Brain metastasis localized to an area of infarction

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Summary

A patient with adenosquamous carcinoma of the cervix developed brain metastases limited to an area of evolving infarction. This preferential localization of tumor in an area of previous tissue injury with neovascularization provides support, in the human, for the importance of local vascular factors in the development of brain metastases.

Introduction

The mechanisms operative in determining the arrest and growth of metastatic carcinoma are multifactorial (1, 2). Of these, local vascular factors are considered important in the arrest of circulating tumor cells and their subsequent course at that site (3–6). Experimental animal work forms much of the basis for this concept. In a few instances, cases of preferential localization of tumor in sites of injury have been noted in humans (7–9). A recent observation of carcinoma metastasizing to the brain only in the area of a four-week-old infarct is the subject of this report and supports the importance of vascular factors in the development of brain metastases.

Case report

A 50-year-old woman initially developed postcoital bleeding proved by laparotomy to be an adenosquamous carcinoma of the uterine cervix, stage IB. She received 5 000 rads of external radiation therapy and additional brachytherapy, and she was asymptomatic for nine months. Two weeks before her final admission she developed symptoms of an upper respiratory tract infection with a fever to 38 °C and a cough. She was treated with intramuscular penicillin, aspirin and cough syrup. At 10 pm on the night of admission, while in bed, her husband noticed that she ‘shook all over’ for several seconds and then was unable to talk or move her right side. She was brought to the hospital, where her temperature was 38.4 °C, respirations were 16 and regular, blood pressure 150/70 and pulse 120 and regular. The physical examination was otherwise normal except for a grade 3/6 holosystolic murmur heard at the base and not noticed on previous admissions. She was awake and alert, globally aphasic, unable to communicate or to comprehend verbal commands. Her eyes were held to the left. There was a right homonymous hemianopia, flaccid hemiplegia with an extensor plantar response. The left side was normal. Admission laboratory work included a hematocrit of 15%, a white count of 16 000/cu mm and a platelet count of 143 000, down from 296 000/cu mm two weeks before. Her prothrombin time was 12.5 sec and partial thromboplastin time 30 sec. The remainder of the chemistries were normal. A two-dimensional echocardiogram of the heart revealed normal left ven-
tricular function with possible thickening of the anterior mitral valve 'perhaps representing vegetations.' An electrocardiogram revealed new small Q waves in 2, 3 and AVF with ST depression and inverted T waves. The chest x-ray was normal. A CT scan of the brain was negative. Multiple blood cultures failed to grow organisms. Serial EKG's and enzyme studies for evaluation of myocardial infarction failed to reveal evidence of that disorder. Her anemia responded to transfusions. During hospitalization her platelet count fell further, the prothrombin time rose to 13.9 sec, and the partial thromboplastin time remained normal at 38.2 sec. The thrombin time was 19.6 sec. A fibrinogen level of 320 mg/l but fibrin split products of 48 mg/l were found. She continued to be intermittently mildly febrile (to 38.2 despite antibiotics); her prothrombin time continued to rise slightly and fibrin split products remained present in the serum. The platelet count dropped to 70 000/cu mm. A factor VIII determination was normal. Melanotic stools were found on several occasions and a diagnosis of low-grade DIC was made with the possibility that the stroke was a result of non-bacterial thrombotic endocarditis. Her neurologic state remained essentially stable. Her coagulogram continued to show evidence of disseminated intravascular coagulation. A chest mass developed on chest x-ray. Twenty-eight days after admission at 12 midnight, she suddenly developed acute pulmonary edema and subsequently became hypotensive. There was also evidence of an acute abdomen. Despite supportive treatment in an intensive care unit, she expired 31 days after admission to the hospital.

The general postmortem examination revealed an acutely perforated pyloric ulcer. Thrombi filled both cardiac atrial appendages, and a small sterile vegetation was found on the posterior leaflet of the mitral valve. Adenocarcinoma exhibited a lymphangitic pattern of spread in the lungs and was found replacing pulmonary hilar and para-aortic lymph nodes. Multiple macroscopic foci of tumor were found in the liver, and microscopic foci were seen in each adrenal gland. Microscopically, there were multiple fibrin thrombi in glomerular capillaries and thrombi in small mesenteric vessels associated with small intestinal necrosis. An organizing thrombus partially occluded the inferior vena cava. Areas of acute infarction in the lungs, kidney and spleen were associated with thromboemboli.

The brain only weighed 1 000 gm. The vessels of the Circle of Willis showed very little atherosclero-

Fig. 1. Small deposit of poorly differentiated adenocarcinoma residing in the area of cerebral infarction (H&E).