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Lower gastrointestinal bleeding during anticoagulant therapy: a life-saving complication?

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Warfarin is commonly used in the prophylaxis or treatment of thromboembolic disease. Haemorrhage is a recognised complication which may be life-threatening. This paper describes eight cases in which lower gastrointestinal bleeding while on warfarin therapy resulted in the discovery of previously unrecognised large bowel malignancy. Diagnosis of an otherwise asymptomatic carcinoma in this way enabled surgery to be carried out at an earlier stage and so may have resulted in a better prognosis for these patients. Bleeding while on anticoagulant therapy is caused by a specific organic lesion in 30% to 50% of cases. This may be the case even when the prothrombin time is very prolonged. It is important, therefore, that such cases are fully investigated, especially in the elderly.

Long-term anticoagulation is widely used in the prophylaxis or treatment of thromboembolic disease. Haemorrhage is a common complication and may be life-threatening. This paper describes eight cases in which bleeding related to anticoagulant therapy may, paradoxically, have been life-saving.

Case reports

Over a 4 year period, eight patients were referred to a general surgical outpatient clinic with rectal bleeding soon after starting anticoagulant therapy with warfarin. In four cases the treatment was started for atrial fibrillation, in two cases for recurrent pulmonary emboli and in two cases for mitral valve disease. The age range was from 61 to 79 years. Rectal bleeding occurred within 2–4 weeks of staring warfarin therapy and none of the patients described any previous gastrointestinal symptoms of significance. No patient had a family history of colon cancer. Haematological investigation revealed the prothrombin time to be within the therapeutic range in each case. Each patient was investigated by either colonoscopy or barium enema.

Results

All eight patients were found to have neoplasms of the proximal large bowel. No other significant pathology was identified within the colon. Six of the tumours were located in the caecum and two in the proximal transverse colon, necessitating either a right hemicolectomy or an extended right hemicolectomy. In addition, one patient had a solitary liver lesion which was resected.

Histology revealed seven of the neoplasms to be adenocarcinomas (two Dukes' stage A and five Dukes' stage B) and one to be a non-Hodgkin's lymphoma. The liver nodule, found in association with a Dukes' B adenocarcinoma, was confirmed as a metastasis. All patients remain alive and well with follow-up ranging from 2 years (lymphoma) to 4 years (adenocarcinoma with liver metastasis).

Discussion

Warfarin is a commonly used anticoagulant, with many patients on long- or short-term therapy. Bleeding is the

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most common complication with 7% to 10% of hospitalised patients and 30% of ambulatory patients having haemorrhage at some stage in their treatment *(1)*. The risk of bleeding is highest in the first year of anticoagulant therapy, with 5% of these haemorrhages being life-threatening and 1% leading to death *(2)*. The most common site of bleeding is the gastrointestinal tract, with haematuria also being a frequent presentation *(1–3)*. Retroperitoneal bleeding, intracranial bleeding and breast haematoma secondary to occult malignancy have also been described *(4,5)*. In 30% to 50% of patients who bleed while on anticoagulant therapy a specific organic lesion can be found as the cause and in 15% to 20% of patients this has not been recognised previously *(1,4,6)*. Mild gastrointestinal bleeding may be attributed to an initial difficulty in achieving correct control of the prothrombin time, especially if the patient is known to have a pre-existing condition such as haemorrhoids. Although there is an increased likelihood of discovering a significant lesion if bleeding occurs despite a prothrombin time within the therapeutic range, 30% of lesions in one series were diagnosed when the prothrombin time was very prolonged (INR > 7.5) *(4,6)*. Investigation of haematuria in a group of anticoagulated patients with prothrombin times within the therapeutic range resulted in pathological findings, ranging from renal calculi to carcinoma, in over 50% of the patients *(1,7)*. Pathological findings when gastrointestinal bleeding occurs in anticoagulated patients include peptic ulcer disease, the most common finding in one series of 52 patients *(8)*, vascular malformations, diverticular disease, adenomas and malignant lesions of the upper and lower gastrointestinal tract *(8,9)*. It is mandatory, therefore, that bleeding from whatever site is regarded as significant and investigated thoroughly. Only when appropriate investigations have excluded a pathological cause for the bleeding can it be attributed solely to poor anticoagulant control.

Bleeding from left colon cancers is traditionally obvious, whereas right colon cancers often present with iron defiency anaemia from occult bleeding. Failure to investigate the cause of iron deficiency anaemia is an important cause of delay in diagnosis of right-sided malignancies *(10,11)*. The right colon, along with the splenic flexure, has been shown to have the lowest incidence of Dukes' A tumours, and tumours found in the right colon are more likely to be poorly differentiated and locally invasive that those of the rectum *(11–13)*. Early diagnosis of right colon cancer in asymptomatic patients results in a better prognosis compared with cases with intestinal symptoms *(10,11,14,15)*. The majority of colon cancers bleed and positive faecal occult blood forms the basis of screening programmes to detect tumours in asymptomatic individuals.

Warfarin therapy will make occult bleeding obvious and may increase the percentage of cancers which bleed. This may lead to earlier presentation and possibly increased 5-year survival.

Conclusion

Although the majority of episodes of gastrointestinal bleeding while on warfarin therapy are related to benign causes, eg peptic ulceration, a few may alert the clinician to the presence of a previously occult malignancy. All bleeding in this situation must be fully investigated as 50% will be linked to a definite pathology. It is likely that warfarin therapy makes occult bleeding from right colon cancers obvious and such bleeding probably occurs more frequently than is recognised. More widespread awareness of this fact may lead to earlier diagnosis of these occult colon cancers and an increased likelihood of survival.

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