Microfibrillar collagen hemostat–induced necrotizing granulomatous inflammation developing after craniotomy: a pediatric case series

Report of 3 cases

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Object. Microfibrillar collagen hemostat (MCH; trade name Avitene) is a partially water-insoluble acid salt of purified bovine corium collagen. This agent has been widely used to control hemorrhage at surgery, and especially during pediatric neurosurgeries at the authors' institution. Despite its effectiveness, rare case reports detailing adverse inflammatory reactions to MCH have been documented. Based primarily on MR imaging, postoperative reactions have most commonly elicited clinical differential diagnoses of tumor recurrence or abscess. According to the literature, MCH induces a very characteristic mixed inflammatory response that is rich in eosinophils; in light of these observations, many authors have suggested an allergy-based pathogenesis.

Methods. The authors retrospectively reviewed 3 pediatric neurosurgical cases treated at their institution, wherein a common histomorphological inflammatory reaction to MCH was elicited at the site of prior craniotomy.

Results. Case 1 is that of a 10-year-old girl whose diagnosis was a right temporal lobe ganglioglioma, classified as WHO Grade I. Case 2 is that of a 9-year-old boy whose diagnosis was a left parietal lobe anaplastic ependymoma, classified as WHO Grade III. Finally, Case 3 is that of a 15-year-old girl whose diagnosis was focal cortical dysplasia Type IIA affecting the left occipital lobe. Each patient presented with new or recurrent seizures 5–6 weeks after the initial resection. The postsurgical reactions incited by MCH mimicked the radiological appearance of either an abscess (Cases 2 and 3) or recurrent tumor (Case 1). Histologically, the mixed inflammatory infiltrate was typified by the presence of MCH-centric necrotizing granulomas that were surrounded by a palisade of macrophages and often several eosinophils.

Conclusions. The findings are in keeping with previous case reports describing the clinicopathological features of adverse reactions occurring due to MCH. Based on the authors' observations, the possibility of an idiopathic inflammatory reaction to MCH should be considered when either seizures, a typical radiological appearance (that is, consistent with tumor recurrence or abscess formation), or both arise shortly after initial surgery. A conservative treatment approach to this type of inflammatory lesion appears to be the most appropriate management strategy. (*DOI:* 10.3171/2010.8.PEDS10248)

KEY WORDS • microfibrillar collagen hemostat • Avitene • necrotizing granuloma • inflammation • textiloma • craniotomy

Mathematical Control Britlan Collagen hemostat (trade name Avitene) is a partially water-insoluble acid salt of purified bovine corium collagen. It is processed into microcrystals and used at the time of surgery to control hemorrhage without the need for sutures. The MCH is applied directly on the bleeding surface and induces platelet aggregation, the thrombotic cascade, and ultimately the formation of a stable hemostatic plug.^{7,13}

It was approved by the FDA in the US in 1977, and since then it has been widely adopted by several surgical subspecialties as an effective bioabsorbable hemostatic agent.^{1,3,8–10,15,16,21,22} The neurosurgical use of MCH is especially beneficial given the danger of postoperative hemorrhage in the closed and confined intracranial space.^{6,17}

This article contains some figures that are displayed in color online but in black and white in the print edition.

Abbreviations used in this paper: FCD = focal cortical dysplasia; MCH = microfibrillar collagen hemostat.

Although the manufacturer (MedChem Products, Inc.) describes several potential adverse effects that may be associated with the use of MCH (including wound dehiscence, abscess formation, adhesion formation, allergic reactions, and foreign-body responses), these reactions are considered rare, and therefore, MCH is generally considered safe.^{1,2,14} However, some of the initial experimental animal literature did describe rare instances of significant postoperative inflammation after the use of MCH.14 Not surprisingly, multiple clinical case reports have since documented adverse postoperative inflammatory reactions to MCH throughout the body.^{1,3,5,10,15,16,18,19,21-23} Various terminologies have been used in the literature to describe these lesions, including textiloma, gossypiboma, and muslinoma.²² These reactions have clinically mimicked abscesses, tumor recurrence, or radiation necrosis.^{1,16,19,21-23} Intracranial reactions are uncommon, and only 1 pediatric case has been described to date.5,18,19,22,23

In addition to reviewing the neurosurgical literature, we report a series that includes 3 pediatric cases in which a histological picture of necrotizing granulomatous inflammation emerged 5 to 6 weeks after the use of MCH. These reactions mimicked tumor recurrence in 1 patient and abscess formation in our other 2 cases.

Methods

Patients at Children's and Women's Health Center of British Columbia with possible clinical or radiological reactions to MCH were identified retrospectively with assistance from the Division of Pediatric Neurosurgery. The clinical charts and pathological materials were reviewed in each case with the approval of our local research ethics board (#H10–01293). Given the age of the histological materials, occasionally slides were recut and stained to facilitate microscopic assessment.

Case Reports

Case 1

This girl originally presented at the age of 7 months with complex partial seizures. A head CT scan obtained at that time revealed a partially calcified and cystic right temporal lobe mass that measured 2.5 cm. When the patient was 10 years old, the seizures became increasingly refractory to medication. Follow-up MR imaging studies revealed enlargement of the cystic component of the lesion and encroachment on the adjacent cerebral peduncle. Despite the history and imaging findings, no neurological or other abnormalities were noted on physical examination.

A selective anterolateral temporal lobectomy was performed at this time. Hemostasis during surgery was achieved using bipolar cautery and application of MCH; after irrigation of the tumor bed, only adherent MCH remained. The temporal lesion was gross totally excised, but a nonresectable subarachnoid component remained in the interpeduncular and ambient cisterns. Microscopy revealed a ganglioglioma (WHO Grade I) (Fig. 1A). Adjuvant therapy was not immediately pursued.

The patient's seizures ceased in the immediate postoperative period. However, approximately 6 weeks after surgery, the patient's typical seizure auras returned, and 2 generalized seizures occurred. Follow-up head CT scanning revealed a suggestion of subarachnoid tumor expansion, as well as a recurrent lesion in the previous resection cavity that was typified by medial enhancement and mass effect (Fig. 1B).

In light of the clinical differential diagnosis, which included a resolving hematoma, tumor progression, or postoperative scar, surgical reexploration was undertaken for the purpose of biopsy sampling. At surgery, a very swollen and firm cavity containing pockets of fluid was encountered. Biopsy samples of the walls of the cavity were obtained and sent for pathological review. Microscopy revealed necrotizing granulomatous inflammation. Acellular, fibrillary, eosinophilic foreign material was closely surrounded by a palisade of epithelioid macrophages. The latter was in turn embedded in dense connective tissue containing a mixed infiltrate of neutrophils, plasma cells, lymphocytes, and multinucleated giant cells (Fig. 1C). Although also present, eosinophils were only scattered.

Twenty-one months later, the patient presented with back and leg pain and right-sided foot drop. Papilledema was noted on examination. The MR imaging revealed obstructive hydrocephalus that was thought to be due to persistent intracranial subarachnoid disease. In addition, diffuse and extensive extraaxial metastatic disease (that was not compressing the spinal cord) was suggested throughout the spinal axis. A ventriculoperitoneal shunt was placed, and the patient received craniospinal irradiation (3600 cGy in 20 fractions over 4 weeks) and chemotherapy. The latter consisted of vincristine and actinomycin D, but this chemotherapy was subsequently halted after 1 cycle due to anorexia and weight loss. A small biopsy of the abnormal tissue noted in the right temporal lobe revealed tumor that was considered to be similar to that obtained in the first surgery (it was reported as "low grade astrocytoma" given the lack of neoplastic neurons in the limited tissue submitted).

Despite the ominous clinical picture 21 months after her initial surgery, the patient, remarkably, improved. At the last follow-up, the patient was 29 years old and was alive and well. She was off medication and free of seizures. Although MR imaging revealed generalized enhancement of the leptomeninges, there was no definitive evidence of residual tumor. The cause of this latter generalized leptomeningeal enhancement was not definitively determined.

Case 2

This 9-year-old boy originally presented to the emergency department with a 2-week history of progressive headache that was associated with vomiting in the morning. Subsequently he developed right-sided weakness manifesting in clumsy hand function. His history also included short periods of headache and neck pain in the months preceding presentation. A CT scan showed a large contrastenhancing left parietal mass that was cystic and calcified.

A gross-total resection was obtained at surgery. Hemostasis was achieved using cotton balls soaked in hydrogen peroxide, followed by the application of MCH. The tumor bed was subsequently irrigated, and only ad-



Fig. 1. Case 1. A: Photomicrograph of a section of the initial right temporal lobe mass reveals a ganglioglioma, WHO Grade I. Note the large abnormal ganglion cells with vesicular nuclei. H & E, original magnification × 200. B: Axial head CT scan obtained at clinical repeat presentation 6 weeks after the initial craniotomy. A contrast-enhancing mass, suspected of being recurrent tumor, is noted in the medial aspects of the prior resection bed. C: Photomicrograph of an H & E–stained section of the mass depicted in B. A palisade of macrophages surrounds the eosinophilic MCH, some of which (upper part of the panel) is necrotic. Multinucleated foreign-body type giant cells are easily identified in the mixed inflammatory infiltrate. Original magnification × 100.

herent MCH was left in situ. The original histological diagnosis was of a supratentorial primitive neuroectodermal tumor, but recent review suggested an alternative diagnosis of an anaplastic ependymoma (WHO Grade III) (Fig. 2 left). Adjuvant treatment included craniospinal radiation and chemotherapy with the CCD-9892 protocol, consisting of vincristine, cisplatinum, and 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (lomustine).

Five weeks after surgery, the patient presented with right-sided focal motor seizures leading to progressive weakness. Head CT scanning revealed a ring-enhancing lesion and surrounding edema at the site of the previous surgery. The clinical differential diagnosis included cerebral abscess (although there was no fever), recurrent tumor, postoperative change, or a reaction to radiotherapy. Antibiotics were commenced and a second craniotomy was performed to better delineate the disease process. At surgery, a cystic cavity filled with xanthochromic fluid was encountered. There was no obvious tumor tissue or pus. The cavity did not look inflamed, but it was firm to the touch. The dura mater was thick and calcified. Biopsy samples of the walls of the lesion were obtained and sent for pathological review. Hemostasis was once again achieved via intracavitary application of MCH, the excess of which was removed by irrigation.

Microscopic examination revealed necrotizing granulomatous inflammation (Fig. 2 right). Partially necrotic basophilic to amphophilic fibrillary material was closely surrounded by a palisade of macrophages. These latter regions were embedded within an eosinophil-rich mixed inflammatory infiltrate that included neutrophils, plasma cells, and multinucleated giant cells. Dense connective tissue deposition was noted, but there was no evidence of microorganisms or tumor.

At last follow-up, 3 years after treatment, the patient was neurologically well and free of disease on neuroimaging.

Case 3

This 15-year-old girl presented with an 8-year history



Fig. 2. Case 2. Left: Photomicrograph of a section of the initial left parietal lobe mass reveals an anaplastic ependymoma, WHO Grade III. Perivascular pseudorosettes are numerous and often contain microvascular proliferation. H & E, original magnification × 100. **Right:** Histological section of the ring-enhancing lesion identified 5 weeks after the original craniotomy. Note the palisade of macrophages that surround the eosinophilic MCH. The background inflammation contains numerous eosinophils and some multinucleated foreign-body type giant cells. H & E, original magnification × 200.

of refractory partial seizures and intellectual impairment. Her seizures were initially characterized by blurring of vision, loss of vision or visual hallucinations followed by nausea, vomiting, eye deviation to the left, occasional cyanosis, eyelid blinking, manual automatisms, and confusion. Her seizures were often associated with generalized body stiffening and jerking, including secondary generalization. Seizures tended to occur in clusters and were more frequent during sleep. She had numerous episodes of status epilepticus, and she suffered from multiple daily seizures that were refractory to anticonvulsants.

An extensive workup, including electroencephalography and neuroimaging (CT scans and MR imaging), suggested a left occipital epileptogenic focus emanating from a subtle region of cortical dysplasia. The patient underwent an occipitoparietal cortical resection, during which MCH was used for hemostasis. The MCH was placed in the resection cavity at the end of the procedure, and the excess was removed via copious irrigation. Microscopic analysis revealed only mild FCD (most consistent with Palmini Type IA: see below).²⁰

Seizures continued despite this initial resection, and the postoperative MR imaging results suggested residual dysplastic tissue. One month later, when the patient was taken back to the operating room for additional tissue resection and the placement of a subdural grid, MCH was again used for hemostasis. The microscopic appearance of this resected tissue was similar to that obtained at the first operation.

Two days after the second resection, seizures were persisting. Subdural grids mapped the epileptogenic focus as medial to the previous surgical sites; therefore, a third resection was performed. Microscopic evaluation revealed definitive FCD with abnormal, large, and disoriented neurons, but no balloon cells (that is, Type IIA) (Fig. 3A). In addition, a marked necrotizing granulomatous inflammatory reaction was observed. Ropy collagen-like material, consistent with MCH, was partially necrotic and surrounded by a palisade of macrophages. The latter was in turn embedded in a sea of chronic inflammation that was rich in eosinophils (Fig. 3B). A mild acute inflammatory reaction was also noted in the regions of previous subdural electrode placement.

Seizure activity stopped after the third surgery. However, the skin wound over the craniotomy site was healing poorly and there was some fluid drainage. Sixteen weeks after the third resection, a small area of exposed calvaria (deep to the scalp incision) was observed, and a subgaleal swab of this site grew methicillin-sensitive Staphylococcus aureus. The patient was well clinically, with no fever or seizures. On CT and MR imaging studies of the head, a possible area of osteomyelitis was demonstrated at the site of bone exposure, and an intraaxial ring-enhancing area was seen near the previous surgical bed (Fig. 3C). The clinical concern was for an abscess. However, the possibility of an inflammatory reaction to MCH was considered in light of the histological findings from the prior resection. Debridement, reclosure of the scalp incision, and aspiration of the cystic lesion were performed. The capsule of the lesion was very firm, and 6 ml of dark red fluid was aspirated. Histological examination of the aspirate failed to reveal outright pus or microorganisms; acute and chronic inflammatory cells were accompanied by nondescript proteinaceous material. Culture results were negative. No other surgical interventions were undertaken, and no antibiotics were administered. A CT scanning study was repeated 3 months later, and revealed resolution of the intracerebral ring-enhancing lesion. In retrospect, the lesion was thought to be most consistent with an MCH-induced inflammatory reaction (that is, a textiloma), given the following: 1) the documented prior inflammatory reaction to MCH 5 weeks after initial craniotomy; 2) the classic abscess-mimicking radiographic appearance of the lesion, as previously described in the MCH literature; and 3) the sterile characteristics of the lesion.

Discussion

Microfibrillar collagen hemostat has been routinely used for hemostasis during craniotomy at our institution



Fig. 3. Case 3. A: Photomicrograph of the original left occipital lobe underlying lesion reveals FCD Type IIA. Note the large, dysplastic, disoriented ganglion cells that are located abnormally high in the laminar architecture of the neocortical gray matter. H & E, original magnification × 200. B: Additional histological section of dysplastic tissue obtained 5 weeks after the initial craniotomy. Ropy MCH is surrounded by a vague palisade of macrophages, which in turn is engulfed by an eosinophil-rich sea of mixed inflammation. H & E, original magnification × 400. C: A T1-weighted axial MR image obtained with addition of Gd, performed 4 months after the initial cortical resection, after persistent wound dehiscence and drainage. The image depicts a left parietooccipital ring-enhancing lesion that was initially clinically suspected of being an abscess.

Postcraniotomy MCH-induced necrotizing granulomatous inflammation

since 1979, and since that time, several hundred procedures have been performed (approximately 100 craniotomies per year). Over this period we identified 3 instances of patients who developed postoperative reactions to MCH. Clearly, in our experience these foreign-body reactions are rare. Each patient presented with new or recurrent seizures 5-6 weeks after the initial neurosurgical procedure that involved MCH administration for hemostasis. On neuroimaging, the lesion in each case displayed enhancement that either mimicked tumor recurrence (Case 1) or abscess formation (Cases 2 and 3). However, clinicopathological workup did not confirm these radiological impressions. In all 3 cases, microscopy revealed necrotizing granulomatous inflammation directed at the residual MCH particles within the resection cavity. The MCH was partly necrotic and surrounded by a palisade of macrophages. In turn, these foci were engulfed by a sea of mixed inflammation that generally contained neutrophils, lymphocytes, macrophages, and plasma cells. In Cases 2 and 3, this inflammatory population was rich in eosinophils. Notably in Case 3, there was a time discrepancy between histological confirmation of an MCH reaction (5 weeks) and the neuroradiological appearance of a ring-enhancing lesion (16 weeks). To our knowledge, this is the first neurosurgical pediatric case series describing postoperative inflammatory reactions to MCH.

In 2001, Kothbauer et al.¹¹ described the only other pediatric case series involving intracranial inflammatory reactions to hemostatic agents. In their report, the authors detailed the occurrence of foreign-body granulomas in 3 boys, in all of whom central primitive neuroectodermal tumor was initially diagnosed. These reactions, which according to the authors all mimicked tumor recurrence, were identified radiologically 2-7 months after the initial surgery. One reaction was attributed to gelatin sponges (Gelfoam), whereas the other 2 were thought to be due to oxidized cellulose (Surgicel). Notably, the presence of an offending hemostatic agent was only confirmed in the case in which gelatin sponges were used. In fact, the authors admit to the use of MCH in the 2 cases in which oxidized cellulose was assumed to have incited the inflammation. Because oxidized cellulose was not histologically identified in these latter 2 cases, and given our experience as described here, we would advocate for the possibility that 2 of Kothbauer et al.'s 3 cases were due to MCHinduced inflammation.

The neurosurgical reports documenting inflammatory reactions to MCH are infrequent (Table 1). Only Case 1 of Ono et al.,¹⁸ reported in 2009, and Case 3 of Gondo et al.,⁵ published in 1989, lacked histological confirmation. Most instances involving inflammatory reactions to MCH have occurred after resection of a supratentorial neoplasm; this latter finding may be in part reflective of patient age, because most of the reported cases have affected adults. Notably, our Case 3 is the only instance of a nonneoplastic lesion antedating the MCH reaction.

Generally, loose MCH is first placed in an Aspeto syringe and puffed onto the resection margins. Occasionally the material is flattened, then placed as a small square onto a specific bleeding point. The applied MCH is then covered with cotton patties, which are subsequently re-

moved. Finally, all excess MCH, aside from that which is adherent to blood clot, is flushed out with copious irrigation. With the exception of our small case series, this surgical approach to the use of MCH has successfully controlled hemorrhage and has not resulted in any significant clinical complications. However, in light these inflammatory reactions at our institution, one could rightly argue against the routine use of MCH, especially given that postoperative hemorrhagic complications rarely occur when MCH is not used.⁴ Unfortunately, our clinicopathological review has failed to reveal a salient explanation for these MCH-induced inflammatory reactions. Although speculative, an underlying and inherent allergy to MCH should be considered in these unusual cases. Support for this hypothesis emanates from a case report by Kitamura et al.¹⁰ published in 1995 that documented a positive postoperative skin reaction to MCH after its use during a cholecystectomy.

With respect to timing, all of the reported neurosurgical cases involving inflammatory reactions to MCH have occurred within 4-8 weeks of the initial operative procedure (see Table 1). This time window would be consistent with animal experiments that suggest complete disappearance of MCH from operative sites 84 days after administration.¹⁴ One exceptional instance is our Case 3, where there was a discrepancy between the histological documentation of the inflammatory reaction (5 weeks) and when the ring-enhancing lesion was noted on imaging (16 weeks). As argued above, we believe that the latter imaging picture in Case 3 is indicative of an MCH reaction, and this would extend the window within which this reaction may be seen intracranially (that is, from 4-8weeks to 4–16 weeks). This would be in keeping with other non-CNS case reports in which MCH reactions occurred several months after initial surgery.^{1,16}

Of the cases in which clinical signs and symptoms were reported, new or recurrent seizure activity appears to be the most frequent symptom correlated with the presence of an MCH reaction (see Table 1). Other common symptoms included weakness (either focal or generalized), emesis, and fever. Given the typical location of these inflammatory reactions (that is, at the site of prior resection), it is not surprising that the postoperative clinical picture often mimics that of the original presentation. Therefore, tumor recurrence is often foremost in the initial clinical differential diagnosis, and is assumed on the basis of repeat neuroimaging. The latter often uncovers ring enhancement and edema, raising the possibility of recurrent tumor, radionecrosis (when clinically appropriate), or abscess.

The MCH-induced inflammatory reaction observed in each of our 3 cases is similar to other descriptions in the literature. An eosinophil-rich mixed inflammatory infiltrate, which typically contains multinucleate foreign-body giant cells, surrounds MCH-centric granulomas. Typically, a palisade of macrophages is seen immediately adjacent to the MCH; Ribalta et al.²² have noted a similarity to the pseudopalisading necrosis that is characteristic of highgrade gliomas. Although the MCH per se may be necrotic (hence "necrotizing granulomas"), the more viable portions of MCH may take on a ropy/fibrillary connective

Authors & Year	Age (yrs), Sex	Primary Diagnosis	Primary Lesion Location	Clinical Interval (wks)†	Clinical Presentation	Neuroimaging Features	Histological Findings
Sani et al., 2008	19, F	dysembryoplastic neuroepithelial tumor	rt parahippocampal gyrus	വ	emesis, generalized weakness (es- pecially in legs), high fevers, gait ataxia, urinary retention, & a positive L'hermitte sign	ring-enhancing 2.5-cm mass w/ significant edema	MCH in approximation w/ foreign-body type giant cells, lymphocytes, plasma cells, histiocytes, & eosinophils
O'Shaughnessy et al., 2006	3, M	medulloblastoma	4th ventricle & ver- mis	ω	 wk of headache, fever, intermittent emesis, bilateral horizontal ny- stagmus/dysmetria, truncal ataxia, & mild rt hemiparesis 	heterogeneous enhancement	broad bands of MCH adjacent to degranu- lating eosinophils; histiocytes, intact eosinophils, & plasma cells in adjacent tissue
Ono et al., 2009							
case 1	55, M	meningioma	rt frontal	3-4	recurrent numbness of It arm & mo- tor weakness	enhancement of surgical cavity wall, w/ surrounding edema	no histological confirmation
case 2	22, M	meningioma	rt ventricular trigone	4-5	headache, focal sz involving lt arm	faint enhancement around resec- tion cavity w/ adjacent marked edema, & midline shift w/ en- largement of inferior horn of lat ventricle	moderate lymphocytic invasion around a basophilic MCH; lymphocytic/neutro- philic angiitis of vessels w/ wall thicken- ing
Gondo et al., 1989							
case 1	22, M	oligodendroglioma	It ventricle	œ	NA	ring enhancement	MCH & "granulation"
case 2	57, F	glioblastoma	It parietal	8	NA	ring enhancement	MCH & necrotic material
case 3	19, M	astrocytoma	It frontal	œ	NA	marked ring enhancement	no histological confirmation
Ribalta et al., 2004							
case 1	30, M	oligodendroglioma	frontoparietal	4	ΝΑ	surgical cavity w/ ring enhance- ment & edema in surrounding parenchyma	degenerating eosinophilic to amorphous MCH surrounded by a zone of palisad- ing macrophages; prominent eosino- phils; foreign-body type multinucleated giant cells
case 2	20, M	anaplastic astro- cytoma	rt frontoparietal	4	NA	ring enhancement & edema in surrounding parenchyma, & fluffy intracavitary material	mixed MCH-cotton granuloma; dense fi- broblastic response & reactive vascular proliferation in surrounding tissue

TABLE 1: Literature review of inflammatory reactions to MCH^*

(continued)

	Age			Clinical			
Authors & Year	(yrs), Sex	Primary Diagnosis	Primary Lesion Location	Interval (wks)†	Clinical Presentation	Neuroimaging Features	Histological Findings
present study							
case 1	10, F	ganglioglioma	rt temporal	Q	typical sz auras returned, plus 2 generalized szs	medial enhancement & mass ef- fect in medial aspect of prior surgical bed, plus expansion of subarachnoid disease	necrotizing granulomatous inflammation; rare eosinophils
case 2	9, M	anaplastic epen- dymoma	lt parietal	5	rt-sided focal motor szs leading to progressive weakness	ring-enhancing lesion & surround- ing edema	necrotizing granulomatous inflammation; rich in eosinophils
case 3	15, F	FCD Type IIA	lt occipitoparietal	5‡	poor wound healing & drainage; szs	ring-enhancing lesion & surround- ing edema	necrotizing granulomatous inflammation; rich in eosinophils
 NA = not applic: The time from t The inflammato 	able; sz he first c rv reacti	 seizure. sraniotomy until the region was first confirmed 	peat presentation. 1 at 5 weeks after the	initial cran	liotomv, but the ring-enhancing lesion	on MR imaging was identified at 16 v	weeks after initial craniotomy.

tissue appearance. On H & E staining, MCH is typically eosinophilic in color, but may be amphophilic to basophilic in appearance; this variability in hue may be related to degeneration, because MCH is eventually absorbed by the host. Moreover, in those cases in which electron microscopy was performed, the collagenous constitution of MCH was confirmed by revealing the typical ultrastructural banding pattern expected of collagen.^{16,22} Both MCHcontaining textilomas reported by Ribalta et al.22 were described as inciting a striking eosinophilic infiltrate that was claimed to be unique to this hemostatic agent. Our Case 1 was somewhat unusual in that eosinophils, although present, were somewhat infrequent. However, on review of the literature, some cases of MCH-induced inflammation may not display conspicuous eosinophils (see Ono et al., Case 2);¹⁸ accordingly, we would argue that an eosinophilic infiltrate, although common, may not be a universal feature of MCH-induced inflammation. As is characteristic of MCHinduced inflammation, microorganisms were not identified by microscopy (or clinically).

Awareness of the possibility of postoperative inflammatory reactions to MCH and the typical clinical presentation are key to diagnosis. Neuroimaging is essential to the workup of these cases, and the differential diagnosis raised usually includes recurrent tumor or abscess. Unfortunately, current MR imaging sequences do not assist in distinguishing MCH-induced inflammation from recurrent tumor or abscess. Likewise, the imaging results from our Case 3 did not reveal a pathognomonic or distinguishing MR appearance with respect to MCH. Martins et al.¹² also described similar nonspecific MR imaging characteristics with respect to an intracranial gossypiboma, which in their case was due to surgical gauze. Nonetheless, in the typical clinical context, the suggestion of a recurrent tumor or abscess-like lesion based on MR imaging findings may be enough to trigger the correct differential diagnosis of a hemostatic agent-induced inflammatory reaction. Because these MCH-induced lesions inherently regress with time, we would recommend a conservative approach to management. The utility of such an approach is borne out by our experience in Case 3, in which the suspected abscess regressed after only minimal intervention (that is, aspiration without resection). A reasonable approach would include a routine infectious disease workup (including detailed history and physical examination, complete blood count with differential, cultures, and prophylactic antibiotics) and, if necessary, biopsy. Although unlikely to be seen, peripheral eosinophilia may suggest the possibility of an allergic-type response and a potential reaction to MCH.10 Moreover, if a reaction to MCH is suspected, some clinicians have sought out skin testing and confirmed an allergic response.¹⁰ It is conceivable that such testing could be performed preoperatively in patients thought to be especially at risk for such a reaction.

Conclusions

We have presented a pediatric neurosurgical case series wherein an inflammatory reaction to MCH developed 5-6 weeks after initial craniotomy. The presentation of all patients included new or recurrent seizures. Neuro-

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imaging suggested abscess in Cases 2 and 3, and tumor recurrence in Case 1. Microscopy revealed necrotizing granulomatous inflammation in all cases, and in keeping with the literature, the areas of reaction in Cases 2 and 3 contained numerous eosinophils. These new cases add to a limited neurosurgical literature regarding adverse inflammatory MCH reactions. Clinical awareness of this entity and consideration of a conservative approach to treatment are key to the appropriate management of these cases.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Dunham. Acquisition of data: all authors. Analysis and interpretation of data: all authors. Drafting the article: Dunham, Apel-Sarid, Cochrane, Steinbok. Critically revising the article: Dunham. Reviewed final version of the manuscript and approved it for submission: all authors. Administrative/technical/material support: Dunham, Apel-Sarid. Study supervision: Dunham.

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