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Successful Removal of a Giant Skull Base Metastasis from Hepatocellular Carcinoma after Direct Ethanol Injection: Case Report

ABSTRACT—Skull metastases from hepatocellular carcinoma (HCC) are extremely rich in vascularity, which sometimes makes surgery dangerous. For minimally invasive surgery, it is very important to diminish the intratumoral vascular flow preoperatively. We report the case of a 69-year-old man with a giant skull base metastasis from HCC that was successfully removed after two sessions of direct ethanol injection into the tumor as a preoperative treatment to diminish the intratumoral vascular flow. Direct ethanol injection is a modification of percutaneous ethanol injection therapy, which is widely used in the treatment of primary HCC. In this article, we describe in detail the practical procedures and the usefulness of this treatment for a giant skull base metastasis from HCC.

In patients with skull metastases from hepatocellular carcinoma (HCC), surgical treatment is usually selected because conservative therapies are controversial.[1–4] However, skull metastases from HCC are extremely rich in vascularity, which sometimes makes them difficult to treat surgically. Especially when they exist in the skull base and are so large as to destroy the normal anatomic structures, surgery is severely dangerous. For minimally invasive surgery, it is very important to diminish the intratumoral vascular flow preoperatively.

Recently, using the direct ethanol injection technique for skull metastasis from HCC, we succeeded in diminishing the vascularity within the tumor, although the tumor was a small calvarial metastasis.[5] This technique is a modification of percutaneous ethanol injection therapy (PEIT), which is widely used for the treatment of small primary lesions of HCC.[6–8] We used this technique as a preoperative treatment to diminish the intratumoral vascular flow in a patient with a giant skull base metastasis from HCC. Here, we described the prac-

Skull Base Surgery, Volume 10, Number 2. Departments of Neurosurgery (TI, HN, TS, JY, KW) and Radiology (TK), Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan. Reprint requests: Toshihiko Isaka, M.D., Ph.D., Department of Neurosurgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, 3 Nakamichi 1-chome, Higashinari-ku, Osaka, 537-8511, Japan. 1052-1453, p;2000,10,02,081,086,ftx,en;sbs00177x

tical procedures and the usefulness of this treatment for giant skull base tumors that are rich in vascularity.

CASE REPORT

A 69-year-old man was referred to our hospital with a giant skull base tumor in June 1998. At another hospital about 2 years previously, he was diagnosed as having a skull tumor 3 cm in diameter in the left petrous apex, which was considered to be a metastasis from HCC. The tumor was treated with gamma knife radiosurgery with a maximum dose of 50 Gy and a marginal dose of 25 Gy. After gamma knife radiosurgery, the tumor continued to enlarge. The patient gradually developed some neurologic abnormalities with an increased subcutaneous mass from the left frontotemporal region to the ipsilateral face, for which he requested another positive therapy. The primary lesion of HCC had been controlled with two sessions of transcatheter arterial embolization and one session of PEIT over the past 6 years.

Examination

On admission, the solid mass was 8 cm in diameter, covered with thin but normal-looking skin, and extended from the left frontotemporal region to the ipsilateral face. Neurologic examination revealed visual loss and total ophthalmoplegia of the left eye, hyperalgesia of the left trigeminal nerve, facial nerve palsy, and hypoglossal nerve palsy on the left side. Magnetic resonance (MR) imaging revealed an expansive, osteolytic, and solid tumor extradurally extending from the anterior and middle cranial fossae into the infratemporal and pterygopalatine fossae, destroying a part of the sphenoid and zygomatic bones (Fig. 1, A–F). The tumor also extended into the subcutis of the frontotemporal region, destroying a part of the frontal, temporal, and parietal bones. On MR images, the lesion showed high intensity on T1-weighted images and was homogeneously enhanced with gadolinium. Computed tomography (CT) revealed that the lesion was isodense and strongly enhanced with contrast medium (Fig. 2, A–C). Angiography showed that the tumor was mainly fed by the external carotid artery and partially by the internal carotid artery and was homogeneously and strongly

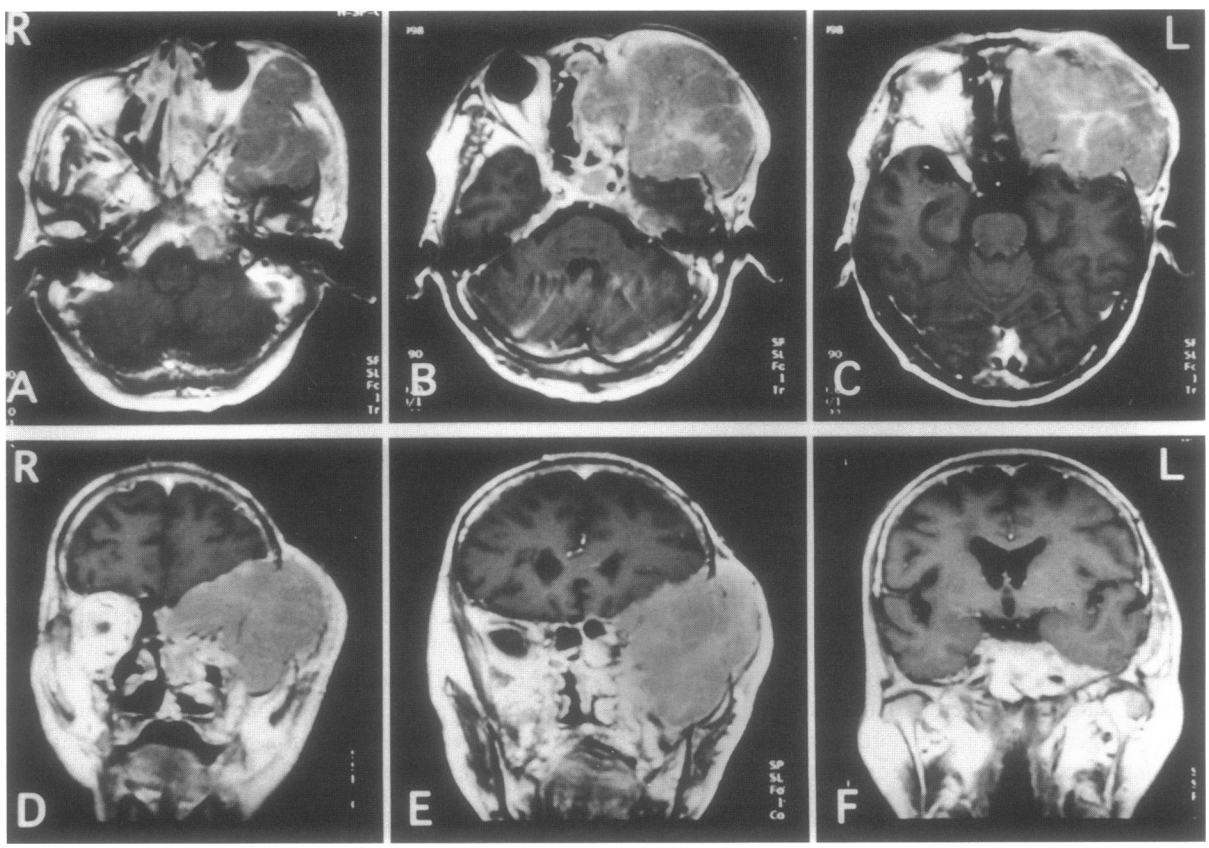

Figure 1. MR images on admission. Enhanced T1-weighted images axial **(A–C)** and coronal **(D–F)** showing an expansive, osteolytic, and solid tumor extradurally extending from the anterior and middle cranial fossae into the infratemporal and pterygopalatine fossae, destroying a part of the sphenoid and zygomatic bones, and also extending into the subcutis of the frontotemporal region, destroying a part of the frontal, temporal, and parietal bones.

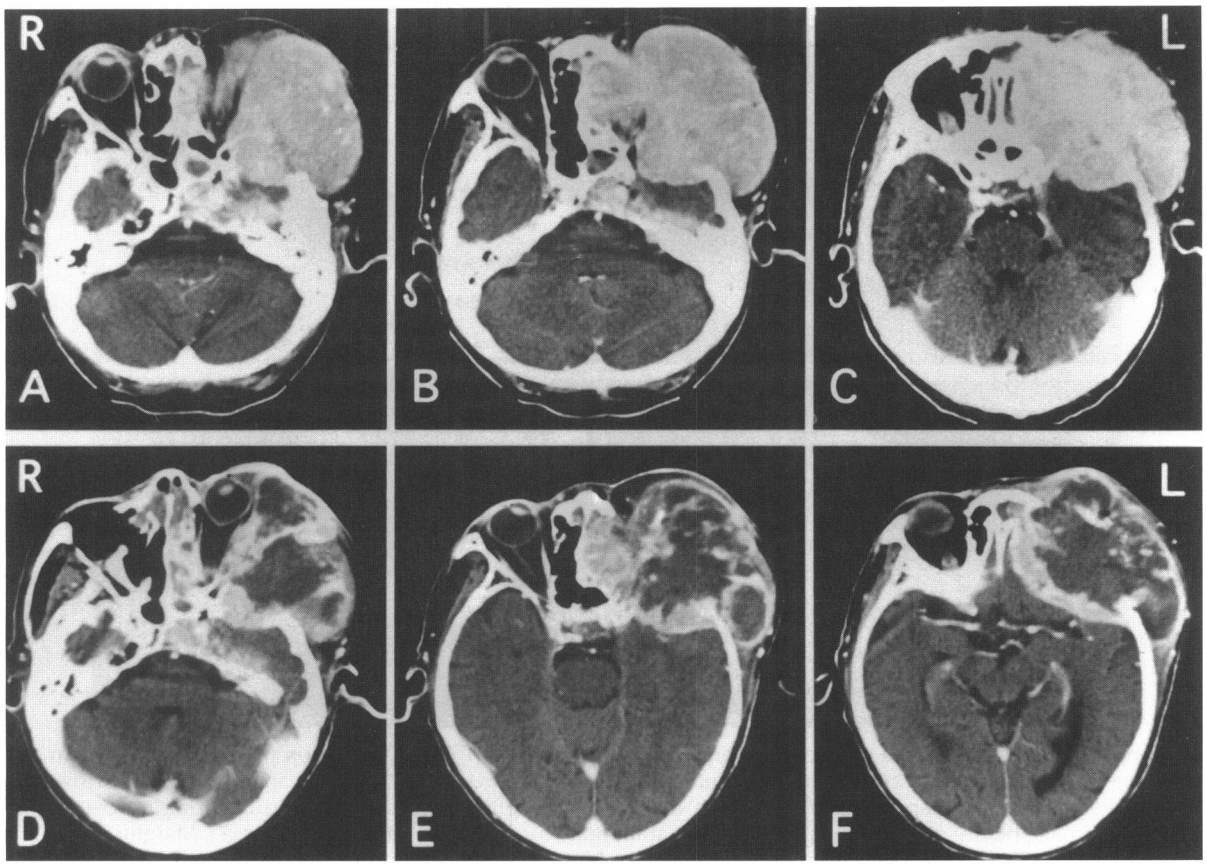

Figure 2. Enhanced axial CT of the tumor. **(A–C)** Enhanced CT showing the tumor before ethanol injection. **(D–F)** Enhanced CT showing nonenhanced broad regions within the tumor 6 days after the second ethanol injection.

stained from the arterial phase until the late venous phase.

Preoperative Treatment

After informed consent was obtained from the patient and his family, direct ethanol injection was performed on June 9, 1998. Under the guidance of an ultrasound (US) scanner (LOGIQ 500MD, GE Yokogawa Medical System, Tokyo, Japan) equipped with a 5.0-MHz convex type probe and CT observation, sterile 99.5% ethyl alcohol (ethanol) was injected into the tumor using a specially designed 21-gauge needle with three side holes and no end hole (PEIT needle, Hakko Shoji Co. Ltd., Tokyo, Japan) (Fig. 3, A and B). The target for ethanol injection was defined as the lesion, excluding the lesion involving the clivus by direct invasion and keeping 10 mm inside from the original tumor margin for safety.

To cover the whole region of the target, 30 ethanol injection sites were selected at regular intervals in three dimensions within the defined target. The volume of ethanol for each injection was 0.5 ml, and a total of 15 ml was injected. Each injection was slowly performed with more than 60 sec, and at the end of injection the needle was left in place for 30 sec to avoid reflux of ethanol along the needle track before it was slowly withdrawn. During the course of the procedure, the vascular flow within the tumor was observed by the real-time power Doppler (PD) imaging. Although the vascular flow within the tumor was abundant before ethanol injection (Fig. 3C), it markedly decreased within the tumor, especially within the target, at the end of the session.

After the session, the patient complained of nausea and dizziness, which had continued for a period of 3 days. However, no other serious complications developed. CT 6 days after the session revealed the nonenhancing wide region within the tumor, especially within the target, and the enhancing region within the tumor, especially outside the target.

In the residual vital lesion enhanced on CT, additional direct ethanol injection was performed on June 16, 1998. The second target for ethanol injection was defined as the lesion enhanced on CT, excluding the lesion involving the clivus by direct invasion and keeping 5 mm inside from the original tumor margin for safety. Twenty ethanol injection sites were selected at regular intervals in three dimensions within the defined second

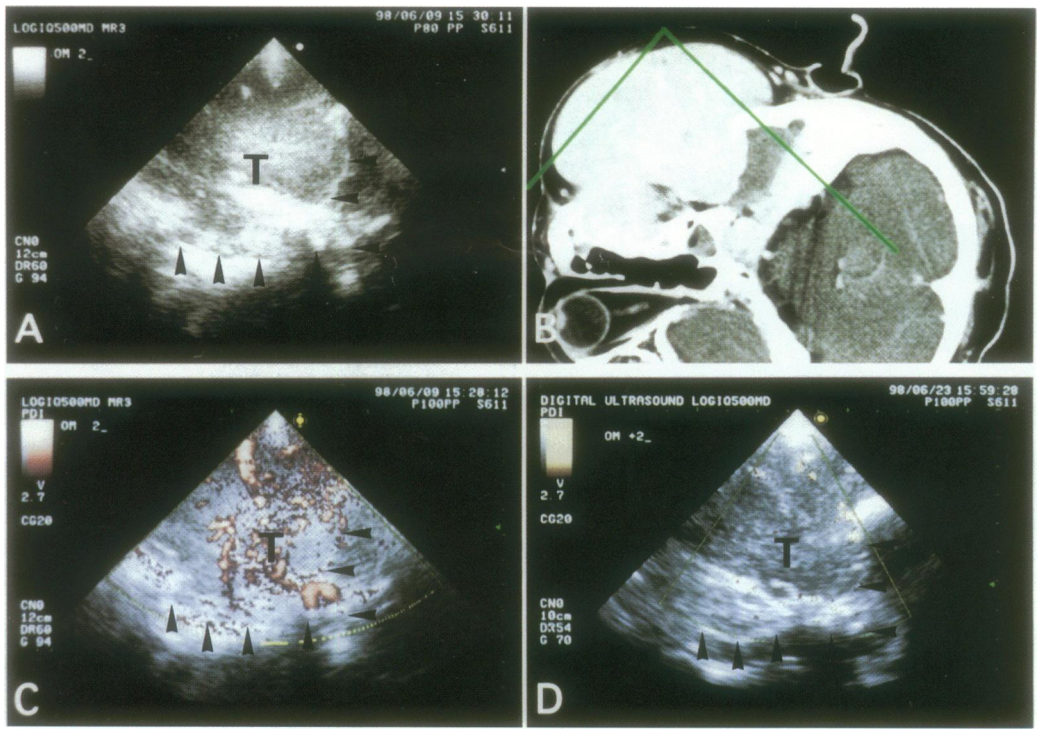

Figure 3. Axial slices of the ultrasound scans **(A, C,** and **D)** and CT **(B)** are made on the plane about 2 cm above the OM line. **(A)** Conventional US image before ethanol injection showing the tumor (T) and its margins (arrowheads). **(B)** Enhanced CT before ethanol injection and the margins of the ultrasound beam (green bars) laid to overlap each other. **(C)** PD image before ethanol injection showing abundant vascular flow within the tumor (T). Margins of the tumor (arrowheads). **(D)** PD image 6 days after the second ethanol injection showing a marked decrease or disappearance of the vascular flow within the tumor (T). Margins of the tumor (arrowheads).

target. The volume of ethanol for each injection was 0.5 ml, and a total of 10 ml was injected. After the session, no complications developed. CT 6 days after the session revealed enlargement of the nonenhancing region within the tumor (Fig. 2, D–F), and PD image revealed a marked decrease or disappearance of the vascular flow within the same region (Fig. 3D).

Operation and Pathologic Examination

Seven days after the second ethanol injection, surgery was performed. The tumor was approached extradurally via a combination of the subfrontal, subtemporal, and preauricular infratemporal approaches. After frontotemporal craniotomy, the tumor in the anterior and middle cranial fossae was dissected from the dural surface and was resected together with the adjoining bone. The tumor in the infratemporal and pterygopalatine fossae was resected by suction irrigation or an ultrasonic aspirator. Bleeding from the tumor treated with ethanol was minimal, but it was severe from the tumor that was not treated. After tumor resection, reconstruction of the skull was performed using a free rib bone graft and Resin plate. Histopathologic diagnosis was a skull metastasis from HCC. The lesion treated with ethanol showed massive necrosis (Fig. 4, A and B).

Postoperative Course

After surgery, hyperalgesia of the left face disappeared and steady improvement of facial nerve palsy and hypoglossal nerve palsy on the left side was recognized with disappearance of the subcutaneous mass. Postoperative MR images demonstrated subtotal removal of the tumor except a part that replaced the clivus and a small amount within the ethmoidal sinus (Fig. 5, A–F). Eleven days after surgery, the patient was discharged and was satisfied with the results.

DISCUSSION

The frequency of skull metastasis from HCC is increasing with longer survival due to recent advances in the treatment for primary lesions.[7,9] Currently, surgical treatment of skull metastasis from HCC is considered to be the best method because other conservative therapies, including radiation and chemotherapy, are contro-

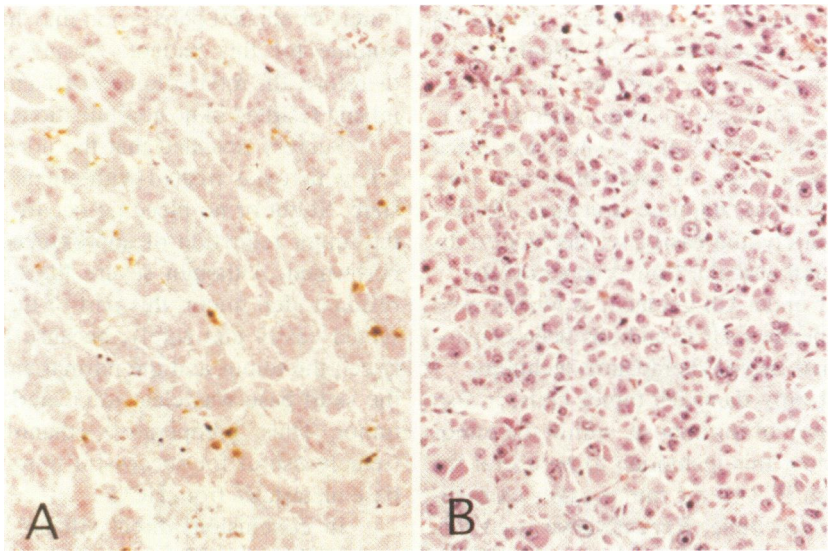

Figure 4. Photomicrography showing the trabecular arrangement of the necrotic cancer cells in the region treated with ethanol **(A)** and the compact arrangement of viable cancer cells from HCC in the region not treated with ethanol **(B)** (hematoxylin and eosin; original magnification, ×200).

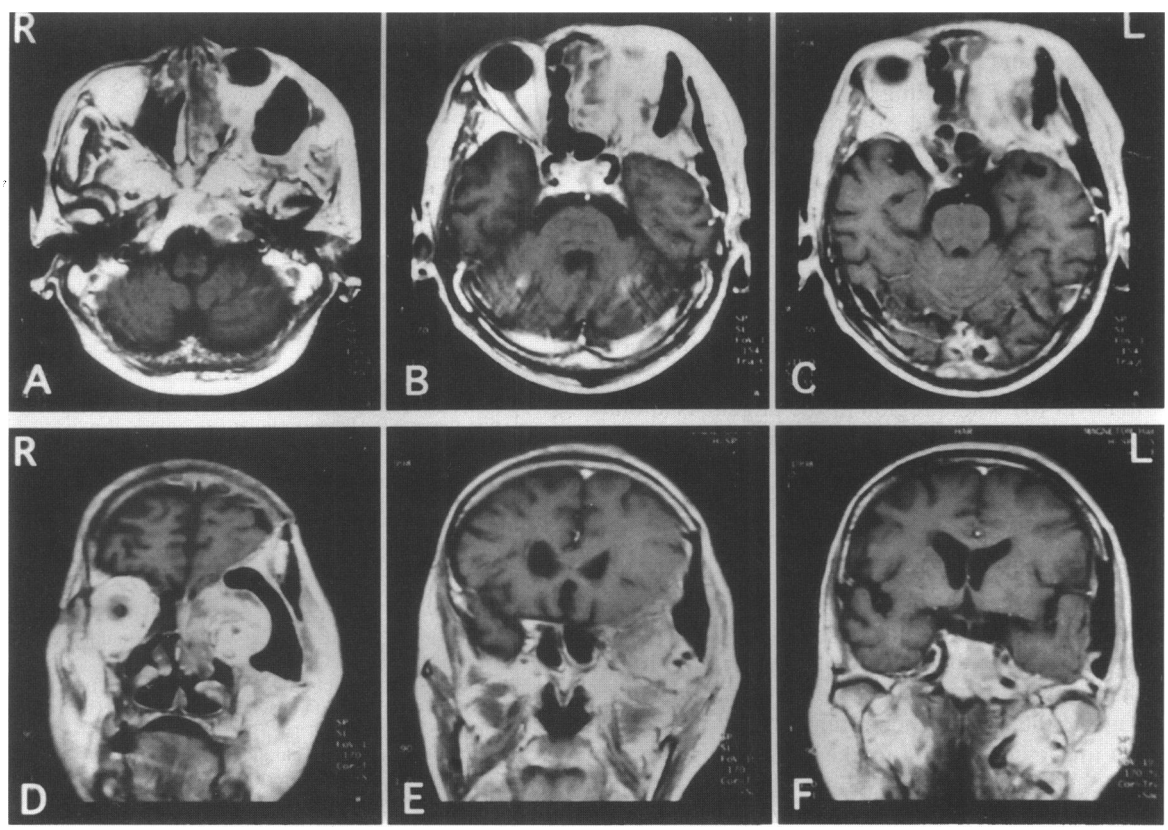

Figure 5. Postoperative MR images of the tumor. Enhanced T1-weighted images axial **(A–C)** and coronal **(D–F)** showing subtotal removal of the tumor except a part that replaced the clivus and a small amount within the ethmoidal sinus, and successful reconstruction performed using a free rib bone graft and Resin plate.

versial.[1–4] However, surgery is sometimes dangerous because the tumors are extremely rich in vascularity.[9,10] In the present case, the tumor was extremely rich in vascularity as shown by radiologic findings, including CT, MR imaging, and angiography, and existed not in the calvaria but in the skull base. In addition, it was very large and destroyed normal anatomic structures. To perform the operation safely and easily, we decided to diminish the intratumoral vascular flow preoperatively.

Currently, PEIT under US guidance is widely used in the treatment of primary HCC and has been considered a safe, easy, and useful therapeutic technique.[6–8] Injected ethanol not only damages tumor cells, it also promotes the formation of thrombosis within the tumor vessel.[11,12] We consider this technique to be useful for skull metastases from HCC if the tumor exists extradurally and has destroyed bone. Recently, we used this technique in a patient with a calvarial metastasis from HCC.[5] In that case, a total of 10 ml of ethanol was injected into the tumor, 4 cm in diameter, without any meaningful complications. The tumor was subsequently resected surgically and histopathologically confirmed to be almost completely necrotic. This finding suggested that this technique is useful for patients with skull metastases from HCC.

In the present study, we performed direct ethanol injection into a tumor to diminish the intratumoral vascular flow preoperatively. Because the tumor was extremely large and located adjacent to important anatomic structures, including the brainstem, cavernous sinus, and orbita, safe and effective ethanol injection was indicated. To avoid injury to the surrounding structures due to leakage and diffusion of ethanol, the injection sites were maintained at more than 5 mm inside the tumor margin and the volume of ethanol for each injection was 0.5 ml. Among the targets of ethanol injection, the lesion involving the clivus by direct invasion was ruled out to avoid injury to the brainstem. The injection sites were dispersed as regularly as possible within the target to cover the whole region of the target. As a total volume of ethanol per session, more than 10 ml was used to diminish the intratumoral vascular flow as much as possible in a few sessions, although less than 10 ml was recommended from PEIT findings.[13]

Enhanced CT and PD images demonstrated the effect of ethanol injection. Based on CT findings after the second session, the nonenhancing tumor volume was calculated by adding the objective regions on multiple parallel slices and multiplying the slice thickness.[14] The percentage of the nonenhancing tumor volume became 80%. PD images revealed a marked decrease or disappearance of the vascular flow within the same region. These results suggested that the operation could be performed without massive bleeding. As a complication of ethanol injection, nausea and dizziness continued for a period of 3 days after the first session, which was considered due to mild alcohol intoxication.[13] Fifteen milliliters of ethanol per session may have been too large a volume for this patient. During the second session, therefore, the total volume of ethanol was reduced to 10 ml and resulted in no complications.

Surgery revealed that the nonenhancing tumor on CT, which was treated with ethanol, was in a necrotic state. Slight or no bleeding occurred in the tumor, and the tumor reduction of approximately 80% was easily performed. Although severe bleeding occurred in the residual vital tumor, this part of the tumor was also resected easily and safely, because the relationship between the tumor and the normal anatomic structures in the skull base was clear after marked reduction of the tumor. Thus, preoperative ethanol injection was extremely useful for successful removal of a giant skull base metastasis from HCC.

In conclusion, direct ethanol injection is a safe, easy, and very useful therapeutic technique to diminish the intratumoral vascular flow preoperatively for giant skull base tumors rich in vascularity, such as a giant skull base metastasis from HCC.

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