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Editorial

Introduction of chemotherapy by omentum for a glioblastoma WHO-IV

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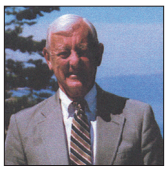

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THE PROBLEM

It is well acknowledged that glioblasts remain a major neurological problem that has existed for decades. When experiments with the omentum were begun in animals[1,2] and humans[3] in the 1970s, no thought was considered for the use of the omentum in the treatment of malignant brain tumors. Glioblasts are routinely excised from the brain, but poor surgical survival results continue to prevail. In fact, current survival statistics following surgery for glioblasts are only moderately improved in comparison to the surgical results obtained by Harvey Cushing more than a century ago. The reason for these clinical failures is the marked ability of blood–brain barrier (BBB) and blood–brain tumor barrier (BBTB) capillaries to prevent chemotherapy from entering the brain.

There are billions of capillaries throughout the body, but the only capillaries that have BBBs are those in the brain. Capillaries outside the brain are fenestrated (open) with endothelial cells that line the wall of these vessels. Throughout this wall of endothelial cells are open gaps that allow biological materials such as water, oxygen, and glucose to enter and exit throughout the body tissues. When these gaps are tight or blocked by specific BBB and BBTB capillaries, chemotherapy is prevented from entering the brain. If there is to be a successful chemotherapeutic treatment for glioblasts, BBB and BBTB capillaries must be bypassed or eliminated.

This paper proposes an operation that will allow the introduction of chemotherapeutic drugs into the brain of patients suffering from a glioblast. The operation requires the placement of the vascularized omentum into a prepared cavity in the brain, in which omental arteries can develop and subsequently penetrate directly and deeply into brain tissue. These omental arteries that enter the brain follow the progression of all arteries, namely, they branch into smaller vascular structures called arterioles which subsequently branch into smaller capillaries that connect the arterial-arterioles system in the body into smaller capillaries which advance blood flow from the heart into the general venous system. It is these specific capillaries in the brain that contain BBBs that prevent chemotherapy from entering the brain.

It had been hoped in the past that the administration of chemotherapeutic drugs offered to patients suffering from a glioblast would be clinically effective. Unfortunately, this did not occur. The BBBs within the brain prevent chemotherapeutic drugs from entering the brain. The operation proposed in this paper bypasses these BBBs.

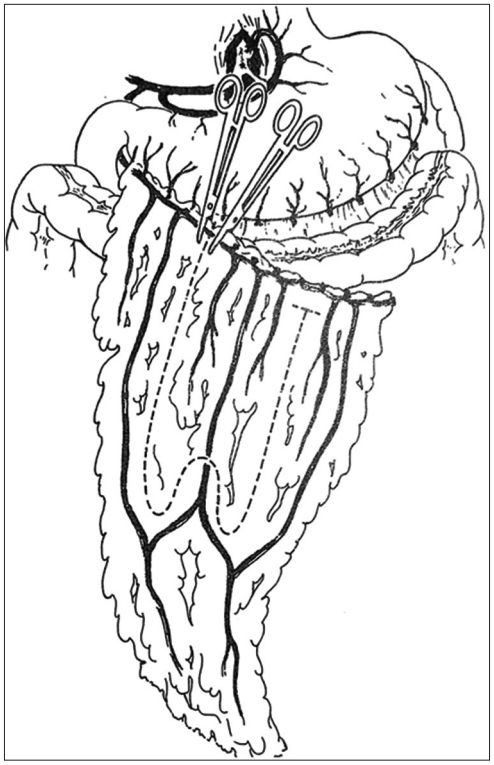

Figure 1: The omental apron is divided to gain increased length with arterial supply being maintained primarily, along the periphery.

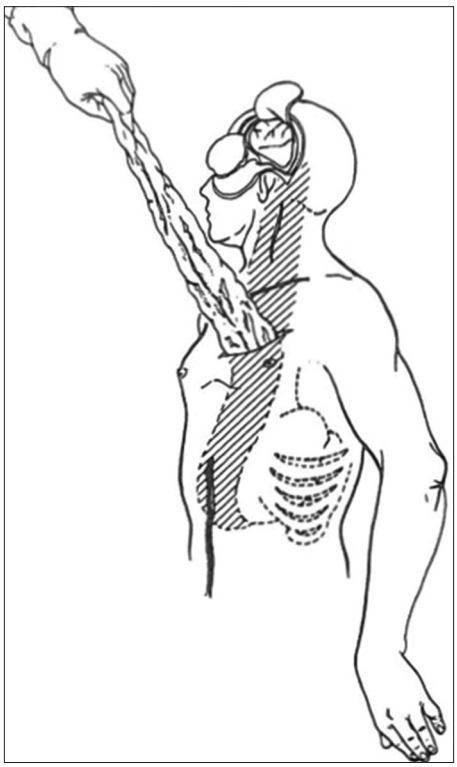

Figure 2: Omentum has been brought through a long subcutaneous tunnel developed between incisions along chest and anterolateral neck, where it exits behind the ear and, then, is placed on the brain.

The first step in the operation is to become familiar with the intra-abdominal presence of the omentum. This is accomplished by making a 4–5-inch upper midline abdominal incision, which makes it easy to observe the placement of the omentum within the abdominal cavity. The technique to elongate the omentum up to the brain begins as follows: The omentum is completely separated from the transverse colon. This step is avascular and simple. This is followed by separating the omentum from its proximal and central attachments to the greater curvature of the stomach, leaving the gastroepiploic artery and vein intact within the omental apron. The left gastroepiploic vessels are then divided to increase omental length.

To gain length to reach the brain, the omentum is surgically tailored with care being taken to preserve intact at least one major artery and vein within the omental apron [Figure 1]. After completing this omental lengthening process, the blood vessels that maintain the vascular integrity of the omental pedicle are the right gastroepiploic artery and vein. The viability of the pedicled omental graft depends on the preservation of these vessels.

Once the omentum has been sufficiently lengthened to reach the brain without any tension, several small transverse incisions are made along the chest wall which is connected by a long longitudinal subcutaneous tunnel [Figure 2]. The omentum is brought through this subcutaneous tunnel up the chest to the neck, behind the ear, and then placed directly on the brain. This omental lengthening technique has been successfully reported when the omentum was placed on the surface of the brain in the treatment of Alzheimer's[4,5,7,8] and cerebrovascular patients.[10,11]

In the operation being proposed, the intact omentum is placed in a recently created brain cavity caused by the surgical excision of the glioblast. The omentum is key since it is the most angiogenic structure in the body, due to extensive amounts of vascular endothelial growth factor (VEGF) which is the most angiogenic substance in the body and its greatest concentration is found within the omentum itself.[13]

Before the surgery being proposed, the patient ingests aminovolumic acid (5-ALA) 3 h before the operative procedure.[12] The distinct coloration of malignant tissue, which fluoresces from the 5-ALA, allows the neurosurgeon to be more exact in the excision of the brain tumor. The final steps in the operation are the excision of the brain tumor and the placement of the omentum into the cavity in the brain caused by the recent excised glioblast. In this location, the omentum begins to extend its extensive angiogenic capability by producing multiple omental arteries that penetrate

Figure 3: Omentum on monkey brain showing omental arteries penetrating deeply into underlying brain tissue. These arteries are devoid of blood–brain barriers.

throughout the circumferential wall of the brain cavity into the surrounding brain tissue [Figure 3]. On the side of the brain in which the malignant tumor has been recently excised, arteries need only to progress a short distance to reach the area, in which recurrent glioblast tissue might be developing. The reason for the short distance that arteries may develop from the omentum in the brain cavity to an area of possible recurrent tumor is that 90% of recurrences of glioblasts occur within 2 cm of the contrast-enhancing margin as depicted by computed tomography scans.[9] This means that most recurrent brain tumors are less than one inch distant from the recently created cavity in the brain (1" equals 3.54 cm). This should allow chemotherapeutic drugs flowing through omental arteries that are devoid of BBBs, to be destructive for recurrent malignant brain tissue in the area. The newly arriving omental arteries are fenestrated, which would allow intravenous chemotherapy to enter the brain and bypass the presence of BBB capillaries in the area.[6]

It is believed that this operation can improve the survival statistics of a glioblast, but the eventual success of the operation may depend on the strength of the chemotherapy that would be flowing into the brain through the omental arteries.

CONCLUSION

In the past, it was hoped that chemotherapy, when administered to patients with a glioblastoma, would be clinically improved by the use of these drugs. However, this did not occur as a result of BBB and BBTB capillaries that are specifically located only in the brain. It is now known that placement of the omental arteries in the brain of patients suffering from a glioblast, could allow chemotherapy to perfuse throughout the brain. Most important will be the strength of the chemotherapy that will be present in the omental capillaries that are devoid of BBB and BBTB vessels. Due to the lethality of glioblasts, it is hoped that clinical investigation of the effect of the placement of the omentum on the brain of glioblast patients will result in an experimental and clinical sense of urgency. For a patient with a glioblast, time is critical.

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