Gamma Knife Radiosurgery and Albendazole for Cerebral Alveolar Hydatid Disease

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Standard treatment of cerebral alveolar hydatid disease consists of open brain surgery and systemic albendazole. We describe a patient with inoperable cerebral alveolar hydatid cysts on whom gamma knife radiosurgery was used instead of open brain surgery. Because of the size of the multicystic lesion, the gamma knife procedure was done in two sessions. Repeated courses of albendazole were given concurrently. Magnetic resonance imaging follow-up studies showed marked shrinkage of the irradiated cystic structures and initially increased perifocal edema. At a follow-up visit 3 years after gamma knife radiosurgery, the polycystic lesion, the perifocal edema, and the neurological symptoms had all markedly decreased. The patient is now stable and has minimal neurological symptoms, and the quality of her life has improved. Gamma knife radiosurgery may be an alternative for patients with cerebral alveolar hydatid disease for whom surgery is not possible.

Alveolar hydatid disease (AHD) is caused by the larval stage of Echinococcus multilocularis. AHD has a restricted geographic distribution with foci in the northern and central parts of North America and in Europe, Asia, and Australia. The incidence of alveolar echinococcosis ranges from 0.18 per 100,000 population in Europe [1] and 65–170 per 100,000 among the Eskimos in Alaska [2] to 410 per 100,000 in central China [3]. Human infections are located primarily in the liver (98%), but primary or metastatic lesions occur in the brain (4%–13% in different series), lungs (9%), mediastinum (3%), and other organs [4, 5].

The multivesicular cysts grow by continuous exogenous budding and then invade and infiltrate into the surrounding tissue, similar to malignant tumors. Cure is possible with radical resection of the entire larval mass, but the resectability rate is as low as 18% among patients with AHD. In situations where radical resection is not possible, chemotherapy with benzimidazole derivatives (albendazole and mebendazole) has been reported to cause arrest of extracerebral lesions (in up to 77% of patients) [6]. Resectability of cerebral AHD cysts is low, and surgical treatment of cerebral hydatid cysts is associated with frequent postoperative complications and a high mortality rate [7, 8].

Mebendazole is not effective for cerebral AHD. Albendazole has been used with success for cerebral AHD [9], but in other studies albendazole was not beneficial [10] or not tolerated [11]. Whenever possible, surgical excision of the cerebral hydatid masses, together with perioperative administration of albendazole, is the treatment of choice [3, 6, 12].

We describe a patient with inoperable cerebral alveolar hydatid cysts for whom gamma knife radiosurgery and albendazole administration were of clinical benefit. To our knowledge, this is the first report on gamma knife radiosurgery for cerebral AHD.

Case Report

A 28-year-old woman had cysts in the liver, lungs, and brain. The diagnosis of AHD was established by needle biopsy of the liver and detection of serum antibodies to E. multilocularis. The cerebral cysts extended into the left parietal lobe, and open excision would most likely have caused extensive right-sided hemiplegia. Treatment was begun with mebendazole, followed by mebendazole plus IFN-γ. While the liver and lung lesions were stable, the cerebral lesion progressed (figure 1); this has been reported previously [13]. When right-sided hemiparesis, headache, and seizures worsened, we considered stereotactic radiotherapy (with the gamma knife) as an alternative to open excision. Therapy with albendazole, which had then become

Figure 1. Therapeutic management of alveolar hydatid disease in a patient with liver, lung, and brain cysts after diagnosis and during follow-up. The gamma (γ) knife was applied only to the cerebral lesion (■ = lesion progressed; ■ = lesion stabilized; □ = lesion regressed).
available in Austria, was started at the time of the first gamma knife surgery (repeated courses of 400 mg b.i.d. for 28 days, followed by a 2-week drug-free interval) and continued for a total of 2 years (figure 1).

Preoperative MRI of the brain showed a polycystic parietal lesion with perifocal edema, compression of the left lateral ventricle, and a midline shift (figure 2A). Because of the overall size of the lesion, two sessions of stereotactic radiosurgery with Leksell’s gamma knife were planned. At the first session the ventrocranial part of the lesion (a volume of 20 mL) was irradiated with 26.7 Gy to the center of the lesion and 12 Gy to the margins at the 45% isodose line.

One day after the procedure, the patient’s hemiparesis and headache worsened, and CT scans showed increased perifocal edema. The symptoms diminished with administration of intravenous dexamethasone and mannitol over 2 weeks. Three months after the first gamma knife session, MRI showed a marked decrease in the size of the irradiated part of the polycystic structure, with decreased edema and resolution of the midline shift (figure 2B). The remaining, dorsal part of the lesion was then irradiated with a maximum dose of 26.7 Gy to the center and 12 Gy to the margins at the 45% isodose line.

Three months later MRI showed a renewed increase in the perifocal edema involving the basal ganglia and the medial parts of the temporal lobe (figure 2C). The recently irradiated part of the lesion had shrunk. Administration of dexamethasone was resumed, and the neurological symptoms diminished. Over the next 6 months the patient developed recurrent fever due to bacterial superinfection of the liver and Cushing’s syndrome, but both resolved with use of intravenous antibiotics and reduction of the dexamethasone dosage.

During follow-up, MRI was repeated every 3–6 months. Three years after the first gamma knife session, MRI scans showed a marked decrease in the size of the polycystic lesion, with only slight residual perifocal edema (figure 2D). Abdominal and thoracic CT scans did not show further progression of the lesions in the liver and the lungs. The patient is now stable and has minimal neurological symptoms, and her quality of life has improved markedly.

Discussion

During treatment with mebendazole and IFN-γ, the lesions in the liver and lungs of our patient were stable, while the cerebral hydatid cysts progressed after 15 months. Treatment was changed to administration of albendazole, which is more readily absorbed than mebendazole and which better penetrates the CSF and cerebral cysts [14, 15]. However, albendazole has more side effects than mebendazole [6, 15], and intolerable and irreversible side effects of albendazole have been reported [11]. Albendazole is parasitostatic rather than parasiticidal [16]. Because the efficacy of albendazole alone for cerebral alveolar hydatid cysts was unclear and because our patient was not a candidate for open excision, we considered stereotactic irradiation with the gamma knife.

This procedure has been reported as an alternative to open neurosurgery in arteriovenous malformation, cerebral metastasis, acoustic neuroma, meningioma, malignant glioma, and trigeminal neuralgia. During the gamma knife procedure, a single high dose of ionizing radiation is delivered stereotactically with exquisite precision to a radiographically defined intracranial target and destroys the target tissue [17]. The intent for our patient was to eliminate the alveolar hydatid tissue, which histologically resembles a brain tumor.

Focal irradiation induced perifocal edema and reaction-tissue volumes that were larger than expected, but both resolved with long-term corticosteroid therapy. During the 3 years of follow-up, the cerebral lesion decreased markedly in size, and the neurological symptoms resolved. The steadily increasing marginal contrast enhancement during the follow-up MRI studies indicated the formation of an inflammatory host-tissue barrier encapsulating the shrunk cystic lesion following radiosurgery. The lesions in the liver and lungs neither increased nor decreased in size and number during the 3-year observation period, probably owing to albendazole treatment.

The part of the cerebral lesion that was irradiated first shrunk more rapidly than the other part, and the size of the extracerebral lesions did not decrease with albendazole treatment alone. This indicates that gamma knife radiosurgery was primarily responsible for shrinking the cerebral cysts. Open excision combined with perioperative administration of albendazole is still the treatment of choice for cerebral AHD, and in our case both the gamma knife and albendazole must be given credit for the successful outcome. Gamma knife radiosurgery should be considered as an alternative for patients with inoperable cerebral AHD; however, clinical trials must still be carried out in a series of patients.

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Figure 2. T2-weighted magnetic resonance images of the brain of a patient with alveolar hydatid disease. A: Preoperatively there is a polycystic lesion with perifocal edema, compression of the left lateral ventricle, and a slight midline shift. B: Three months after the first and immediately before the second gamma knife session, the irradiated part of the polycystic lesion has shrunk, the edema has decreased, and the midline shift has disappeared. C: Three months after the second gamma knife session, the perifocal edema has increased and now involves the basal ganglia and medial parts of the temporal lobe. The midline shift has reappeared and slightly impresses the brain stem. The recently irradiated part of the lesion has shrunk. D: Three years after the first gamma knife procedure, the polycystic lesion has shrunk markedly, and there is only slight residual perifocal edema.
References