

Multiple Cerebral Infarctions In The Context Of Malignancy

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Abstract

Coagulation disorders are common in patients with malignancy, sometimes leading to arterial and venous thrombosis. Such patients are therefore at increased risk for ischaemic stroke. Though usually occurring in advanced stages of cancers, sometimes stroke can be the first manifestation of a hidden, yet undiagnosed, malignancy. In this report, I present a case of recurrent strokes secondary to malignancy-related thromboembolism in a 63-year old gentleman.

Key Words

Malignancy, Hypercoagulability, Stroke

Case Presentation

A 63-year old man presented to A&E department with altered mental status. He was found by his wife attempting to turn on the switch but being unable to locate it with his right hand. He also had dysarthria and was somewhat confused. He had a history of type II diabetes mellitus, hypertension and dyslipidaemia. Moreover, he had suffered an ischaemic stroke 3 months previous to this admission affecting the right middle cerebral artery territory. His medications included the antiplatelet agents aspirin and dipyridamole, the hypoglycaemic agent metformin and the HMG-CoA reductase inhibitor simvastatin. He had stopped smoking 15 years previously.

This patient thus suffered two ischaemic strokes in different vascular territories in 3 months and a coagulopathy was considered to be the cause. A chest x-ray revealed a lesion in the right lung base, which was confirmed on CT; the latter also detecting right hilar and supracarinal lymphadenopathy. CT-guided biopsy of the lung lesion was then carried out which showed adenocarcinoma of the lung. Right lower lobectomy was performed but merely two weeks after surgery, the patient presented again with another left-sided stroke; the third one in four months. While an in-patient, he also had a deep vein thrombosis, despite being anticoagulated with enoxaparin. His general condition was very poor and he was treated palliatively until he passed away.

Discussion

The relationship between malignancy and hypercoagulability is well known and actually thromboembolic events occur in around 11% of patients with cancer and account for the second leading cause of mortality in cancer.¹ Almost all cancers are associated with coagulopathy but especially myeloproliferative disorders as well as cancers of the pancreas, prostate, colon, gallbladder, stomach and lung adenocarcinoma.²

This association between cancer and hypercoagulability was first described by Armand Trousseau in 1865, and since then malignancy-associated thromboembolic disorders have been termed Trousseau syndrome.³ Its clinical manifestations include arterial thrombosis, recurrent venous thrombosis, non-bacterial thrombotic endocarditis and disseminated intravascular coagulation (DIC) as well as accelerated ischaemic heart disease and peripheral vascular disease.⁴⁻⁵

There are various pathogenic mechanisms, which explain the hypercoagulable state of malignancy. Tumour cells produce pro-coagulant factors like interleukin-1, interleukin-6, tumour necrosis factor-1, factor X and factor XII.⁶ Moreover, adenocarcinomas produce a lot of mucin; high molecular weight, heavily glycosylated proteins that result in platelet-rich microthrombi.⁷⁻⁸

Malignancy can result in hypercoagulability in a variety of other ways. Some chemotherapeutic agents like mitomycin and some hormonal agents like tamoxifen are prothrombotic.⁹⁻¹⁰ Trauma, as a result of surgery, can also play an important role by exposing subendothelial tissue factor, activating the extrinsic

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coagulation pathway. Decreased mobility is also another risk factor.

Cancer patients with thromboembolic disease often have biochemical evidence of an activated coagulation cascade. Many have thrombocytosis, as well as high PT and APTT, and elevated levels of fibrinogen and D-dimers. However, since cancer can cause deranged clotting activity and many patients with thrombosis have normal levels of these markers, studies have shown that they are clinically neither specific nor sensitive to malignancy-associated thromboembolism.¹¹⁻¹²

Although cerebrovascular events are quite frequent in cancer patients, stroke as the first manifestation of cancer, as happened in this case, is uncommonly reported.¹³ When presented with multiple bihemispheric infarctions on diffusion-weighted imaging, early relapse or anaemia, one must consider the possibility of an occult cancer. In their study, Hiraga and colleagues claimed that the commonest cancer in stroke patients in the West is lung cancer, followed by gastrointestinal cancer. They recommend that a proper cancer work-up should be done in cases where the aetiology of stroke is unknown or where there are recurrent strokes and systemic thromboses, including thoracic imaging and measurement of tumour markers like CEA and CA19.9.¹⁴

The prognosis of patients with malignancy-associated thromboembolism is poor and management is very difficult. Recurrent arterial and venous thromboses mean that these patients should be on long-term anticoagulation. However warfarin is not a very good choice in these patients because of its narrow therapeutic window, need for frequent monitoring and tendency to interact with numerous other drugs. In a randomized controlled trial, Lee and colleagues compared warfarin against heparin in patients with active cancer and a confirmed DVT/PE. They found that fewer patients on heparin had recurrent venous thrombosis and the mortality rate was also less. On the other hand, there was no statistically significant difference in the rate of bleeding.¹⁵ Recent studies have also shown a trend towards decreased mortality with low-molecular-weight heparin as compared to unfractionated heparin.¹⁶⁻¹⁷

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