The oncotic pressure of fluid from subdural hematomas and subdural hygromas was compared to that of simultaneously drawn venous blood in 20 patients. There was no significant difference in the oncotic pressure of fluid from subdural hematomas and venous blood; however, the oncotic pressure of fluid from subdural hygromas was significantly less than that of blood. This finding fails to support the Zollinger and Gross modification of Gardner's theory, that chronic subdural hematomas grow and produce symptoms after a latent interval because they attract fluid from the blood via dural vessels.

Key Words: oncotic pressure, colloid osmotic pressure, subdural hematoma, subdural hygroma

Almost 50 years ago, Gardner placed cellophane sacs of blood in the subdural space or rectus muscle of dogs, and, after 3 to 18 days, found a gain in weight of 39% to 103%. He also placed one "inner" subdural membrane containing 17 cc of subdural fluid inside a beaker containing 52 cc of cerebrospinal fluid (CSF), and found an increase in volume of 2.9% for the hematoma after 16 hours in a refrigerator. On this basis, he hypothesized that subdural hematomas grew in volume because blood components broke down with time into smaller molecules, thereby increasing the oncotic pressure within the hematoma, which in turn sucked water into the sac from the CSF. This theory gained almost instant acceptance, and is still widely held.

Zollinger and Gross suggested that the hematoma gained its fluid, not from the CSF, but from the intravascular compartment. Using oxalated or hemolyzed blood in cellophane sacs placed in isotonic saline, they found increases in volume of the "hematomas" despite the fact that the osmotic pressure, as measured by freezing-point depression, was the same on both sides of the cellophane. They implied that the dynamic mechanism by which hematomas expanded was a difference in colloid osmotic pressure (oncotic pressure) between hematoma and blood, not a difference in oncotic pressure between hematoma and CSF.

Osmotic pressure is generated by a movement of water across a semipermeable membrane in an effort to equalize the concentrations of solute on either side. The size of the membrane's pores must be such that the water but not the solute molecules can traverse them. Water flows from a region of lower to higher osmotic pressure. Osmotic pressure varies with the number of molecules in solution, and one molecule of low molecular weight exerts the same osmotic pressure as any huge organic molecule. Oncotic pressure (synonymous with colloid osmotic pressure) is the pressure resulting across a membrane, of which the pores are sufficiently large that they are impermeable only to such large organic molecules as albumin, but allow many smaller molecules in addition to water to pass freely. This pressure is of great importance in the movement of fluids across capillary walls, of which the openings permit many molecules in addition to water to pass. Albumin, with a molecular weight of 69,000 and a plasma concentration of 3.6 gm/dl, generates a pressure of 16.4 mm Hg. The remaining plasma proteins generate a pressure of about 3.6 mm Hg. In addition, approximately 30% of the total pressure results from the unequal distribution of electrolytes in an ionized colloidal system caused by the Gibbs-Donnan phenomenon. In our hospital, the normal range of serum oncotic pressure is 22 to 28 mm Hg.

With the recent development of membrane oncometers with fast response time, it has become feasible to measure oncotic pressure of biological samples. It was felt that the direct, simultaneous measurement of the oncotic pressure of fluid from subdural hematomas and venous blood could provide a new approach to the study of the growth of chronic hematomas.

The present study was undertaken to determine the oncotic pressure of fluid from subdural hematomas and subdural hygromas and to compare it with that of simultaneously drawn venous blood in 20 patients. The patients were divided into two groups: Group 1, 10 patients with subdural hematomas, and Group 2, 10 patients with subdural hygromas.

The oncotic pressure of fluid from subdural hematomas and venous blood was compared in 20 patients. There was no significant difference in the oncotic pressure of fluid from subdural hematomas and venous blood; however, the oncotic pressure of fluid from subdural hygromas was significantly less than that of blood. This finding fails to support the Zollinger and Gross modification of Gardner's theory, that chronic subdural hematomas grow and produce symptoms after a latent interval because they attract fluid from the blood via dural vessels.

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Oncotic pressure of subdural fluids

TABLE 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Fluid</th>
<th>Oncotic Pressure (mm Hg)</th>
<th>Total Protein (gm/dl)</th>
<th>Albumin (gm/dl)</th>
<th>Total Hemoglobin (gm/dl)</th>
<th>Supernatant Hemoglobin (gm/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>subdural hematoma</td>
<td>blood</td>
<td>25.9 ± 1.7</td>
<td>6.6 ± 0.2</td>
<td>3.8 ± 0.2†</td>
<td>13.2 ± 0.6</td>
<td>—</td>
</tr>
<tr>
<td>(14 cases)</td>
<td>hematoma fluid</td>
<td>27.5 ± 1.9</td>
<td>6.5 ± 0.4</td>
<td>2.7 ± 0.3†</td>
<td>11.3 ± 1.1</td>
<td>2.6 ± 0.6</td>
</tr>
<tr>
<td>subdural hygroma</td>
<td>blood</td>
<td>20.3 ± 2.2†</td>
<td>6.0 ± 0.3†</td>
<td>2.8 ± 0.3‡</td>
<td>11.7 ± 0.9</td>
<td>—</td>
</tr>
<tr>
<td>(6 cases)</td>
<td>hygroma fluid</td>
<td>7.2 ± 3.2†</td>
<td>1.2 ± 0.7</td>
<td>0.6 ± 0.4‡</td>
<td>0</td>
<td>—</td>
</tr>
</tbody>
</table>

*—: test not done. Values are means ± standard error of the means.
†Paired t-test: p < 0.001.
‡Paired t-test: p < 0.01.

Clinical Material and Methods

Twenty patients with subdural fluid collections operated on during 1979 at the University of Alberta Hospitals were studied. The oncotic pressure of subdural fluid and simultaneously drawn venous blood was measured. A burr hole was made, and the dura was punctured with a No. 18 sharp needle and fluid aspirated. A 2- to 3-mm circle of dura and outer membrane (if any) was excised and submitted for routine histological examination. Most patients had a Jackson-Pratt drain placed in the subdural cavity when the fluid had been evacuated. All patients had pre- and postoperative computerized tomography (CT) scans, except for two (Cases 3 and 4) who did not have postoperative scans. Computerized tomography was by EMI scanner, using a 160 × 160 matrix.*

The specimens obtained were spun down in an ordinary centrifuge, and the supernatant fluid was examined for oncotic pressure using an oncometer.† The electrophoretic pattern of the fluids was determined using clear cellulose acetate membranes in a scanner.‡ Results are given as means ± the standard error of the means.

Results

In 14 patients, opaque fluid, red to brown in color, was aspirated, and they were considered to have hematomas. Six had clear yellow fluid aspirated, and they were classified as having hygromas. The mean oncotic pressure, total protein, albumin, and hemoglobin contents of the subdural hematomas and hygromas are given in Table 1. There was a significant difference in oncotic pressure of venous blood and hygroma fluid but not venous blood and hematoma fluid. Statistical tests of the quantitative variables were carried out (Pearson “product movement” correlations). The oncotic pressure of subdural fluid correlated with the total protein of subdural fluid (p < 0.001), the free hemoglobin in subdural fluid (p < 0.01), the total hemoglobin in subdural fluid (p < 0.01), the albumin in venous blood (p < 0.01), the albumin in subdural fluid (p < 0.05), and the oncotic pressure of venous blood (p < 0.05). The oncotic pressure of venous blood correlated highly significantly with the albumin of venous blood (p < 0.001) and with the total protein of venous blood (p < 0.001).

Oncotic pressure was not related to age. There was no significant difference between samples from patients with a history of head injury less than 6.5 weeks, from those with history longer than 6.5 weeks, and from those with no known instance of head injury. The oncotic pressure for the three groups was 25.7 ± 3.3, 25.6 ± 2.7, and 32.3 ± 3.7 mm Hg, respectively.

Paired t-tests showed no significant difference between the oncotic pressure of subdural hematoma fluid and venous blood; a significant difference would have supported the Zollinger-Gross theory (see Table 1). Similarly there was no significant difference in the total protein of subdural hematoma fluid and venous blood, although the former had significantly less albumin (p < 0.001). On the other hand, there was a highly significant difference (p < 0.001) in the oncotic pressure of subdural hygroma fluid and venous blood, as well as the total protein of hygroma and blood (p < 0.001) and albumin of hygroma and blood (p < 0.01).

The highly significant relationship between the oncotic pressure and the total protein of subdural fluid (both hematoma and hygroma) is illustrated in Fig. 1. The oncotic pressure of subdural fluid equals 0.01 + 4.12 × total protein.
FIG. 1. Graph showing the oncotic pressure of subdural fluid by total protein of fluid. \( y = 0.01 + 4.12x \).

A composite diagram of the electrophoretic patterns of the two classes of fluids is shown in Fig. 2. Subdural hematoma fluids show hemoglobin breakdown products migrating with the alpha and beta globulins. Subdural hygroma fluids did not show this, and, in addition, four of six samples showed pre-albumin, typically seen in CSF and not blood serum. Albumin in the subdural hematomas was 2.7 ± 0.3 gm/dl by the bromcresol green assay, and 2.3 ± 0.4 gm/dl using the electrophoretic method. The corresponding figures for subdural hygromas were 0.6 ± 0.4 and 0.6 ± 0.4 gm/dl. The oncotic pressure of seven isodense collections (on CT scan) was 28 ± 3.6 mm Hg, for four hypodense examples it was 29.9 ± 2.3 mm Hg, and for three hyperdense cases 23.3 ± 1.3 mm Hg.

FIG. 2. Composite electrophoretic patterns aligned by the albumin peak. alb = albumin, Hgb = hemoglobin breakdown products, pre-alb = pre-albumins.

Discussion

The present study suggests that chronic subdural hematomas do not progressively increase in size because of an oncotic pressure gradient between the interior of the hematoma sac and the blood stream. A previous study was also unable to find evidence in support of the osmotic theory of growth by direct measurement of the osmotic pressure (by freezing-point depression method) of hematoma fluid, blood, and CSF.

Modern theories of transcapillary fluid movement have become more complex than the original Starling hypothesis, which considered that the main factors were a positive outward pressure at the arterial end of the capillary and a negative pressure at the venous end, these balances depending on net hydrostatic and oncotic pressures. Additional influences on fluid movement are lipid solubility, pore size of the capillaries, and the presence of cytoplasmic vesicular transport mechanisms. Factors that would act to cause a fluid shift into a subdural hematoma or hygroma would be as follows: 1) increased hydrostatic pressure in the neomembrane's capillaries; 2) increase in permeability of these capillaries; 3) increase in the surface area of the capillary network; 4) increased water production as a result of the metabolism of the neocapillaries; 5) decreased resorption of fluid by the neocapillaries into the blood or through the dural-arachnoidal layer into the CSF; and 6) decreased tissue hydrostatic pressure, that is, intracranial pressure. A decrease in the osmotic or oncotic pressure within the lumen of the neocapillaries or an increase in the hematoma could also theoretically cause a fluid shift.

There are several commonplace observations, by no means new, which must be explained in any theory on the pathogenesis of chronic subdural hematoma. Subdural hematoma fluid usually does not clot. Regardless of the age of the hematoma, it contains fresh erythrocytes. Routine pathological examination shows that the outer membrane of the hematoma has a neocapillary network of obvious fragility because of the presence of numerous areas of microhemorrhage. In conjunction with these observations, we should consider the findings of Labadie and Glover that subdural hematoma fluid accelerates the intrinsic clotting system, produces defective clot formation, and stimulates the fibrinolytic system. Ito, et al., have shown that fibrinogen is absent from hematoma fluid, that fibrin degradation products are greatly increased, and that mean daily hemorrhage into a chronic hematoma (chromium-51-labeled erythrocytes) accounted for an estimated 10.2% of its volume. Sato and Suzuki carried out electron microscopic studies of subdural hematoma membrane. They found endothelial fenestrations as well as open gaps between adjacent endothelial cells in the neocapillary bed. Friede and Schachennay believed that neomembranes are not de novo proliferations of tissue from
Oncotic pressure of subdural fluids

smooth inner dural surface, but result from the proliferation of the normal layer of dural border cells. They suggest that the dural-arachnoidal junction is tight, and that subdural hematomas are actually intradural. Macrophages engulfing erythrocytes and their subsequent intracytoplasmic disintegration were illustrated. Lindenberg commented that new hematomas can develop on the outer aspect of an old one, within its membrane.

Translated into everyday clinical practice, a multifactorial concept for the origin of chronic subdural hematomas is consistent with the known occurrence of chronic hematomas following repeated minor trauma, intracranial hypotension (postshunting), decreased brain volume (aging), impaired blood coagulability (alcoholism and use of anticoagulants), structural vascular abnormality (dural neoplasm or infection), and central venous hypertension.

Some of our cases showed no outer membrane, fluid lacking hemoglobin or erythrocytes, protein concentrations similar to CSF but not to blood, and a low attenuation coefficient on the CT scan. These cases had low oncotic pressure. Some also showed prealbumin, the concentration of which increases when the flow of CSF is obstructed. It seems possible that an arachnoidal tear could create a one-way valve and a sequestration of CSF in the subdural space. Some of these collections are clearly unilateral and space occupying. Other bilateral collections are more likely enlargements of the subarachnoid space over the cortex as the initial event in the development of communicating hydrocephalus, rather than the more common initial ventricular enlargement.

It is remarkable that the simple removal of the chronic subdural hematoma fluid by a burr hole is so often curative since almost the entire neocapillary membrane is left in situ. Presumably the explanation lies in the fact that the hemorrhagic fluid contains the anticoagulation factors that lead to a self-perpetuating cycle of bleeding, and without these factors hemo- stasis and fibrosis can occur. Some fluid is transported out of the hygroma into the compartment with the lower oncotic pressure. This does not, however, show a progressive increase in volume.

The low oncotic pressure of subdural hygroma compared to blood suggests that there is an effective fluid barrier between the subdural compartment in such cases and the blood stream, otherwise fluid would shift out of the hygroma into the compartment with the higher oncotic pressure.

In summary, when bleeding occurs into the subdural space, then the normal homeostatic response is to attempt to remove the debris. To accomplish this, scavenging macrophages must get to the offending erythrocytes, and for that to happen a neocapillary network must be laid down. In many circumstances, this healing progresses uneventfully and fibrosis occurs. In some cases, however, the “leaky” new vessels lose more erythrocytes than they remove. The microhemorrhages are aggravated by the fibrinolytic activity of the fibrin degradation products. It no longer seems necessary to postulate that a late increase in volume occurs either because of an osmotic or oncotic mechanism.

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References


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