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CASE REPORT

Immunohistochemical analysis of a ruptured basilar top aneurysm autopsied 22 years after embolization with Guglielmi detachable coils

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SUMMARY

The authors report on the histologic and immunohistochemical analyses of a cerebral aneurysm embolized with platinum coils and with the longest observation period. A 58-year-old woman presenting with subarachnoid hemorrhage due to ruptured basilar top aneurysm was treated with Guglielmi detachable coils (GDC) 22 years ago. She was the 15th case since the GDC was introduced. After she died of unrelated causes, an autopsy and thorough histologic examination were performed. Gross examination revealed no adhesion between the aneurysm wall and the surrounding brain tissue. Histologic and immunohistochemical analyses demonstrated that the cavity of the aneurysm was filled with homogeneous collagenous fibrous tissue, while the neck was completely covered by a dense collagenous neointima and a smooth muscle cell layer. The unique histologic results of this case may contribute to a better understanding of the long-term evolution of the healing process in intracranial aneurysms successfully treated with the GDC.

BACKGROUND

Since Guglielmi detachable coils (GDC) were introduced for clinical use in April 1990, this is the 15th patient who was treated with the device. The patient died of unrelated causes 22 years after the treatment. Thorough histopathologic analysis, including immunohistochemistry, was performed to investigate the final healing process of the treated aneurysm with the longest observation time.

CASE PRESENTATION

A 58-year-old woman with a history of hypertension who smoked one pack of cigarettes per day developed sudden-onset severe headache while driving. Within days she developed right facial

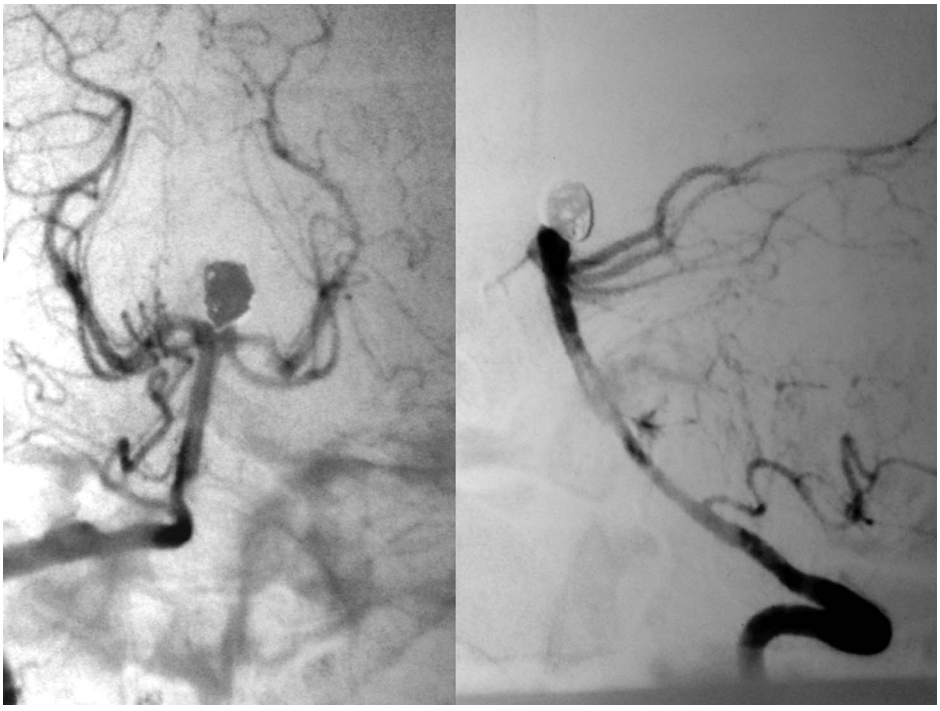

Figure 1 Follow-up angiograms performed in 1996. Anteroposterior (left) and lateral (right) views demonstrate complete occlusion of the treated aneurysm. The contrast filling defect between the coil mass and the parent artery described as the 'white collar' sign is also seen.

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numbness and a sense of fatigue. These lasted for 2 weeks but disappeared spontaneously.

She underwent brain CT and MRI, both of which showed a basilar top aneurysm. Cerebral angiography confirmed the aneurysm, which measured approximately10 mm at its largest diameter.

TREATMENT

Surgical exploration was performed, but clipping of the aneurysm was not done because the branches of the large posterior thalamoperforating artery were closely adhered to the dome of the aneurysm.

Two weeks after surgery the patient was treated with coil embolization using two GDCs (40 cm and 15 cm in length, respectively) by two neurointerventionalists. The immediate postoperative angiogram showed complete occlusion of the aneurysm (Raymond 1). The patient had an uneventful clinical recovery and was asymptomatic on her periodic neurosurgical follow-ups. Cerebral angiograms performed in January 1992 (1 year and 2 months post-embolization) and July 1996 (5 years and 8 months post-embolization) both showed complete occlusion of the aneurysm (figure 1).

However, medical problems including hypertension, coronary artery disease, congestive heart failure, carotid artery disease, and chronic lymphocytic leukemia gradually developed. She died in May 2012 at the age of 80 years, approximately 22 years after the GDC embolization. An autopsy was performed at Hudson Valley Neurosurgery in Suffen, New York, USA. Pathology specimen was processed using 10% formalin and the tissue block was sent to the UCLA Medical Center for histologic studies.

OUTCOME AND FOLLOW-UP

The surface of the treated aneurysm and adjacent structures were examined using a stereoscopic microscope (figure 2A). The aneurysm measured 8×8×5 mm and was surrounded by numerous perforating arteries from the bilateral posterior communicating arteries and P1 segments of the bilateral posterior cerebral arteries. There were no adhesions between the aneurysm and the surrounding brain tissue (eg, upper pons and cerebral peduncles). Both posterior cerebral arteries were intact. The implanted GDCs were visible through the thin aneurysm wall (figure 2B) and even partially protruded from the cavity of the aneurysm, while thick neointimal tissue completely covered the aneurysm neck (figure 2C).

A 13×16×8 mm tissue block that included the aneurysm was cut from the original tissue block and embedded in paraffin. To remove the coil materials, 1 mm sections of the paraffin block were made using an IsoMet Low Speed Saw (Buehler, Lake Bluff, Illinois, USA). Using a stereoscopic microscope, the coils were manually removed. Each 1 mm paraffin section was then re-embedded in the paraffin and 10 µm sections were finally made using a microtome. Technical details were as previously described.[1 2] Various staining techniques such as H&E, Masson Trichrome, α smooth muscle actin (αSMA), and factor VIII were performed.

Under low magnification, H&E staining demonstrated that the aneurysm cavity was replaced by solid homogeneous connective tissue with minimal cellular components (figure 3A). The coils were evenly distributed and there was a thick neointima across the neck of the aneurysm. Masson Trichrome staining showed that the entire cavity was replaced by homogeneous collagenous tissue (figure 3A), while the orifice was covered with even denser collagen-rich tissue. Factor VIII staining showed scant neovascularization (figure 3B), while αSMA staining revealed that the aneurysm wall lacked a layer of smooth muscle cells (figure 3C).

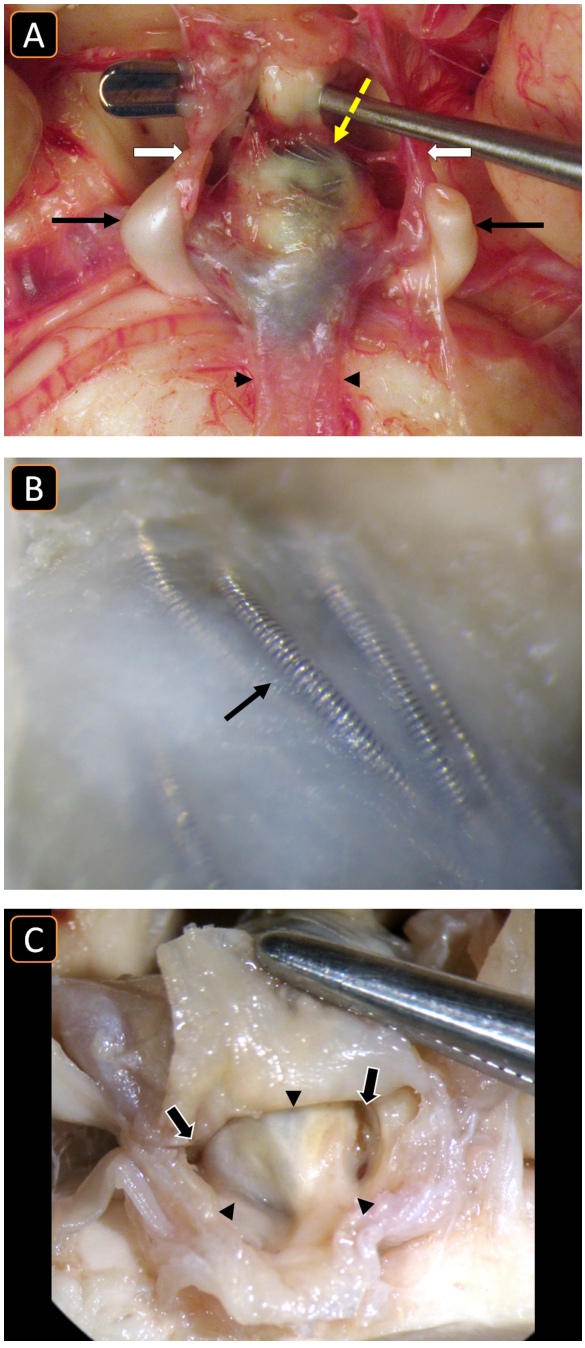

Figure 2 (A) Macroscopic view of the resected specimen. The aneurysm (dotted arrow) is surrounded by numerous perforating arteries from the bilateral P1 segments of the posterior cerebral and posterior communicating arteries. There are no adhesions between the aneurysm and these perforating arteries or the surrounding brain tissue. White arrows, bilateral posterior communicating arteries; black arrows, bilateral oculomotor nerves; between the arrowheads, basilar artery. (B) Magnified view of the surface of the resected aneurysm. Twenty-two years after implantation, the morphologic structures of the coils remain intact. (C) Magnified view of the orifice of the resected aneurysm. The orifice is covered by a thick neointima (arrowheads). The bilateral posterior cerebral arteries are patent and there is no evidence of stenosis or dilation. Black arrow, ostia of the bilateral posterior cerebral arteries.

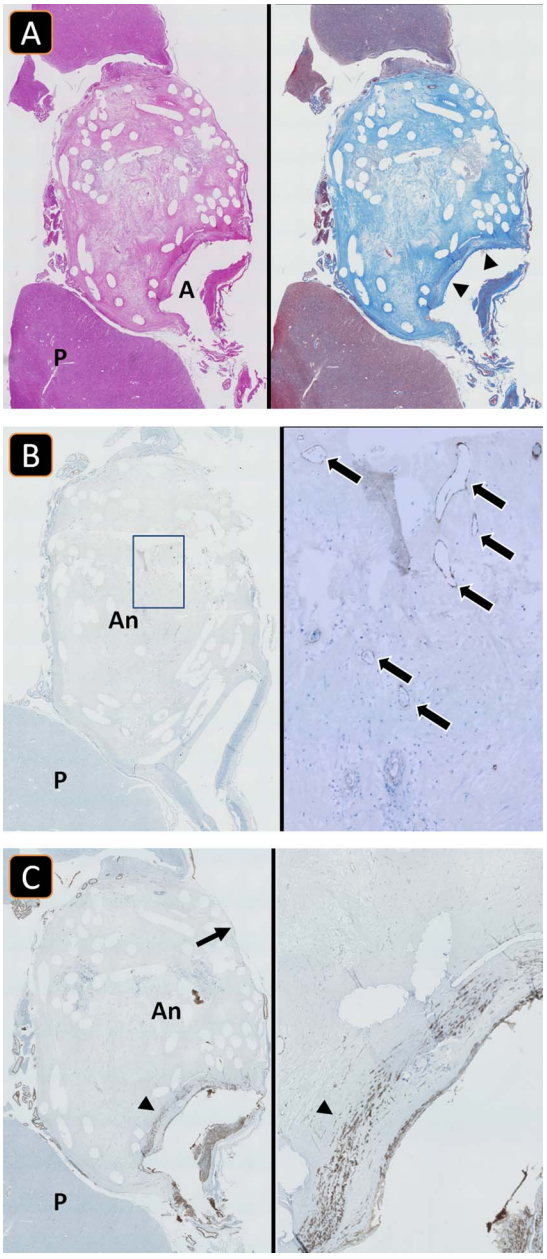

Figure 3 (A) Microscopic view of the resected aneurysm by H&E and Masson Trichrome stainings. Under H&E staining (left), the cavity of the aneurysm is replaced by a solid homogeneous connective tissue with minimal cellular components. The coils are evenly distributed and there is a thick neointima across the neck of the aneurysm. Under Masson Trichrome staining (right), the entire cavity is replaced by homogeneous collagenous fibrous tissue and the orifice of the aneurysm is covered by an even denser collagen-rich neointima (arrowheads). A, patent artery lumen; P, pons. (B) Immunohistochemical analysis of the resected aneurysm by factor VIII staining. Lower magnification (40×, left) shows scant neovascularization in the aneurysm, indicating that the thrombus is in the final stage of the organization process. A magnified view (100×, right) of the rectangular area at the center is shown. (C) Immunohistochemical analysis of the resected aneurysm by α smooth muscle actin staining. Lower magnification (40×, left) shows that the aneurysm wall lacks any layer of smooth muscle cells (arrow). Two layers of smooth muscle cells (arrowhead) can be seen across the neck of the aneurysm. A magnified view of the neointima (right) reveals that the superficial layer of smooth muscle cells, a thinner layer, can be seen immediately beneath the endothelium while a relatively deeper and thicker layer is seen beneath the neointima.

Magnified views of the same staining samples near the orifice of the aneurysm demonstrated two well-developed layers of smooth muscle cells migrating into the intima across the orifice (figure 3C). A superficial thinner smooth muscle cell layer was seen immediately beneath the endothelium and a deeper thicker layer was seen beneath the neointima.

DISCUSSION

Several reports have described histologic changes in aneurysms treated with coil embolization.[3–8] Szikora *et al*[8] reported a histopathologic analysis of 12 aneurysms previously treated by GDC embolization. In their report, in which 36 months was the longest observation time, the aneurysm sacs were mostly filled with organized thrombus and some remnants of unorganized thrombus and fresh blood. Bavinzski *et al* performed histopathologic analysis on 17 patients who underwent GDC embolization, with the longest observation time of 54 months. They reported that partially unorganized thrombus was still seen 54 months after treatment.[3]

The present case has an observation time of 22 years, the longest in the current literature on coil embolization of brain aneurysms. Thorough observation of the aneurysm surface using a stereoscopic microscope revealed that the implanted coils were visible through the extremely thin wall of the aneurysm. Some coils even protruded from the wall. On the other hand, the orifice of the aneurysm was completely covered by a thick and opaque neointima.

One of the technical challenges in the histologic analysis of coiled aneurysms is the preparation process of the samples. Since a microtome cannot cut the paraffin block containing metal, an embedding method using methacrylate-based resins is the commonly used method. However, these samples provide few optimal slices due to the much thicker microtome sections. Thus, the number of available stains is limited and the quality of the staining is inferior to that of paraffin embedded samples. In the present report, the tissue samples were processed using previously described paraffin embedding techniques.[1 2] The coils were manually removed under guidance by a stereoscopic microscope and prepared using a variety of stains for multiple immunohistochemical analyses.

Previously, with non-specific staining techniques, histologic findings were mostly speculative interpretations based on morphologic features. In this case, prominent migration of smooth muscle cells (αSMA staining) combined with a thick layer of collagen fibers (Masson Trichrome staining) across the neck of the aneurysm confirmed the complex layered structure of the neointima covering the orifice of the aneurysm. The aneurysm cavity was filled with collagenous fibrous tissue (Masson Trichrome

Learning points

- Thorough histopathologic analyses, which included immunohistochemistry, were performed to investigate the final healing process of an embolized aneurysm with the longest observation time period.
- After 22 years, the treated aneurysm was filled with dense collagen-rich fibrous tissue and minimal microvasculature. The coil materials inside were seen through the extremely thin aneurysm wall. The aneurysm orifice was covered with thick neo-intima and multiple layers of smooth muscle cells.

staining) with few microvasculatures (factor VIII staining) and scarce cellular components (H&E). The thrombus was in the final stage of the organization process or 'scar tissue formation'. With the longest observation time in the current literature, the histopathologic findings in this patient may contribute to the understanding of the final stages of the healing process in aneurysms treated with GDCs.

Contributors IY: planning, conducting and reporting the study. GG, GD conducted the surgery. DS: planning, conducting surgery, follow-up and reporting. MF, HT: histologic analysis. RJ, ST, YM: planning. FV: planning and conducting the project.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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