Subdural hematoma associated with disseminated intravascular coagulation in patients with advanced cancer

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Nontraumatic subdural hematoma following disseminated intravascular coagulation (DIC) due to advanced cancer was encountered in four patients. It is suggested that DIC plays an important role in the formation of subdural hematoma in cancer patients.

KEY WORDS—subdural hematoma· disseminated intravascular coagulation· cancer

NONTRAUMATIC subdural hematoma is found only rarely in patients with advanced cancer.2-5,7,9,11,12 So far, it has been assumed that this type of hematoma is a result of obstruction of the dural veins by tumor cells.2-4,9 We have recently encountered four cases of subdural hematoma, which seemed to be secondary to disseminated intravascular coagulation (DIC) due to advanced cancer. We believe that not only the vascular obstruction but also DIC plays a role in the formation of nontraumatic subdural hematoma in patients with advanced cancer.

Summary of Cases

Four patients, all females varying in age from 17 to 64 years, were admitted to the Nagoya University Hospital or its affiliated hospitals between 1979 and 1981. The clinical and pathological findings in these cases are summarized in Table 1. These patients were referred to our department because of deterioration in consciousness level, anisocoria, stiffness of the neck (Cases 3 and 4), and seizures (Case 2), all of which developed while the initial examination and treatment were being performed.

Two patients (Cases 1 and 2) had a history of gastrectomy for adenocarcinoma of the stomach. One of these patients (Case 1) had undergone a gastrectomy 3 years before and an oophorectomy for metastasis to the pelvic cavity 5 months before admission. She entered an affiliated hospital with complaints of anorexia, headache, and vomiting. The next day she became semicomatose and exhibited anisocoria, and was referred to our department. The other patient (Case 2) had undergone a gastrectomy for Borrman III type cancer 2 months before admission. She was suffering from excessive gingival bleeding. Seven days after admission, she became unconscious following seizure, and anisocoria developed.

The two other patients (Cases 3 and 4) suffered from malignant tumors. One (Case 3) was hospitalized with the complaint of difficulty in closing her mouth due to progressive buccal swelling. Biopsy from the region and bone marrow aspiration disclosed that the tumor was rhabdomyosarcoma, with metastasis to the bones. Four weeks after admission, she complained of headache followed by vomiting. Several days later, she became lethargic, and exhibited anisocoria and stiffness of the neck. The fourth patient (Case 4) entered an affiliated hospital complaining of lumbago from pathological fracture, and tarry stool which suggested gastrointestinal malignancy with metastasis to the spine. A radioisotope bone scan showed high uptake in virtually all bones. Five days after admission, this patient became drowsy and evidenced anisocoria and stiffness of the neck.

In no case had chemotherapy been indicated; there was no history of head trauma. In three patients (Cases 1, 2, and 3), some petechiae were recognized over the extremities on admission. All four patients...
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### TABLE 1

Summary of data in four cases of subdural hematoma associated with DIC due to advanced cancer

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Symptoms</th>
<th>Hematoma Location</th>
<th>Metastasis</th>
<th>Microscopic Findings</th>
<th>Admission to Operation (days)</th>
<th>Postop &amp; Survival (days)</th>
<th>Primary Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38, F</td>
<td>semicoma, anisocoria</td>
<td>rt frontoparietal</td>
<td>yes</td>
<td>not done</td>
<td>1</td>
<td>2</td>
<td>stomach adenocarcinoma</td>
</tr>
<tr>
<td>2</td>
<td>31, F</td>
<td>lethargy, anisocoria, seizures, hemiparesis</td>
<td>rt frontoparietal</td>
<td>unknown</td>
<td>not done</td>
<td>7</td>
<td>1</td>
<td>stomach adenocarcinoma</td>
</tr>
<tr>
<td>3</td>
<td>17, F</td>
<td>lethargy, anisocoria, stiff neck</td>
<td>lt temporo-parietal</td>
<td>yes</td>
<td>not done</td>
<td>28</td>
<td>cured</td>
<td>rhabdomyosarcoma</td>
</tr>
<tr>
<td>4</td>
<td>64, F</td>
<td>lethargy, anisocoria, stiff neck</td>
<td>lt frontotemporal</td>
<td>yes</td>
<td>tumor cells within dural vessels</td>
<td>5</td>
<td>15</td>
<td>stomach adenocarcinoma</td>
</tr>
</tbody>
</table>

* DIC = disseminated intravascular coagulation.

### TABLE 2

Summary of laboratory data in four cases

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Platelets (/cu mm)</th>
<th>Hb (gm/dl)</th>
<th>Ht (%)</th>
<th>Fibrinogen (mg/dl)</th>
<th>FDP (µg/ml)</th>
<th>BT (min)</th>
<th>PT (sec)</th>
<th>PTT (sec)</th>
<th>TT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65,000</td>
<td>9.1</td>
<td>27.7</td>
<td>139</td>
<td>40</td>
<td>33</td>
<td>20.5</td>
<td>46.9</td>
<td>47.3</td>
</tr>
<tr>
<td>2</td>
<td>33,000</td>
<td>9.8</td>
<td>29.8</td>
<td>100</td>
<td>40 &lt;</td>
<td>11.7</td>
<td>11.8</td>
<td>36.0</td>
<td>42.7</td>
</tr>
<tr>
<td>3</td>
<td>19,000</td>
<td>9.2</td>
<td>25.5</td>
<td>298</td>
<td>40</td>
<td>10</td>
<td>14.5</td>
<td>11.5</td>
<td>36.0</td>
</tr>
<tr>
<td>4</td>
<td>90,000</td>
<td>6.7</td>
<td>21.4</td>
<td>160 &lt;</td>
<td>40</td>
<td>5</td>
<td>12.0 (10.8)</td>
<td>39.0 (40.0)</td>
<td>39.0</td>
</tr>
</tbody>
</table>

* All but the second column indicate levels on admission. Second column gives data for 4 weeks (Case 3) and 5 days (Case 4) after admission, respectively. Control values are in parentheses. Hb = hemoglobin; Ht = hematocrit; FDP = fibrin-fibrinogen degradation products; BT = bleeding time; PT = prothrombin time; PTT = partial thromboplastin time; TT = thrombotest.

Exhibited evidence of DIC in laboratory examinations (Table 2). As a treatment for DIC, heparin, aprotinin (Trasylol), and/or gabexate mesilate (FOY) were administered in each case. In Case 3, intravascular clotting was ameliorated by daily administration of heparin (5000 to 10,000 units) and 2000 mg of FOY 4 weeks after admission, just before surgery.

Computerized tomography (CT) scanning was diagnostic of subdural hematoma, showing crescent-shaped low-density areas in all four cases (Fig. 1). These hematomas were assumed to be responsible for the herniation signs. Evacuation of all hematomas was undertaken. In every case, dark brown fluid was drained through burr holes. Two patients (Cases 1 and 3) had a thin neomembrane covering the hematoma. Postoperatively, three patients (Cases 1, 2, and 4) never regained consciousness and died within 15 days. The other patient recovered from surgery without neurological deficit.

**Fig. 1.** Case 3. Plain computerized tomography scan showing subdural hematoma in the left temporoparietal area. Midline shift with collapse of the left lateral ventricle is evident.
Autopsy was permitted only in Case 4, and revealed adenocarcinoma of the stomach with metastases to the lymph nodes, lung, adrenal glands, and bones. Microscopic examination of the dura adjacent to the subdural hematoma revealed obstruction of the vascular channels by tumor cells (Fig. 2). There were no metastatic nodules in the brain parenchyma.

Discussion

There have been few reports of nontraumatic subdural hematomas developing in cancer patients. In 1904, Westenhoeffer\(^1\) first reported a case associated with metastatic gastric cancer, and applied the term "pachymeningitis hemorrhagica interna." Since then, Wohlwill,\(^12\) Russell and Cairns,\(^9\) and Meyer and Reah\(^5\) have reported similar cases, using the same term. In the past decade, Braun, \textit{et al.},\(^3\) Leech, \textit{et al.},\(^4\) Ambiavagar and Sher,\(^2\) and Ng Tang Fui, \textit{et al.},\(^7\) have described some similar cases as subdural hematoma.

The well accepted explanation for the mechanism of hematoma formation was advanced by Russell and Cairns.\(^9\) They postulated that the hematoma results from obstruction of veins by tumor cells within the outer dense layer, followed by dilatation and rupture of capillaries within the inner areolar layer of the dura. The formation of the hematoma neomembrane was regarded as a consequence of dilatation, engorgement, and rupture of the capillaries of the areolar layer. Braun, \textit{et al.},\(^3\) and Leech, \textit{et al.},\(^4\) supported this explanation based on their observations in dura specimens, which evidenced emboli of tumor cells within the dilated dural vessels. A similar finding was recognized in Case 4 under microscopic study. Ambiavagar and Sher\(^2\) accepted the above explanation, but also pointed out the possible role of a coagulation

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Summary of data in previously reported cancer patients with nontraumatic subdural hematoma*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case No.</td>
<td>Authors, Year</td>
</tr>
<tr>
<td>1</td>
<td>Braun, \textit{et al.}, 1973</td>
</tr>
<tr>
<td>2</td>
<td>Leech, \textit{et al.}, 1974</td>
</tr>
<tr>
<td>3</td>
<td>Ambiavagar &amp; Sher, 1978</td>
</tr>
<tr>
<td>4</td>
<td>75, M</td>
</tr>
<tr>
<td>5</td>
<td>Ng Tang Fui, \textit{et al.}, 1978</td>
</tr>
</tbody>
</table>

* Only reports with clinical and laboratory data are included. Hb = hemoglobin; Ht = hematocrit.
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defect in formation of the hematoma because one of their cases showed marked thrombocytopenia. Ng Tang Fui, et al.,7 also reported a case of nontraumatic subdural hematoma associated with drug-induced thrombocytopenia ascribed to chemotherapy. Table 3 summarizes the clinical, laboratory, and pathological findings in previously reported cases. It is notable that thrombocytopenia, the main stigma of DIC, was present in all but Case 4 in Table 3.

Disseminated intravascular coagulation is not an uncommon complication in the advanced stages of cancer.1 Most patients with disseminated cancer undergo a hypercoagulable state, which is related to the release into the circulation of thromboplastic tissue components from neoplastic cells. The coagulation mechanism of these patients is delicately balanced with compensatory overproduction of some of the consumed coagulation factors and easily tipped toward DIC by minor stimuli.6,8 Although no evidence of DIC was reported in the previous studies, all but Cases 4 and 5 listed in Table 3 may also have had DIC. For these reasons, we believe that formation of the hematoma begins with obstruction of the dural veins by tumor cells and then is precipitated by DIC.

In advanced stages of cancer, a serious investigation for the cause of neurological deficits is not always conducted. This has been partly attributable to the lack of effective means to pinpoint intracranial lesions without imposing a burden on cancer patients. The widespread use of CT scans may indicate that cases such as presented here are far more frequent than considered thus far. Based on the fact that dural metastasis is not a rare complication of advanced cancer,10 as well as DIC, it is reasonable to suggest this explanation as a possibility. In any case, one should be aware of the possible development of a subdural hematoma associated with DIC when neurological deficits are encountered in cancer patients. A recovery may be possible, as in our Case 3.

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References


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