Aneurysm treatment response prediction in follow up black blood magnetic resonance imaging. A case series study

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Abstract
Black blood magnetic resonance imaging (MRI) is a promising imaging tool in predicting aneurysm rupture. Could it be also valuable in evaluating the treatment effect of endovascular and conservative treated aneurysms? Two patients were treated with stent and coil and one with Aspirine (ASS). Correlation of treatment response and contrast enhancement of the aneurysm wall is examined. In the first case stenting failed to treat the aneurysm and contrast enhancement in the wall did never subside during follow up black blood MRI. In the second case the aneurysm responded well to stenting and decreased in size, which was correlating significantly with attenuation of contrast enhancement in black blood MRI. In the third case the aneurysm responded to ASS treatment by decreasing in size as shown in follow up MR-angiography and the contrast enhancement in its wall decreased after 8 months of therapy. Black blood MRI seems to be a promising tool not only in predicting aneurysms at risk of rupture, but also in observing treatment responses after endovascular procedures or even Aspirine administration. When contrast enhancement decreases, aneurysm treatment seems to be successful as can be shown in decreasing size in the follow up angiography.

Introduction
Decision to treat un-ruptured aneurysms relies on semiobjective criteria of the treating physicians. There are scoring systems developed for guidance on which aneurysm should be treated, which help calculating the rupture risk.1 Because of a non-neglecting complication rate during aneurysm treatment, there is more than anytime before, the need of objective criteria to predict which aneurysms are dangerous and need to be treated. Especially today where an increase of cranial magnetic resonance images (MRI) identifies more and more patients with non-ruptured, incidental aneurysms.2 Pathophysiological processes in the aneurysm wall play a crucial role in its development and rupture.3,4 Inflammation in the aneurysm walls has been showed in a number of studies to contribute in aneurysm growth.4 Hemodynamic stress leading to endothelial damage which initiates an inflammatory cascade with macrophage and lymphocyte invasion and a change of vascular smooth muscle cells towards a pro-inflammatory phenotype has been shown as a catastrophic event cascade.5,6 With high resolution magnetic resonance imaging or the black blood MRI, inflammation in the aneurysm wall can be shown, as well as the thickness of the aneurysm wall.3,7,8 There are still some technical and interpretation problems of the method, which allows criticism and opens gates for more research in the field. In the present case series we show the correlation of contrast wall enhancement of aneurysms in response to their treatment. Of course the black blood MRI should not be the gold standard for follow up examinations. Faster MRA imaging shows the aneurysms size well. However, we performed the black blood MRI in a follow up manner in this pilot study only to examine the status of wall inflammation after treatment. Especially for patients with coiling or stenting the follow up imaging is a conventional MRA. For patients treated only with Aspirine though, MRA and black blood analysis in the first follow up imaging is recommended.

Methods: case series of 3 patients
Cranial MRI was performed on a 3T MR scanner (Magnetom Skyra, Siemens, Erlangen) with a 20-channel head coil. The protocol included a 3 D T1 space sequence with fat saturation (SPAIR) and blood suppression (field of view 179*230, repetition time 693 ms, echo time 18 ms, matrix 256x256, spatial resolution 0.9x0.9x0.9 mm) before and after administration of gadolinium (0.2 mL/kg/BW, maximum 20 mL; ProHance, Bracco Imaging, Germany). Total scan time was 7:55 min. With the black blood MRI contrast enhancement is visualized in the aneurysm and vessel wall whereas the arterial lumen is black.

Case Reports
Case #1
A 67-year-old female with a history of forgetfulness was admitted to the neurosurgical department. MR imaging demonstrated a large incidental fusiform aneurysm in the posterior cerebral artery on the right side. MRA and black blood MRI showed enhancement within the aneurysm walls, suggesting wall inflammation. An initial treatment with ASS to decrease inflammation showed no change in the aneurysm size or the contrast enhancement in the BB MRI. A coiling with Stent (5x bioactive hydrogel coils (Microvention); 2 x Leo + Stent, 3.5 x 50 mm) was applied (Figure 1A and B) which obliterated the aneurysm partially and reduced the flow in the aneurysm significantly.

Further therapy with Clopidogrel 75 mg and ASA 100 mg followed for at least 3 months. Due to aneurysm thrombosis ischemic areas in the posterior cerebral artery territories developed, which did not lead to neurological disturbance.

Three weeks after endovascular intervention and under ASS and Clopidogrel the patient developed a spontaneous subarachnoid hemorrhage (SAH). No treatment of the SAH was required and the patient was discharged to rehabilitation with a slight left-sided hemiparesis, horizontal visual palsy and moderate amnestic disturbances.

In the control MRA at 3 months after initial treatment the aneurysm showed no decrease of its size nor a difference in the BB MRI contrast enhancement. At 8 months the aneurysm was growing and the BB MRI showed a strong contrast enhancement in the walls of the aneurysm.
and thrombotic material in the aneurysm cavity (Figure 1C and D). A further stenting was performed with implantation of 2 Derivo Flow diverter stents (3.5x25 mm). This resulted in a stagnation of the inflow into the aneurysm (Figure 1E and F, 2 months follow up after last treatment). However, the BB MRI did not show any significant reduction of contrast enhancement in the aneurysm wall (data not shown). The patient died about 3 months after the last treatment of a subarachnoid hemorrhage for unknown reason. The BB MRI correlated with the treatment nonresponse by showing a strong contrast-enhancing wall through the whole treatment period.

Case #2

The second case is that of a 53 y.o. female patient with mirror aneurysms of the cavernous segment of the internal carotid artery (Figure 2A). She was suffering from headaches for years but in the last examination in the outpatient clinics she had double vision caused by abducent nerve palsy on the right side. Since the right aneurysm became paralytic we proceeded to treat the aneurysm with a flow diverter stent, reducing intra-aneurysmal flow significantly. Figure 2B shows the angiography with the stent. The CT-angiography before treatment and 3 months after treatment showed a significant decrease of aneurysm size (Figure 2C and D). Interestingly the BB MRI showed a significant decrease of contrast wall enhancement between the initial and the 3 months follow up MRI in the treated (right) aneurysm (Figure 2E and F). The untreated (left) aneurysm showed no difference in the BB MRI between the 2 examination time points (Figure 2E and F). The initial BB MRI shows a stronger contrast enhancement in the paralytic, right aneurysm compared with the left aneurysm (Figure 2E). The double vision subsided. The left aneurysm was untreated (extradural, non growing, asymptomatic). The BB MRI correlates with the excellent treatment response by showing a decrease of contrast enhancement together with aneurysm size decrease as shown in the CTA.

Case #3

This is a 47-year-old man presented to our outpatient clinic with headaches and intermittent visual disturbances, as well as tinnitus and left sided facial hemihypesthesia. The MRA showed a left fusiform aneurysm of the vertebral artery (VA), which appeared to be partially thrombosed and compressing the brain stem (Figure 3A). Cerebral digital subtraction angiography confirmed the findings. BB MRI demonstrated a strong contrast enhancement of the aneurysm wall of the VA aneurysm, which was most likely to be reconciled with inflammatory vessel wall changes (Figure 3B and C). Because of the length of the fusiform aneurysm we decide not to treat by stenting and first to try anti-inflammatory treatment with Aspirine. Therefore the patient was treated conservatively with ASS for 8 months. Serial MRI/MRAs and BB MRIs every 2-3 months follow up after the second stenting shown in 3d angiography reconstruction; F) CTA after the second stenting. No residual aneurysm is seen.
months were performed. After 8 months of ASS the aneurysm was decreased significantly in size and contrast enhancement in the BB MRI correlated with this size reduction by a significant less wall enhancement (Figure 3D and E).

**Discussion and Conclusions**

There is a growing body of evidence showing that MRIs examining the aneurysm wall will gain their place in treatment decision finding. Park et al. could measure the wall thickness of brain aneurysms with black blood MRIs, although technical difficulties did only allow estimations with a significant degree of overestimation.8,9 Other studies showed a contrast wall enhancement in symptomatic aneurysms, i.e. ruptured aneurysms, giant, progressively growing and paralytic aneurysms indicating a correlation of contrast enhancement and malignant behavior.3 It is still not clear what exactly the reason for the contrast enhancement is, but it correlates with rupture risk. In the present case series we show a dynamic change of contrast wall enhancement in response to aneurysm treatment. In the first case the aneurysm did not respond to treatment, kept growing and eventually lead to the patient’s death. The contrast wall enhancement did not change during the whole time of follow up indicating that the treatment was failing. In the second case the aneurysm became progressively smaller after stenting and the contrast enhancement in the wall correlated significantly with this response by almost disappearing. In the third case the aneurysm responded to Aspirine treatment and the decrease in size correlated with a decrease in contrast enhancement.

![Figure 2. 53 y.o. female with mirror aneurysms of the extradural internal carotid artery: A) CTA showing the 2 aneurysms. The right aneurysm caused an abducent nerve paralysis; B) angiography after stent implantation; C) CTA 1 day after stent. Around the stent there is still the aneurysm seen; D) CTA 3 months after stenting shows the decrease in aneurysm size; E) the initial black blood MRI shows perimetric contrast enhancement of both aneurysms with a stronger signal in the right (symptomatic) side; F) 3 months after stent the contrast enhancement on the treated aneurysm always disappears.](image-url)
There are optimistic signs that the black blood MRI could not only be used for predicting aneurysms rupture but could also be of value in evaluating the treatment response in aneurysms after stent or even Aspirine treatment. If the black blood MRI identifies inflammation or not is still unclear but does not change the fact that we have a correlation of contrast enhancement and aneurysm behavior. The three cases show the response of aneurysm treatment. It is also shown that in a specific aneurysm entity, which remains to be investigated and clearly defined, Aspirine alone could lead to a cure. The response to Aspirine can be monitored easily by a BB MRI.

Figure 3. 47 y.o. male with fusiform aneurysm of the vertebral artery: A) CTA reconstruction showing the dilated vertebral artery; B) initial black blood MRI showing a strong contrast enhancement of the aneurysm wall (transverse section); C) same as panel B (sagittal section); D) 8 months after Aspirine treatment shows a decrease in aneurysm size with less contrast enhancement; E) same as panel D (sagittal section).
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