Tumor seeding following stereotactic biopsy of brain metastases

Report of two cases

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In a series of 22 patients treated with gamma knife surgery for brain metastasis in whom biopsy specimens were obtained via stereotactically guided procedures before the radiosurgical treatment was administered, two cases with evidence of tumor seeding were observed on subsequent follow-up examination. These findings contradict the opinion that the risk for tumor spread after a biopsy is negligible. This evidence may be explained by the fact that radiosurgery leaves the surrounding tissue unaffected by the treatment, which results in preserved anatomy around the tumor. This allows the surgeon to define the previous biopsy channel and, consequently, whether a distant tumor recurrence may have resulted from tumor seeding related to the biopsy procedure. Additionally, radiosurgical treatment leaves tumor cells that may have been spread as a result of the biopsy unaffected, giving them the potential to divide and develop into a new tumor. In contrast to this, microsurgical removal of the tumor will affect the surrounding tissue, making it impossible to detect whether new metastases are resulting from seeding. Furthermore, conventional fractionated radiation therapy will sterilize tumor cells that may have spread, thus making it impossible for these cells to regrow.

The authors conclude that the risk for tumor seeding following a stereotactically guided biopsy may be higher than previously assumed.

KEY WORDS • brain metastasis • stereotactic biopsy • tumor seeding • radiosurgery
tween tumor cell implantation and visible tumor on computerized tomography (CT) and/or magnetic resonance (MR) studies, all 76 patients who lived less than 60 days after the gamma knife surgery were excluded from the study, leaving 415 patients in the group.

In 52 of the cases, a histological analysis was available from an earlier brain metastasis and in 49 a specimen of the treated metastasis was preserved after microsurgery, making biopsies unnecessary. We were aware of a primary tumor disease in 256 patients, making a biopsy redundant in these cases. Biopsy specimens were not obtained because of patient refusal or for medical reasons in 15 patients. One patient received fractionated radiation therapy after the biopsy. Of the remaining 42 patients, biopsy was performed before gamma knife treatment in 22 cases. The time between biopsy and gamma knife treatment was 0 to 30 days, with a median of 6 days. In 20 cases, the biopsy was obtained after gamma knife surgery, and in these cases both operations were performed on the same day.

In two cases, evidence of tumor seeding caused by the biopsy procedure could be visualized on MR images. The time between biopsy and proven tumor seeding in Cases 1 and 2 was 26 and 18 weeks, respectively. In both patients, the biopsy had been performed before gamma knife treatment, resulting in a 9% incidence of tumor seeding in this group of 22 patients.

Case Reports

Case 1

This 47-year-old woman had a 3-week history of headache, vertigo, and double vision and no history of malignant tumor. A diagnostic MR image disclosed a contrast-enhanced left-sided infratentorial lesion. A CT-guided stereotactic biopsy was performed, and the diagnosis was adenocarcinoma. The patient was treated with gamma knife surgery 5 days after the biopsy, based on a stereotactic MR examination (Fig. 1 left). The tumor was well delineated and there were also signal changes and a slight contrast enhancement along the trajectory of the biopsy needle. A follow-up CT scan was obtained 6 weeks post-treatment and showed a decrease in the size of the tumor and no enhancement in the biopsy channel. A routine follow-up evaluation 6 months after the treatment revealed a further decrease in the size of the previously treated tumor; additionally, a new tumor was found. This tumor was also treated with gamma knife surgery. The stereotactic MR images obtained before the treatment clearly showed that the new tumor was located in the biopsy channel (Fig. 1 right). The patient died 2 years later as a result of generalized tumor spread in the brain, without the primary tumor having been diagnosed.

Case 2

This 69-year-old previously healthy man had a 1-week history of right-sided weakness. A CT scan revealed an expanding lesion in the right motor area, and a biopsy was performed to ascertain the pathology of the lesion. The specimen showed evidence of a metastatic lesion from a renal cell carcinoma, and the lesion was treated with gamma knife surgery the same day. The primary tumor was surgically removed. A routine follow-up examination 14 weeks after gamma knife treatment revealed a new tumor adjacent to the treated lesion, but showed no evidence of contrast enhancement in the biopsy channel (Fig. 2 upper left and right). The patient subsequently developed neurological symptoms indicating increased brain tumor activity. He was retreated with gamma knife surgery, and the stereotactic MR images clearly showed contrast enhancement in the whole biopsy channel, indicating tumor seeding there. It could also be seen that the new tumor was located where the tip of the biopsy needle had penetrated the tumor (Fig. 2 lower left and right). All of this new contrast-enhanced tissue was included in the second gamma knife treatment field. A follow-up scan 1 month later revealed a decrease in the tumor size, and the patient’s neurological condition had improved. Also, there was no remaining contrast enhancement along the biopsy trajectory. However, the patient died 3 months after the second treatment because of generalized primary disease in spite of the fact that the brain tumor was still controlled.
In the literature, reports of tumor seeding following biopsy procedures are sparse. In one paper, seeding following multiple needle aspirations of a craniopharyngioma was reported. Also, seeding following stereotactically guided biopsy of a pineoblastoma has been reported. To the best of our knowledge, tumor spread following biopsy of a cerebral metastasis has not been reported. The cases reported in this paper indicate, however, that the risk of seeding following a stereotactic biopsy may be higher than previously assumed.

This apparently contradictory finding may be explained by the following: a common rationale for performing a biopsy when a metastasis is suspected is to obtain histological verification before treatment. If the planned treatment is conventional radiation, the tumor cells that may have been spread by the procedure will be sterilized by the treatment. If surgery is performed, the anatomy will be altered and it will be impossible to judge whether a local or distant recurrence is the result of a seeding from the previous biopsy. After radiosurgery the situation is different. With a reported probability of local tumor control of approximately 90%, and with no effect on tumor cells seeded in the biopsy channel, the cells that may have been spread also have a possibility of survival, ultimately resulting in a new metastasis. Thus, the incidence of seeding in a radiosurgical series will most likely give a more accurate estimation of the risk of tumor spread than experience based on surgical series or on patients who have undergone fractionated radiation therapy.

Clinical Consequences of a Higher Risk for Seeding

It can be assumed that the risk for seeding is higher after surgery than after biopsy. Thus it is logical to assume that patients will benefit from fractionated radiation therapy added after microsurgical tumor removal. There are no
prospective randomized studies published in which surgery followed by fractionated radiation therapy is compared with surgery alone, but retrospective studies exist in which the benefit of fractionated radiation therapy is strongly suggested.9,15,22,23 If the mechanism of fractionated radiation therapy is mainly to sterilize the tumor cells spread by the surgical procedure, the positive experience reported in the aforementioned studies cannot be used to justify this therapy after gamma knife surgery. Of course, fractionated radiation therapy may have other points of attack, and there are published reports suggesting that patients treated with the gamma knife also benefit from added fractionated radiation therapy.12

The findings described in this paper are also a rationale for performing gamma knife surgery before biopsy. This strategy also excludes the possibility that the mass shift, which may occur because of swelling or hemorrhage after a biopsy, will affect the dose given to the tumor. If a mass shift occurs, the tumor localization will also change. If this is not taken into consideration before the gamma knife treatment, part of the radiation will be directed at the surrounding brain tissue instead of the tumor.

The disadvantage of treating lesions before they are histologically verified is obvious. A lesion that is considered a metastasis and treated accordingly may later prove to be something else. This has happened at our institution: of the 27 cases treated with the gamma knife before biopsy on the assumption that the lesion was a metastasis, histological examination verified the assumption in 20 cases. Histological studies were inconclusive in four cases, revealed a glioblastoma in two cases, and a lymphoma in one. Of the inconclusive cases, two proved to be glioblastomas as diagnosed later via a surgical procedure and two were malignant tumors; whether primary or secondary could not be defined. Of the latter patients, one died shortly after gamma knife treatment and the other is still alive more than 6 years later with no evidence of ongoing disease. In all cases in which the histological examination revealed a primary malignant brain tumor, fractionated radiation therapy was added to the gamma knife treatment given earlier.

References

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