Foreign body reaction to hemostatic materials mimicking recurrent brain tumor

Report of three cases

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Chemical agents routinely used in neurosurgery to achieve intraoperative hemostasis can cause a foreign body reaction, which appears on magnetic resonance (MR) images to be indistinguishable from recurrent tumor. Clinical and/or imaging evidence of progression of disease early after surgical resection or during aggressive treatment may actually be distinct features of granuloma in these circumstances.

A series of three cases was retrospectively analyzed for clinical, imaging, surgical, and pathological findings, and the consequences they held for further disease management.

All patients were boys (3, 3, and 6 years of age, respectively) and all harbored primitive neuroectodermal tumors. Two tumors were located in the posterior fossa and one was located in the right parietal lobe. Two boys exhibited clinical symptoms, which were unexpected under the circumstances and prompted new imaging studies. One patient was asymptomatic and imaging was performed at planned routine time intervals. The MR images revealed circumscribed, streaky enhancement in the resection cavity that was suggestive of recurrent disease. This occurred 2 to 7 months after the first surgery. At repeated surgery, the resected material had the macroscopic appearance of gelatin sponge in one case and firm scar tissue in the other cases. Histological analysis revealed foreign body granulomas in the resected material, with Gelfoam or Surgicel as the underlying cause. No recurrent tumor was found and the second surgery resulted in imaging-confirmed complete resection in all three patients. Because recurrent disease was absent, the patients continued to participate in their original treatment protocols. All patients remain free from disease 34, 32, and 19 months after the first operation, respectively.

During or after treatment for a central nervous system neoplasm, if unexpected clinical or imaging evidence of recurrence is found, a second-look operation may be necessary to determine the true nature of the findings. If the resection yields recurrent tumor, additional appropriate oncological treatment is warranted, but if a foreign body reaction is found, potentially harmful therapy can be withheld or postponed.

KEY WORDS • foreign body reaction • granuloma • tumor recurrence • primitive neuroectodermal tumor • astrocytoma
cotton as the source of these reactions. This has been reported experimentally,30 as well as after cranial 6,9,11,18,28,31, 32,35 and spinal10 operations. Fibrin sealant (Tissucol or Tisseel; Baxter AG, Vienna, Austria), in use since the mid-1980s,4,23 to our knowledge has not been reported in the neurosurgical literature as the source of a granulomatous reaction.

Case Reports

Case 1

This 6-year-old boy underwent surgery for a hemispheric cerebellar PNET at another hospital. He was then treated according to a CCG protocol for standard-risk medulloblastoma (CCG No. A9961). During radiation therapy, the patient displayed signs of raised intracranial pressure and a new MR image revealed a ring-enhancing structure that was believed to be recurrent tumor (Fig. 1). Because of this finding, the patient underwent a second operation approximately 2 months after the first surgery. At the second surgery we observed a glasslike mass with the macroscopic appearance of Gelfoam. The mass was removed from the resection cavity and microscopic analysis confirmed the intraoperative impression that it was Gelfoam. The patient did well after the second operation, although he required placement of a ventriculoperitoneal shunt. He eventually completed his treatment protocol and continues to be free from disease 34 months after the first operation.

Case 2

This 3-year-old boy underwent surgery during which an inferior vermis medulloblastoma was completely resected. He was treated with chemotherapy according to a CCG protocol (CCG No. 99703). During the course of his treatment a surveillance MR image revealed an enhancing mass in the resection cavity, close to the lower brainstem, which was suggestive of recurrent tumor (Fig. 2 left). Repeated surgery was performed 4 months after the initial operation. We found a firm mass that was tightly adherent to the right side of the lower brainstem and completely resected it (Fig. 2 right). Histological examination revealed no evidence of a neoplasm, but instead a foreign body granuloma with necrosis and multinucleated giant cells (Fig. 3). The patient recovered well and treatment was resumed according to the CCG protocol. Because we do not routinely leave Gelfoam in the resection cavity, but often cover its walls with a layer of Surgicel, we considered that hemostatic material to be responsible for the granulomatous reaction. The boy continues to do well, without disease progression, 32 months after the first operation.

Case 3

This 3-year-old boy presented with a short history of headache. Because the child had previously undergone local embolization of a skin and soft-tissue arteriovenous malformation of the left auricle and adjacent areas, MR imaging was recommended. A right posterior parietal tumor with enhancement was seen on the MR image and the tumor was completely resected. The histological diagnosis was PNET. The patient was started on a chemotherapeutic protocol (Head Start II). Follow-up MR images displayed some streaklike enhancement in the resection cavity and, particularly, along the dura. At the end of the chemotherapy cycles, the question of whether to prescribe craniospinal or local radiation therapy hinged on the presence or absence of residual tumor. Thus a second surgery was performed 7 months after the first. The resected tissue displayed a granulomatous foreign body reaction. Surgicel, which had been used to cover the walls of the resection cavity, was thought to be responsible for this reaction. The patient continues to do well and is free from disease 19 months after the first surgery.

Discussion

Following surgery for malignant brain tumors, most patients are enrolled in a chemotherapeutic protocol.20,21,33,36 Magnetic resonance imaging is routinely performed at regular intervals to follow residual disease or to detect recurrence. On examination of event-free survival curves of patient groups treated for medulloblastoma, it becomes clear that it is extremely rare to find a recurrence only a few months after complete surgical resection or during chemo- or radiation therapy.21 When a patient exhibits progressive neurological symptoms during therapy, and
when a new enhancing lesion is found in the operative site on MR images, however, tumor recurrence must be suspected. This may warrant additional surgery and longer or more aggressive chemo- as well as radiation therapy. It is, therefore, very important to ensure the absence of disease in these cases. In addition, recurrence of a PNET after complete resection carries a poor prognosis. Thus it is essential to ascertain the diagnosis of a recurring mass that has the imaging appearance of tumor, so that prognostic expectations can be correctly related to patients and their families in a realistic way.

The three patients reported here had harbored PNETs and were enrolled in experimental treatment protocols. In all three cases, the seemingly recurring lesions had been completely resected and no evidence of recurrent tumor was found. No changes were made to the treatment protocols in these cases.

Granulomatous reactions to foreign bodies, such as suture material, cotton pads, cadaveric or synthetic dural grafts, and shunt catheters have been described in numerous publications. In an experimental study assessing osseous regeneration in the presence of one of four hemostatic agents, bone wax was shown to result in a granulomatous reaction, whereas gelatin sponge, oxidized cellulose, and microfibrillar collagen did not have a comparable effect.

On the basis of operative reports, pathological findings, and our own neurosurgical practice it was determined that gelatin sponge was the causative agent in Case 1 and oxidized regenerated cellulose was the agent in Cases 2 and 3.

It is not our practice to leave Gelfoam pieces in a resection field because of the enormous ability of Gelfoam to absorb fluid and swell. Nevertheless, many neurosurgeons apparently do leave Gelfoam as a hemostatic cover in a resection field and, certainly, most of the time there are no subsequent problems. Gelfoam was the active agent in Case 1; this is consistent with earlier reports on granulomas caused by that material.

In Cases 2 and 3, oxidized regenerated cellulose is the most likely cause of the foreign body reactions. Similar cases, in which granulomas were believed to be tumors on the basis of their appearances on imaging studies, have been reported as well. Microfibrillar collagen has also been reported to cause foreign body granulomas that have an appearance similar to recurrent tumor. Although this material may have been used in some of the cases presented here, we commonly irrigate and suction this substance away after several minutes of application. Thus, there is no direct evidence linking it to the observed granuloma. Fibrin glue was not used in any of these cases.

Several questions remain unanswered by this report. We do not have evidence to explain why Gelfoam and Surgicel caused the observed reactions. In the absence of other plausible explanations, we believe them to be the causative factors. Whether there are any unknown promoting factors that may trigger such reactions in a few individuals, but not in most others, is open to further observation and study.

Whether it is a coincidence that the patients in whom such a reaction was found had harbored PNETs cannot be known. It is a possibility that, for some unknown reason, after resection of PNETs such reactions are more likely to occur than after resection of other tumors. We favor the explanation that, in patients with PNETs, the distinction between real tumor and unspecific postoperative changes in the wall of a resection cavity is so essential for the long-term treatment plan that a repeated surgery was considered necessary. This would not be the case generally after resection of benign tumors with small residual fragments or uncertain MR imaging findings.
All three patients are male, but we believe there is no evidence to indicate that this is more than a coincidence. Anecdotal evidence that commonly used materials for chemical hemostasis may cause a granulomatous reaction that may mimic recurrent or progressive neoplasm on imaging studies should not discourage the use of these materials. Gelfoam, Surgicel, and Avitene, if properly used, are excellent and essential tools for safe control of minor bleeding in neurosurgery. Such an adverse reaction should be remembered, however, and taken into account when unusual tumor progression is seen, or when a malignant tumor seems to recur during aggressive treatment. Second-look surgery may be advised to ascertain the diagnosis. This lifts the burden of uncertainty from the patient and the treating physician and allows for a more conservative treatment plan.

References


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