

Intracranial Hemorrhage as the Initial Presentation of Disseminated Intravascular Coagulation in Association with Malignancy

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A 76-year-old man presented with a sudden disturbance of consciousness and right hemiplegia. An initial computed tomographic examination revealed multiple hematomas. The laboratory studies were highly suggestive of disseminated intravascular coagulation, although the underlying diseases were unknown at the time of admission. Despite various attempts at management, including replacement therapy, bleeding was not controlled and the patient died on day 5. An autopsy revealed the presence of prostate and rectal cancers. This case illustrates the fact that a fatal intracranial hemorrhage can be the first manifestation of disseminated intravascular coagulation in association with malignancy. **Key Words:** Disseminated intravascular coagulation—intracranial hemorrhage—prostate cancer—rectal cancer.

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Disseminated intravascular coagulation (DIC) is characterized by the systemic intravascular activation of coagulation, leading to the widespread deposition of fibrin in circulation.¹ Hemorrhage into the brain parenchyma or the subdural or subarachnoid space can result from acute DIC in cancer patients.³⁻⁸ The clinical signs of cerebral hemorrhage in association with DIC are fulminant and may be fatal.⁶ We report a rare case of multiple intracranial hemorrhage as the first manifestation of cancer-related DIC.

Case Report

A 76-year-old man with no significant medical history was admitted to our department because of unconsciousness and right hemiplegia. A computed tomographic (CT)

examination revealed an unusual hemorrhage distribution (Fig 1A). Upon admission, the patient was afebrile and his blood pressure was 153/79 mm Hg, with a regular pulse of 86 beats per minute. Laboratory studies revealed a platelet count of 99,000/mm³ (normal; 150,000-350,000/mm³), an international normalized ratio of 1.73, a fibrinogen level of <50 mg/dL (normal; 200-400mg/dL), a fibrin degradation product level of >640 µg/mL (normal; <10 µg/mL), and a D-dimer level of >320 µg/mL (normal; <0.4 µg/mL), suggesting DIC based on the criteria of the Japanese Ministry of Health Labour, and Welfare. Extensive gastrointestinal bleeding was also recognized on the admission. However, a CT scan of his body did not reveal any abnormal findings except for the presence of gallstones. Despite treatment using gabexate mesylate and transfusion, a CT examination on day 2 revealed multiple hematomas in the brain parenchyma and subarachnoid space that were not obvious on the initial CT images (Fig 1B). The patient's general condition deteriorated and the patient died on day 5. An autopsy revealed multiple hematomas, massive cerebral edema, and uncus herniation with no signs of neoplasm (Fig 2A). Microscopic examination revealed necrotic changes in the left basal ganglia and the right frontal lobe (Fig 2B). The autopsy also revealed a moderately differentiated rectal

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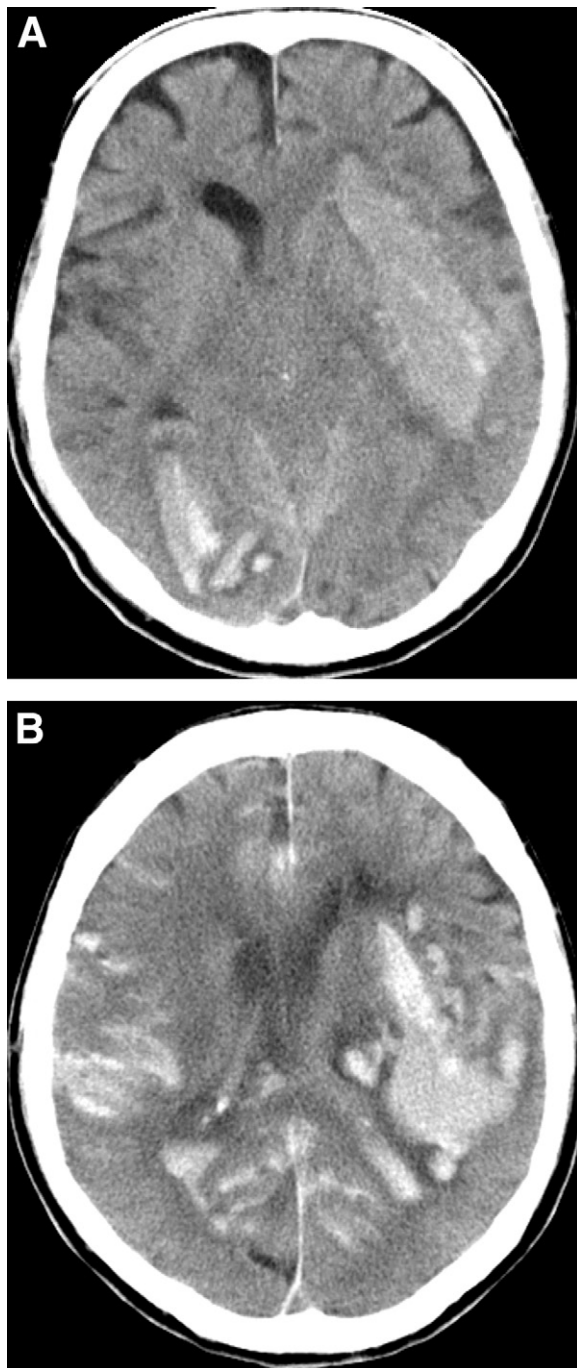


Figure 1. (A) Computed tomographic (CT) scan obtained upon admission shows hemorrhages in the left basal ganglia, the right posterior lobe, and the ventricles. (B) CT scan obtained on the following day shows multiple hematomas in the cerebral parenchyma and subarachnoid space that were not obvious on the initial CT images.

adenocarcinoma 4 cm in diameter (Fig 2C and 2D) and a moderately differentiated prostate adenocarcinoma 4.5 cm in diameter (Fig 2E and 2F). The rectal adenocarcinoma had infiltrated the muscle layer and the vein, without bone or lymph node metastases. The prostate adenocarcinoma revealed invasion to the capsule and metastases to the bone and lymph nodes.

Discussion

Spontaneous intracerebral hemorrhages have several main etiologies, including hypertension, amyloid angiopathy, vascular malformations, aneurysms, neoplasm, and DIC.⁹ In cancer patients, intracranial hemorrhages are most commonly caused by acute DIC.^{3,7} A recent retrospective study analyzing 208 adult cancer patients diagnosed as having an intracranial hemorrhage also concluded that the intratumoral hemorrhage and coagulopathy accounted for the majority of the hemorrhages, whereas hypertension was rare.⁵ DIC occurs as a complication of an underlying disorder.^{1,2} Excessive thrombin production leading to the increased consumption of platelets, coagulation factors, and coagulation inhibitors is speculated to be responsible for DIC in patients with cancer.⁷

In the present case, a CT examination performed upon admission revealed unusual distribution of the intracranial hemorrhages. Considering the laboratory data, we suspect that the intracranial hemorrhage was a result of DIC. The hypercoagulable state that accompanies DIC is a common pathophysiology for cerebrovascular complications.⁷ Patients with DIC often develop intracranial sinus thrombosis, which may cause infarction or parenchymal or subarachnoid hemorrhage.⁶ DIC associated with malignancy is also easy to suffer a cerebral infarction and subsequent hemorrhagic infarction.⁶ In our case, the most plausible pathophysiology was an infarction caused by the hypercoagulable state secondary to DIC, possibly leading to the multiple parenchymal hematomas followed by the rapid expansion of the hematomas under the extensive hemorrhagic state created by the DIC. However, we could not determine whether the multiple necrotic changes detected in the brain specimen were truly caused by DIC. Considering the multiplicity of the distribution of the hematomas, hypertension was unlikely to be the cause of the intracranial hemorrhage in our case. However, we could not completely rule out the possibility of hypertensive hemorrhage in the left basal ganglia.

A postmortem autopsy revealed multiple cancers. The association of DIC-related central nervous system bleeding is higher for prostate cancer than for other solid tumors.³ The DIC in the present case was likely caused by the prostate cancer.

Regarding treatment for DIC, attempts should be made to treat the underlying pathophysiologic condition and to replace clotting factors.^{6,7} In the present case, the underlying disease remained unknown while the patient was alive. Despite supportive management, the intracranial hemorrhage progressed during the clinical course. Any treatment was unlikely to have been effective unless the underlying disorder could have been well controlled.

A case with multiple hemorrhagic strokes as the initial manifestation of DIC associated with occult large cell

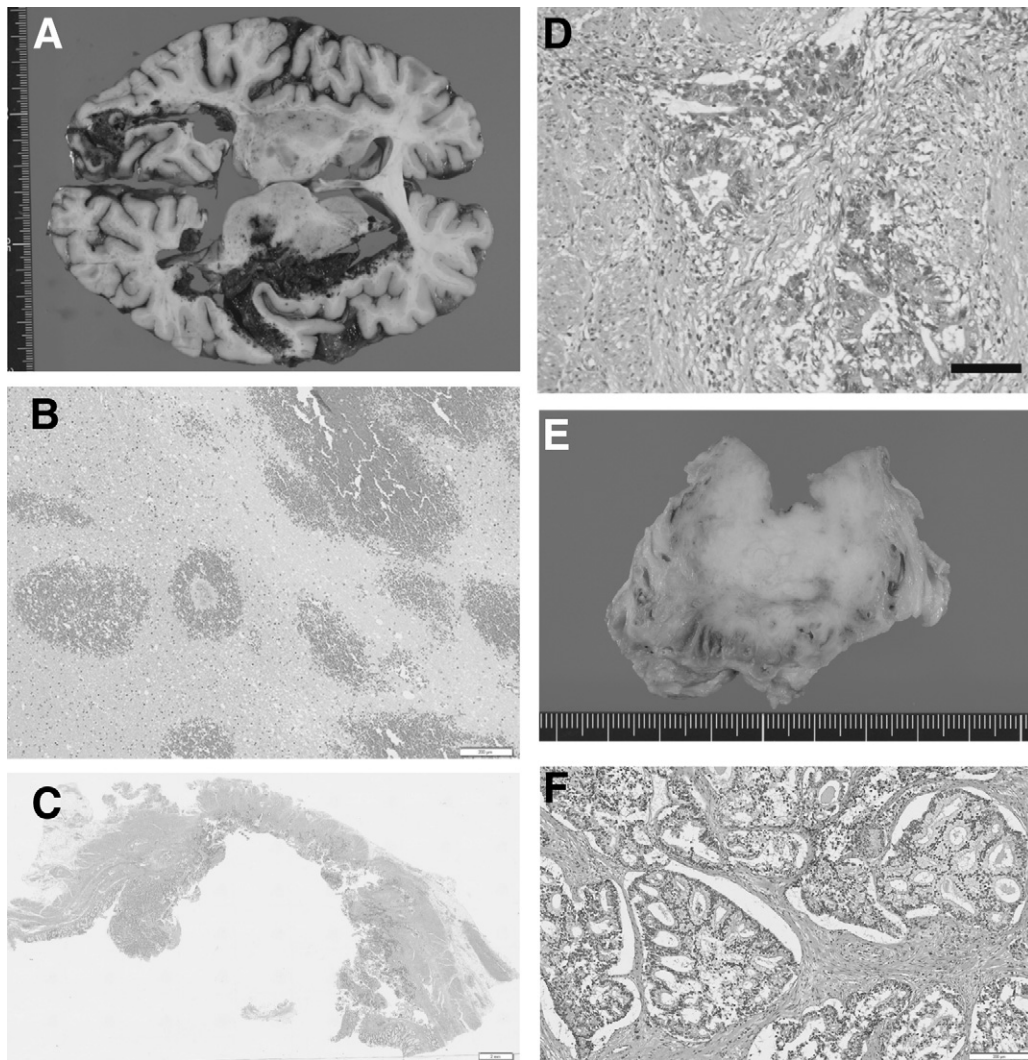


Figure 2. (A) Macroscopic image of the brain. Hematomas were recognized mainly in the left basal ganglia, the right posterior lobe, and the subarachnoid space. (B) Microscopic image of the left basal ganglia. Necrosis was seen adjacent to the hemorrhagic foci. No signs of neoplasm were seen. (C) Low-magnification microscopic image of the rectum. (D) High-magnification microscopic image of the rectal adenocarcinoma. The rectal adenocarcinoma had infiltrated the muscle layer. (E) Macroscopic image of the prostate. (F) Microscopic image of the prostate adenocarcinoma. The prostate adenocarcinoma had invaded the capsule. (Scale bars: B, 200 μ m; C, 2 mm; D, 100 μ m; and F, 200 μ m).

carcinoma has been previously reported.⁴ To the best of our knowledge, however, no previous reports have described a fatal intracranial hemorrhage as the first presentation of DIC arising from occult cancer. Our case illustrates the fact that fatal intracranial hemorrhages can be the first manifestation of DIC secondary to occult cancer. A systematic workup should be considered in patients with atypical intracranial hemorrhage if the initial laboratory studies are highly suggestive of DIC, because the rapid diagnosis and treatment of the underlying disease is crucial.

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