11 cases, there were 6 patients receiving definite surgical repair and diverting stoma for GIP, but one (16.6%) expired despite surgical intervention. The perforation sites included 1 case at colon where tumors located, 3 cases at stomach, and 1 case at terminal ileum. One of the three patients with gastric perforation had history of gastric ulcer. The other 5 cases under medical management without surgical intervention all expired. The mean interval from first dose of bevacizumab to onset of the perforation was 119 days (range, 10-409 days).

Table 1. Demographics of reported GIP cases

No.	Gender	Age	Indication	Onset interval of GIP	Peforation site	Surgical intervention for GIP	Patient outcome
1	F	56	Colorectal cancer	Unknown	Bowel, NOS	No	Death
2	M	70	Colorectal cancer	Unknown	Bowel, NOS	Yes	Resolved
3	F	55	Sigmoid colon cancer	88	Bowel, NOS	No	Death
4	F	49	Non-small cell lung cancer	10	Gastric	Yes	Resolved
5	F	82	Colorectal cancer	245	Gastric antral	Yes	Resolved
6	M	59	Gastric cancer	54	Bowel, NOS	No	Death
7	F	24	Sigmoid colon cancer	25	Sigmoid colon	Yes	Resolved
8	M	57	Pancreatic cancer	31	Gastric	No	Death
9	F	69	Colon cancer	105	Bowel, NOS	Yes	Death
10	M	64	Renal cell carcinoma	409	Terminal ileum	Yes	Resolved
11	M	28	Colon cancer	103	Bowel, NOS	No	Death

Abbreviation: F, Female; M, Male; NOS, Not Otherwise Specified

Conclusions

Bevacizumab-associated GIP is an uncommon life-threatening complication with poor prognosis. The mechanism responsible for GI perforation is still unknown. Patients with history of gastric ulcer and the location of the tumors along the gastrointestinal tract may be at greater risk. Patients with history of gastric ulcer should be well treated before initiation of bevacizumab. Patients with surgical repair had better prognosis in our study, so surgical intervention is advised whenever GIP is diagnosed. Physicians treating with bevacizumab should be aware of patient presenting with acute abdominal pain or peritonitis which may be the early signs and symptoms of GIP.