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Case Report

Regression of Neointimal Hyperplasia of an Intracranial Stent: 6 Years Follow-up of A Wide-Necked Aneurysm

İntrakranial Stentte Neointimal Hiperplazi Regresyonu: Geniş Boyunlu Anevrizmanın 6 Yıllık Takibi

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ABSTRACT

We present a case of wide-necked giant aneurysm located at the P1-P2 segment of the posterior cerebral artery. The initial goal for treatment of the aneurysm was hemodynamic flow redirection with subsequent thrombosis so the procedure and involved stent placement to the neck of the aneurysm without any filling material. During follow up, significant in-stent stenosis due to intimal hyperplasia was found at the 6th month on digital subtraction angiography. Regression of in-stent neointimal stenosis at the 18th month and a total disappearance at the 76th month were observed on follow-up angiograms. Illustrating the reversibility of neointimal hyperplasia during a long follow up period was the main goal of this case report.

KEYWORDS: Intracranial stent, Aneurysm, Neo-intimal hyperplasia

ÖZ

Bu makalede, posterior serebral arter P1-P2 segmentine oturmuş geniş boyunlu anevrizmada endovasküler tedavinin uzun dönem sonuçları bildirilmiştir. Tedavide anevrizma embolizasyonu yapmadan boyun kısmına yerleştirilen stent ile hemodinamik akım yönü değişikliği yapılması amaçlanmıştır. Dijital anjiyografi ile takipte, 6. ayda stent içi ciddi darlık (neo-intimal hiperplazi) saptanmıştır. Sonraki anjiyogramlarda, 18. ayda neo-intimal hiperplazinin regrese olduğu, 76. ayda ise tamamen kaybolduğu dikkati çekmiştir. Neo-intimal hiperplazinin uzun süreli takipte geri-dönüşümlü olabileceğinin gösterilmesi başlıca amacımızdır.

ANAHTAR SÖZCÜKLER: İntrakranial stent, Anevrizma, Neo-intimal hiperplazi

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INTRODUCTION

The two primary indications for the deployment of microstents in intracranial vessels are stent-assisted coil occlusion of wide-necked or fusiform aneurysms and treatment of atherosclerotic stenosis (9).

This report presents a case of a wide-necked giant aneurysm of the P1-P2 segments of the posterior cerebral artery (PCA) that has a favorable outcome at the end of a 76 month follow-up after treatment with a balloon expandable stent. Reversibility of in-stent neointimal stenosis is highlighted in this particular case

CASE REPORT

A 47-year-old woman, who had a history of increasing episodes of headache and anisocoria due to the left 3rd nerve palsy, was transferred to our care after diagnosis of a giant intracranial aneurysm on computed tomography (CT). Magnetic resonance imaging (MRI) revealed an ischemic infarct in the left thalamic region in addition to the aneurysm (Figure 1). Digital subtraction angiography revealed the presence of a non-thrombotic wide-necked aneurysm measuring 2.5 cm x 2.0x 2 cm in the P1-P2 segment of the left PCA. The angiogram also showed hypoplasia of the P1 segment of the right PCA and presence of both posterior communicating arteries (PCoAs). Late filling of the left PCA territory was observed secondary to preferential filling of the aneurysm (Figure 2A). Vertebral artery injection during left internal carotid artery compression showed termination of the left PCoA within the aneurysm (Figure 2B). After evaluation of risks, benefits, and treatment alternatives, the patient selected to have endovascular treatment.

Under general anesthesia, the right common femoral artery was catheterized with a 7-French (F) sheath, through which heparin was administered intra-arterially (loading dose; 5000 Units (U) maintenance dose; 1000 U/hour). After visualization of the aneurysm, the 6-F Envoy guiding catheter (Cordis, Endovascular, Miami Lakes, Fla, FL) was navigated to the left vertebral artery, and a digital subtraction road map was made. Access to the neck of the aneurysm could be achieved using a microguidewire (Transend extrasoft, 300 cm, /Target

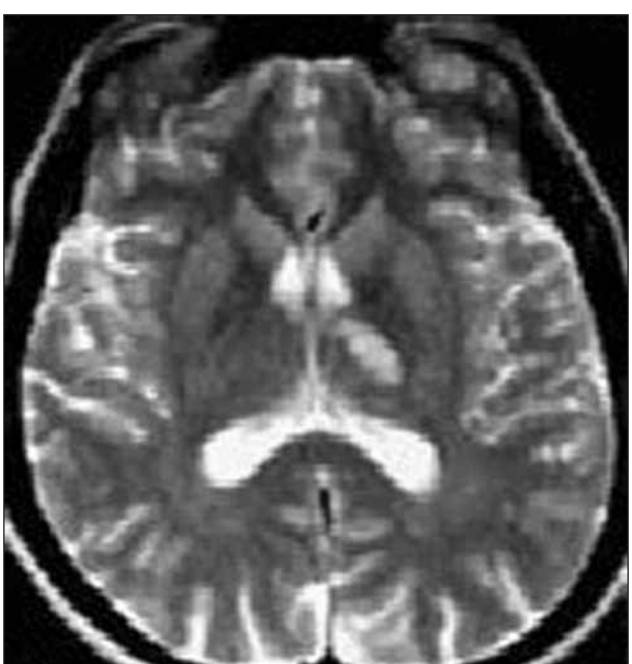

Figure 1: *Large ischemic infarction in the left thalamus is seen on axial T2-weighted MRI.*

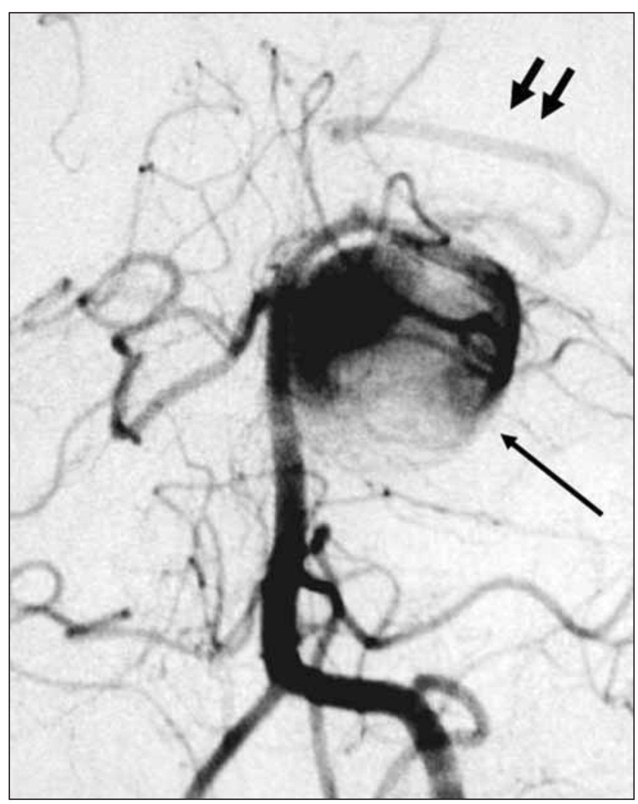

Figure 2A: *Filling of wide-necked PCA aneurysm (long arrow) and late perfusion on the ipsilateral PCA territory (short arrows) due to the turbulent flow in the aneurysmatic sac are seen on left vertebral artery angiogram.*

Figure 2B: *The patency of the posterior communicating artery (asterisk) and its connection with aneurysm as secondary inflow is demonstrated on the left vertebral artery injection during compression of the left internal carotid artery.*

Therapeutics/ Boston Scientific, Natick, MA) passed through the inside of the aneurysm lumen (Figure 3A). After positioning the wire at the P1-P2 segment, a 2.5 mmx9 mm balloon expandable stent (Medtronic, AVES660 Arterial Vascular Engineering, Inc., Santa Rosa, CA) was preloaded (Figure 3B). Under high-magnification fluoroscopic road-map guidance, the stent was appropriately positioned across the neck of the aneurysm. It was deployed after balloon inflation up to 4 atm. A control angiogram was performed which showed slow filling of the aneurysm cavity with significant stasis noted (Figure 4). Because of persistent filling, it was decided that the PCoA orifice of internal carotid artery which directly ended within the aneurysm should be obliterated. A single Guglielmi detachable coil (GDC-10, 2 mm x 4 cm, Boston Scientific/ Target Therapeutics) was used for embolization.

The patient had been preloaded with clopidogrel 4x75 mg before the treatment. After intervention, the patient was prescribed clopidogrel 1x75 mg/day for 4 months and 100 mg/day aspirin during whole follow up period.

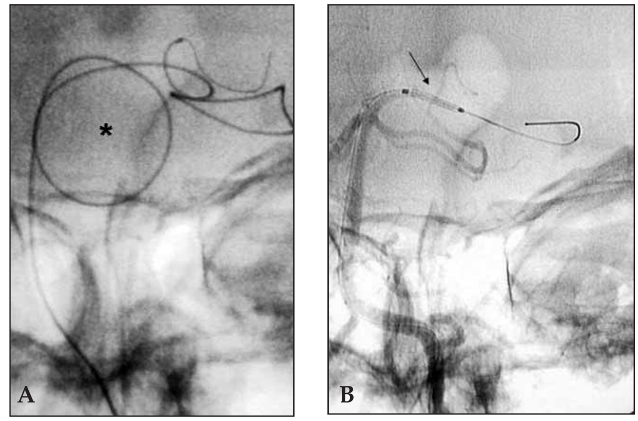

Figure 3: *The difficult manipulation of microguidewire-microcatheter combination in the aneurysm sac before preloading of the stent (**A**) and positioning of the 2.5x9 mm balloon-expandable stent across the neck of the aneurysm (**B**) are shown.*

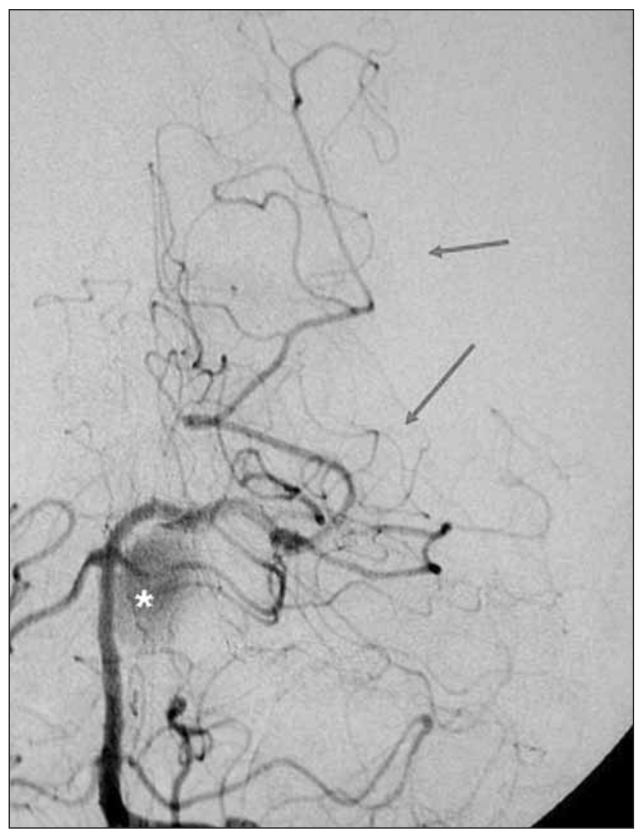

Figure 4: *Immediate left vertebral artery injection after stent deployment shows the reduction of filling in the sac (asterisk) and better perfusion of PCA territory (long arrows).*

During the follow up period, the persistence of slight anisocoria was observed. However, the patient reported significant decrease in headache episodes after treatment.

Imaging follow up

The patient was followed by DSA, CT and MRI at regular intervals. Partial filling of the aneurysm was observed on the first control angiogram (1st week of treatment). Total thrombosis was seen on CT at the 1st month of treatment. Shrinkage of the aneurysm in addition to total thrombosis was observed at the 6th month on CT and MR examination (Figure 5).

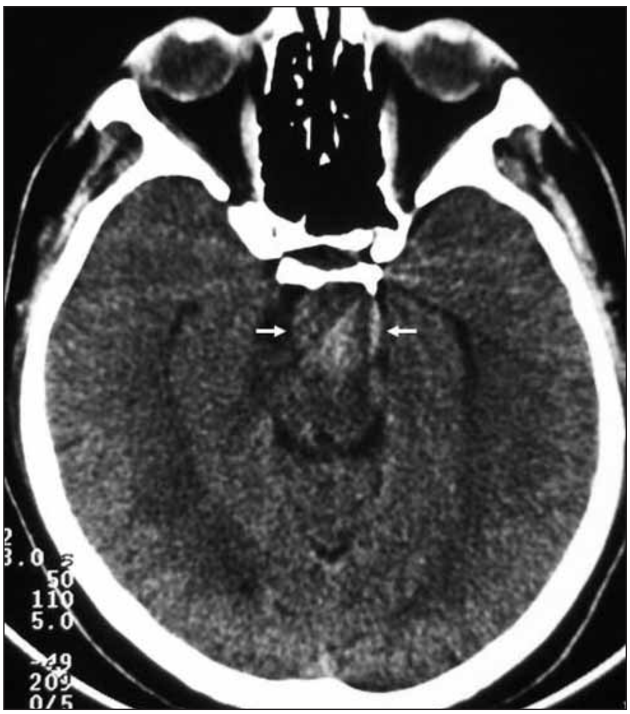

Figure 5: *On CT image, the aneurysm (arrows) with similar density to the brain parenchyma shows thrombosis. Also notice the streak artifacts on the aneurysm originating from coil embolization.*

Presence of aneurysm recanalization and patency of the intracranial stent were evaluated by DSA at 6, 18, and 76 months after treatment. In-stent stenosis due to neo-intima formation was noted in the left P1-P2 segment on the 6-month follow-up angiogram (Figure 6). Significant irregularity of neo-intima with regression of in-stent stenosis was seen at the 18th month of treatment (Figure 7). On the last DSA (at the 76th month of treatment), we interestingly observed the near complete resolution of stenosis and irregularity of in-stent neo-intima. Incidentally noted on the final angiogram was a change in the convexity of the stent body secondary to shrinkage of the adjacent aneurysm sac (Figure 8).

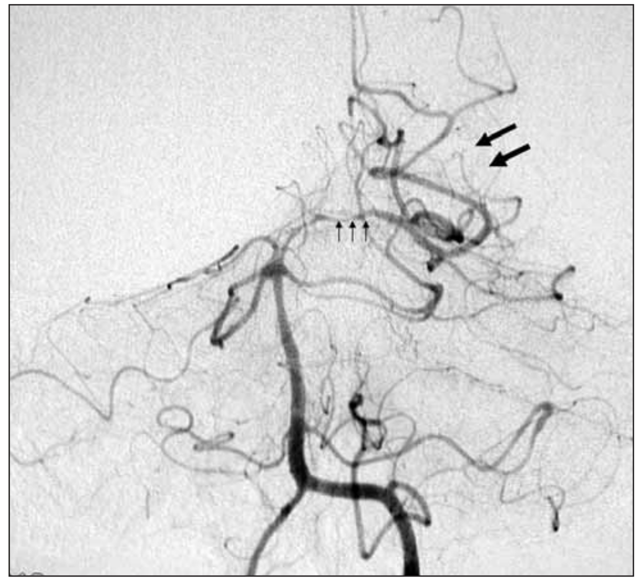

Figure 6: *Significant in-stent stenosis (short arrows) is seen at the 6th month of treatment. Also notice the good perfusion of left PCA territory (long and thick arrows) and no filling of the aneurysm sac.*

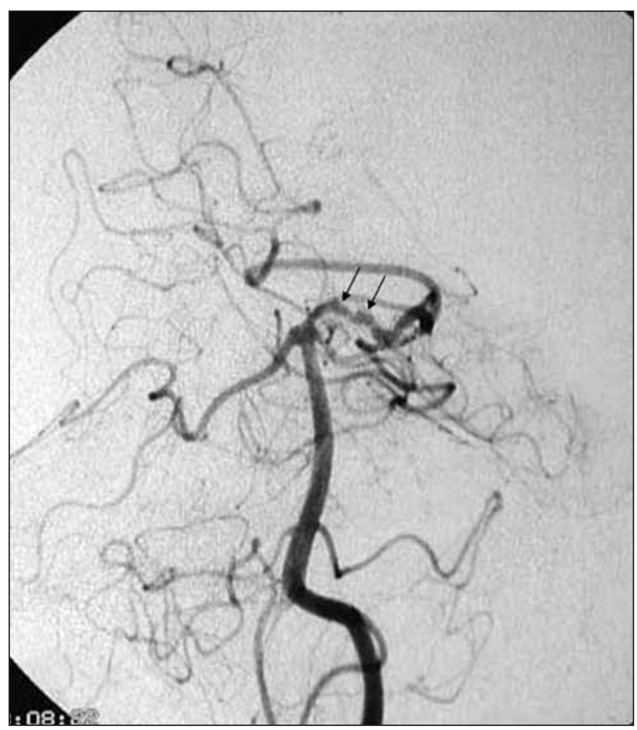

Figure 7: *Partial regression of neointimal hyperplasia with continuing irregularity is seen at 18th month of treatment.*

DISCUSSION

Several endovascular approaches have been used to treat complex intracranial aneurysms with wide-necks or fusiform shape. Parent artery occlusion in the presence of sufficient collateral flow (1) and

Figure 8: Almost total regression of in-stent stenosis and displacement of left P1 to its normal position is observed at 76th month of treatment.

embolization with different filling materials (coils, liquid polymer agents etc) with or without neck protection are the two most common techniques performed. Neck protection can be obtained by using a balloon remodeling technique or with Trispan (Target Therapeutics/ Boston Scientific, Natick, MA). Radioactive coils, bioactive coils and hydrogel coils cause accelerated healing reactions at the neck of the aneurysm. Onyx (Micro Therapeutics, Inc., Irvine, CA), a liquid polymer agent, has been used as a filling material with the help of a balloon remodeling technique (6). There are a limited number of reports about intracranial aneurysm treatment with grafted stents (4,8,14). Porous stent implantation with or without filling materials is another alternative technique used in wide necked aneurysms (12).

We took into account different treatment possibilities while selecting the unique technique for the case. Total occlusion of the sac with multiple coils without balloon remodeling is a relatively simple procedure; however, it was disregarded in this case due to the possibility of PCA territory infarction. Protection of the left PCA using the balloon remodeling technique was another option; however, we did not choose it due to an anticipated high rate of recanalization. The third option, preferred in this case, was to use a technique based on changing the flow dynamics of the parent artery. Our aim was to establish a new hemodynamic situation by changing the vessel curves with a rigid stent at the neck region. A balloon expandable stent without filling material was placed across the neck of the aneurysm in this case. This treatment approach resulted in decompression and shrinkage of the aneurysm with the additional benefit of diminished mass effect on the adjacent 3rd cranial nerve.

The idea of using porous stents to treat aneurysms without embolizing material is based on the assumption that the metallic struts induce alteration in blood flow dynamics within an aneurysm and therefore induce and promote thrombus formation (12).

A stent alters the blood flow and redirects the shear stress. Several reports about hemodynamic alteration have been published as experimental studies (3,5,13). Following stent implantation, it has been shown that the maximum velocity decreases in an aneurysm lumen, turbulent flow as a counter vortex at the dome of the aneurysm disappears, wall shear stress especially at the dome of the aneurysm decreases, and viscosity increases (13). This case was unique because inflow through the PCoA was present in addition to the neck at the P1-P2 segment. Complete hemodynamic alteration therefore did not occur until after the PCoA orifice was embolized as well. In addition to flow redirection, a stent also provides a physical matrix for endothelial growth, facilitating the remodelling of the aneurysm neck as well as the parent vessel in the region of the neck. Due to shear stress of balloon angioplasty or stent deployment, new endothelial growth called "neointima" occurs. The content of neointima changes over time. The early neointima contains a large quantity of proteoglycans, which provide both the volume of the neointima due to high water content, and facilitate cell migration and proliferation. However, as the neointima ages, it loses the bulky, hydrated proteoglycans, which results in reduction in the neointimal volume and the stimulus for smooth muscle cell proliferation. Meanwhile, the collagen matures, transforming from the fibrillar type to the cross linked type and the smooth muscle cells also change their phenotype from synthetic to contractile cells, with the cell content remaining relatively stable (10). As a result, neointimal regression may occur after 6 months (10) or 18 months (11). Late angiographic improvement has been proposed to be probably due to fibrotic maturation of in-stent neointima (2). We observed neointimal regression at the 18th month of treatment, but we don't know exactly when it began to occur.

The usage of self expandable neurostents was first reported in 2002. Before 2002, balloon expandable coronary stents were used in the treatment of intracranial atherosclerotic lesions and aneurysms. The major disadvantage of the balloon expandable coronary stent is its relatively poor flexibility and pushability, which often makes it impossible to navigate the systems to a suitable position. The new generation of self expandable neurovascular stents (Neuroform, Boston Scientific, Wingspan, Smart Therapeutics/Boston Scientific and Enterprice, Cordis Neurovascular), can be delivered more distally because of their flexibility, tractability and increased radio-opacity. Despite the technical advantages of these stents, it is reported that the noncompliant nature of balloon expandable stents does provide the advantage of a greater metal surface area than the Neuroform stent. Coronary stents would therefore be expected to have a greater impact on flow dynamics as well as on the rate of endothelization and intimal remodeling (7).

Although a flexible stent is the best choice in most cases, sometimes the best stent for treatment strategy should have enough rigidity for changing the deployed vessel. Not having standard vascular anatomic structures in every case, our technical standardization is also limited. The changing diameter of intracranial arteries at bifurcations is also another drawback in the production of an optimum intracranial stent.

In conclusion, changing hemodynamics with adjuvant materials (such as stents) may be a good alternative treatment in some wide neck aneurysm cases. Flow direction and maintaining new hemodynamics may lead to in-stent neointimal remodeling, reduction, and even total disappearance. During the follow-up period, the treating physician should consider the possibility of a spontaneous regression to prevent an unnecessary second treatment for in-stent restenosis.

REFERENCES

1. Arat A, Islak C, Saatci I, Kocer N, Cekirge S: Endovascular parent artery occlusion in large-giant or fusiform distal posterior cerebral aneurysm. Neuroradiology 44:700–705, 2002
2. Asakura M, Ueda Y, Nanto S, Hirayama A, Adachi T, Kitakaze M, Hori M, Kodama K: Remodeling of in-stent neointima, which became thinner and transparent over 3 years: Serial angiographic and angioscopic follow-up. Circulation 97:2003-2006, 1998
3. Baráth K, Cassot F, Fasel JH, Ohta M, Rüfenacht DA: Influence of stent properties on the alteration of cerebral intra-aneurysmal haemodynamics: Flow quantification in elastic sidewall aneurysm models. Neurol Res 27:120-128, 2005
4. Burbelko MA, Dzyak LA, Zorin NA, Grigoruk SP, Golyk VA: Stent-graft placement for wide-neck aneurysm of the vertebrobasilar junction. AJNR Am J Neuroradiol 25:608-610, 2004
5. Canton G, Levy DI, Lasheras JC: Hemodynamic changes due to stent placement in bifurcating intracranial aneurysms. J Neurosurg 103:146-155, 2005
6. Cloft HJ, Joseph GJ, Tong FC, Goldstein JH, Dion JE: Use of three-dimensional Guglielmi detachable coils in the treatment of wide-necked cerebral aneurysms. AJNR Am J Neuroradiol 21:1312–1314, 2000
7. Fiorella D, Albuquerque FC, Deshmukh VR, McDougall CG: Usefulness of the neuroform stent for the treatment of cerebral aneurysms: results at initial (3-6 mo) follow up. Neurosurgery 56:1191-1202, 2005
8. Islak C, Kocer N, Albayram S, Kizilkilic O, Uzma O, Cokyuksel O: Bare stent-graft technique: a new method of endoluminal vascular reconstruction for the treatment of giant and fusiform aneurysms. AJNR Am J Neuroradiol 23:1589-1595, 2002
9. Kessler IM, Mounayer C, Piotin M, Spelle L, Vanzin JR, Moret J: The use of balloon-expandable stents in the management of intracranial arterial diseases: A 5-year single-center experience. AJNR Am J Neuroradiol 26: 2342–2348, 2005
10. Kim WH, Hong MK, Virmani R, Kornowski R, Jones R, Leon MB: Histopathologic analysis of in-stent neointimal regression in a porcine coronary model. Coron Artery Dis 11:273-277, 2000
11. Kimura T, Yokoi H, Nakagawa Y, Tamura T, Kaburagi S, Sawada Y, Sato Y, Yokoi H, Hamasaki N, Nosaka H: Three-year follow-up after implantation of metallic coronary-artery stents. N Engl J Med 334:561–566, 1996
12. Krings T, Hans FJ, Möller-Hartmann W, Brunn A, Thiex R, Schmitz-Rode T, Verken P, Scherer K, Dreeskamp H, Stein KP, Gilsbach J, Thron A: Treatment of experimentally induced aneurysms with stents. Neurosurgery 56:1347-1360, 2005
13. Ohta M, Wetzel SG, Dantan P, Bachelet C, Lovblad KO, Yilmaz H, Flaud P, Rüfenacht DA: Rheological changes after stenting of a cerebral aneurysm: A finite element modeling approach. Cardiovasc Intervent Radiol 28:768-772, 2005
14. Saatci I, Cekirge HS, Ozturk MH, Arat A, Ergungor F, Sekerci Z, Senveli E, Er U, Turkoglu S, Ozcan OE, Ozgen T: Treatment of internal carotid artery aneurysms with a covered stent: Experience in 24 patients with mid-term follow-up results. AJNR Am J Neuroradiol 25:1742-1749, 2004