

# Aseptic Meningitis after Embolization of Cerebral Aneurysms Using Hydrogel-Coated Coils: Report of Three Cases

## CASE REPORT

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**SUMMARY:** We report the development of aseptic meningitis in 3 patients with aneurysms treated with hydrogel-coated coils. Patients presented with febrile meningeal syndromes during the 24 hours following the procedures and responded to corticosteroids. One of them developed delayed hydrocephalus that required treatment with a ventriculoperitoneal shunt. Aseptic meningitis is one of the important complications related to hydrogel-coated coils that should be recognized. More information based on the posttreatment surveillance after use of hydrogel-coated coils is required.

Hydrogel-coated coil (HydroCoil Embolic System, MicroVention, Aliso Viejo, Calif) is one of the biologically active detachable coils that were developed to achieve more durable aneurysm occlusion by improved volumetric percentage occlusion of the aneurysmal cavity.<sup>1,2</sup>

Chemical aseptic meningitis accompanied by hydrocephalus after use of bioactive second-generation coils has been reported by Meyers et al.<sup>3</sup> They suggested that the concurrent use of hydrogel and polymer polyglycolic-lactic acid (PGLA)-coated coil systems (Boston Scientific/Target, Fremont, Calif) in large aneurysms may cause an exuberant inflammatory response. To our knowledge, there are currently no reported cases documenting this type of inflammatory response specific to using hydrogel-coated coils alone as bioactive coils. The authors present the periprocedural complications in 30 unruptured cerebral aneurysms treated with hydrogel-coated coils and compare them with historic control data regarding unruptured aneurysms treated with bare platinum coils alone.

### Case Reports

Endovascular occlusion of the aneurysm was performed with the patient under general anesthesia, with systemic hepaticization. Meticulous aseptic technique was maintained throughout each procedure. Prophylactic intravenous antibiotics were not administered to the patients during the perioperative period. In the presented cases, a combination of bare platinum coils and hydrogel-coated coils was used to maximize the theoretic benefits of each coil type to achieve complete and durable occlusion of large aneurysms. Bare platinum coils were used to frame the aneurysms, whereas hydrogel-coated coils were used to fill the aneurysms.

#### Patient 1

A 56-year-old previously healthy woman was admitted for endovascular treatment of an incidentally detected aneurysm of the right internal carotid artery (ICA) (8.2 × 7.6 × 7.5 mm). The aneurysm was occluded with 1 Guglielmi detachable coil (GDC) (Boston Scientific/

Target) and 7 hydrogel-coated coils. Volumetric packing attenuation of 64% was achieved with these coils. After the procedure, the patient recovered from the anesthesia and was transferred to the general ward for further observation. She remained afebrile and neurologically intact. The following morning (18 hours after the procedure), she described a febrile sensation (>38°C). By evening (28 hours after the procedure), she had fever (>39°C), headache, chills, and malaise. Neurologic examination revealed nuchal rigidity. The CSF white blood cell count (WBC) was 1017 × 10<sup>6</sup>/L. The CSF protein and glucose concentrations were 43 mg/dL and 48 mg/dL, respectively. The patient was treated with empiric antibiotics during the interim, pending negative findings on cultures. Complete septic work-up failed to identify an organism. Clinically, she improved on a course of intravenous corticosteroids. After discharge, the patient experienced continual headache, inattention, and somnolence. Six months after discharge, she was re-admitted because of progressive headache, memory disturbance, and gait instability. MR angiography demonstrated stable occlusion of the aneurysm and enlarged ventricles. The radio-isotope shunt flow study showed no obstruction of the CSF pathway. She received a ventriculoperitoneal shunt for hydrocephalus and was discharged home in good condition.

#### Patient 2

A 66-year-old woman with left ptosis and double vision was found to have an aneurysm of 7.2 × 8.1 × 7.9 mm in diameters at the left ICA. By use of a balloon remodeling technique, the aneurysm was obliterated with a total of 9 coils comprising a total length of 91 cm (3 GDCs and 6 hydrogel-coated coils). An aneurysm volumetric packing attenuation of 68% was achieved with these coils. Postembolization control angiography revealed embolic occlusion of the angular artery of the left middle cerebral artery (MCA), and an intra-arterial bolus of 8 mg of abciximab was given. Continuous intravenous infusion of heparin was recommended because of residual embolic occlusion of the left angular artery. She recovered from anesthesia and was neurologically intact. By 22 hours after the procedure, the patient had a febrile sensation (>38°C), headache, and generalized weakness. Neurologic examination revealed nuchal rigidity. The CSF WBC was 3700 × 10<sup>6</sup>/L. The CSF protein and glucose concentrations were 93 mg/dL and 65 mg/dL, respectively. No organism was identified on any culture specimen. Clinically, she improved on a course of intravenous corticosteroids.

#### Patient 3

A 68-year-old man was admitted for endovascular treatment of an incidentally detected 6.0 × 5.9 × 4.8 mm aneurysm of the right MCA

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bifurcation. The aneurysm was occluded with 1 GDC, 1 TruFill DCS (Cordis, Miami Lakes, Fla), and 3 hydrogel-coated coils. Aneurysm volumetric packing attenuation of 75% was achieved with these coils. He had no postoperative neurologic deficits. High fever ( $>39^{\circ}\text{C}$ ) developed 20 hours after procedure. He had severe persistent headache, chills, and agitation. Neurologic examination demonstrated meningismus, but findings were otherwise normal. The CSF WBC was  $1656 \times 10^6/\text{L}$ . The CSF protein and glucose concentrations were 73 mg/dL and 74 mg/dL, respectively. CSF cultures were negative for bacterial meningitis. His symptoms resolved following administration of systemic corticosteroids. He was discharged on the 7th hospital day. Two weeks after treatment, sudden left upper extremity weakness developed. Acute multifocal ischemic infarctions in the right parietal lobe were demonstrated on brain MR imaging. Cerebral angiography revealed durable occlusion of the aneurysm and a small amount of clot at the site of the aneurysm. Antiplatelet medication was recommended. The patient subsequently recovered and was discharged home.

## Discussion

Second-generation new platinum detachable coil systems with biologically active properties are under development to enhance more durable aneurysm occlusion.<sup>1,4</sup> Hydrogel-coated coils are platinum coils coated with polymeric gel composed of cross-linked acrylamide/sodium acrylate that absorbs water by diffusion in an optimal acid-base environment of whole blood, resulting in swelling to improve the volumetric occlusion of aneurysms.<sup>1</sup> Perhaps humans occasionally have an inflammatory reaction to the hydrogel, even though such a reaction has not been demonstrated yet in animals.<sup>5</sup>

Thirty patients with unruptured aneurysms were treated with hydrogel-coated coils in combination with bare platinum coils or PGLA-coated coils in 1 patient, from September 2003 to February 2006. Of these patients, aseptic meningitis developed in 3. Diagnosis of aseptic meningitis was based on the clinical presentation and presence of supportive CSF findings in these patients. Small asymptomatic thrombosis was a complication in 5 patients, and delayed thromboembolic event, a complication in 1 patient. Aseptic meningitis or related hydrocephalus was not identified in 126 patients with 143 intracranial unruptured aneurysms treated with bare platinum coils alone during the same period. Our experience suggests that aseptic meningitis is a complication of HydroCoil use, which is not seen when platinum coils are used alone.

Two cases of aseptic meningitis and related hydrocephalus have been reported as a complication of combined use of hydrogel- and PGLA-coated coils.<sup>3</sup> In our patients, aseptic meningitis developed after treatment with hydrogel-coated coils

and bare platinum coils. The combined use of hydrogel- and PGLA-coated coils did not cause meningitis in our 1 patient.

HydroCoil-associated chemical meningitis can cause symptomatic hydrocephalus on the basis of our 1 patient. Patients who experience acute meningitis symptoms after use of hydrogel-coated coils should be evaluated by brain CT whenever they have symptoms indicative of hydrocephalus. For a patient showing clinical signs of meningitis shortly after an endovascular treatment procedure, the possibility of aseptic meningitis should be considered in patients treated with hydrogel-coated coils, though thorough evaluation and treatment for presumptive bacterial meningitis is also required in such patients.

Treatment was mainly supportive and included analgesics, antipyretics, and maintenance of fluid balance. Systemic corticosteroid therapy was given to modulate the coil-induced inflammatory response and resulted in good clinical response in all 3 patients. There was no clinical evidence for the presence of bacterial meningitis, and empiric antibiotic therapy was instituted during the interim, pending negative findings on cultures.

Although hydrogel-coated coils were approved by the United States Food and Drug Administration in 2002, studies of their clinical use remain limited. Although hydrogel-coated coils may presumably achieve enhanced volumetric occlusion of the aneurysms, additional risks of these coils should not outweigh the potential added benefits from their clinical use. There were 191 aneurysms treated in the HydroCoil for Endovascular Aneurysm Occlusion (HEAL) study,<sup>2</sup> with 1 case of aseptic meningitis (H.J. Cloft, personal communication, April 26, 2006). Our report of aseptic meningitis and related hydrocephalus after the use of hydrogel-coated coils suggests that a more judicious clinical use of this new device is warranted and that manufacturers should evaluate these issues during product development.

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