# Ankylosing Spondylitis associated with intracranial aneurysms: report of 2 cases

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## ABSTRACT

Cerebral aneurysms are the major cause of subarachnoid hemorrhage. Common ascribed etiologies are hemodynamic factors such as atherosclerosis, hypertension, infection, trauma, polycyctic kidney disease, connective tissue disorders like Ehlers-Danlos disease, Marfan syndrome, and familial predisposition. However, its association with ankylosing spondylitis (AS) is not clear. Here, we report 2 patients with AS who presented with subarachnoid hemorrhage which was finally confirmed to be due to cerebral aneurysms, one in posterior communicating artery and the other in basilar artery tip). The patients had no history of hypertension or any other disease. Our data may not strongly suggest that vascular changes due to AS are etiological factors for developing intracranial aneurysm, but this report may show the possibility for existence of an association between these diseases, which has to be confirmed by more genetic and pathologic studies.

**Keywords:** Ankylosing spondylitis; Etiology; Intracranial aneurysm

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## INTRODUCTION

Cerebral aneurysms are the major cause of subarachnoid hemorrhage and cause a significant disease burden annually. Their prevalence is estimated to be 2.3%, with an overall risk of rupture around 1% per year[1]. Contrary to extracranial aneurysms, the exact etiology and pathogenesis of intracranial aneurysms remains unclear. Some studies state acquired risk factors as etiology, while others support the role of genetic factors. Common acquired or genetic etiologies which have been acknowledged for cerebral aneurysms are hemodynamic factors such as atherosclerosis and hypertension, infection, trauma, Autosomal Dominant Polycyctic Kidney Disease, connective tissue disorders like Ehlers-Danlos disease, and Marfan's syndrome. Familial occurrence of intracranial aneurysms has also been reported[2].

Ankylosing spondylitis (AS) is a potentially disabling form of seronegative spondyloarthropathies. The major etiologic factor of AS is genetic predisposition, HLA-B27 being the most important. Both familial and sporadic AS has been described. In familial AS, HLA-B27 positivity is more prevalent than sporadic cases. Moreover, patients with familial AS are younger at symptom onset. Many studies have reported the association of AS and abdominal, thoracic, and coronary artery aneurysms. However, up to date, only one report has described a patient with concomitant AS and an unruptured cerebral aneurysm, albeit this report also did not contribute the aneurysm to AS[3]. Here, we report 2 patients with known previous histories of AS who presented to our institution (Shohada Tajrish Hospital, Tehran, Iran) with subarachnoid hemorrhage which was finally confirmed to be due to cerebral aneurysms, one a saccular posterior communicating artery and the other a saccular basilar artery tip aneurysm.

## CASE PRESENTATION

### Case 1

The patient was a 47 year old man, who was a known case of AS since 25 years ago, presenting by low back pain and a gradual decrease in lumbar range of motion and stiffness. He had a positive HLA B-27, and negative Rheumatoid Factor, Anti-Nucleus Antibody, anti double strand DNA, ANCA, C3, C4, and CH50. He had no history of hypertension or any other accompanying medical disease.

He was on a treatment regimen of indomethacin 75 mg, bid and prednisolone 2.5 mg daily for AS. He was referred to our emergency ward with a history of transient loss of consciousness and severe acute onset headache. He had recovered his full state of consciousness in a few hours. He had experienced an episode of acute severe headache, without a decrease in consciousness or seizure 10 days before, which had been assessed in another centre by a brain computed tomography (CT) scan first. As a thick peri-mesencephalic subarachnoid hemorrhage (SAH) was diagnosed then, a brain 4 vessels angiography was performed, yielding to a normal angiogram result. The patient was discharged then without further workup. On his second presentation, the Glasgow Coma Scale was 15/15, and the patient was alert and oriented. His Mini Mental State Exam scored 30/30. His neurologic exam was thoroughly normal (Hunt and Hess grade 2).

On general and rheumatologic examination, he had no evidence of chest problems or arthritis in peripheral joints. He had only marked limitation of lumbar extension and flexion. On the first CT scan, peri-mesencephalic thick SAH was seen with an IVH component in the posterior horn of right lateral ventricle without hydrocephalus, severe edema, or intracerebral hemorrhage (Fisher Grade 4). On digital subtract brain 4 vessels angiography, a saccular aneurysm was seen on posterior communicating artery segment (P segment) of right internal carotid artery with a 5 mm neck and lateral projecting dome (Figure 1).

The patient underwent a right fronto-temporal craniotomy and clipping of the aneurysm. No complication relating to the general anesthesia or the procedure itself occurred in the peri- or post-operative period. The patient discharged from the hospital 6 days after surgery. He had no further complications in the follow-up visit 18 months after surgery.

### Case 2

A 54 year old man who was a known case of AS from 20 years ago was referred to our hospital with a complaint of severe sudden-onset headache, nausea, vomiting and loss of consciousness 10 days before. After the ictus, he had fallen down from a 3 meters height. The patient had also a history of ischemic stroke 6 years ago, with a remnant right hemiparesis, motor dysphasia, and facial nerve paresis. He had no history of hypertension. He had abandoned the treatment for AS after the stroke, and did not receive any treatment for AS then.

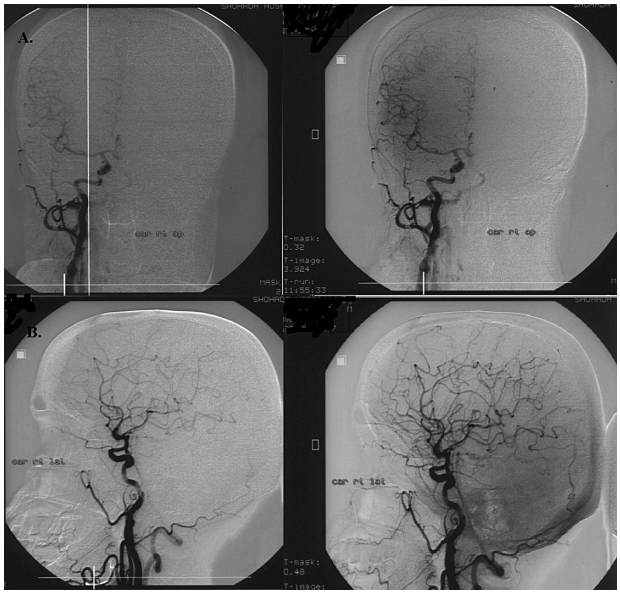


**Figure 1.** Preoperative evaluation in case 1. Brain 4 vessels angiography in AP (A) and lateral (B) views shows an aneurysm in posterior communicating artery segment of right internal carotid artery.

In physical examination, he was conscious but showed motor dysphasia. He had bilateral 6$^{th}$ cranial nerve and right 7$^{th}$ cranial nerve palsy. Motor examination showed quadriparesis, more severe in right side than the left. On whole spine X-Ray series, he had diffuse bambooing of thoracic and lumbar vertebra, indicator of his AS, and a fracture with dislocation in T11-T12 level (Figure 2). Brain CT scan, performed on the day of referral to our

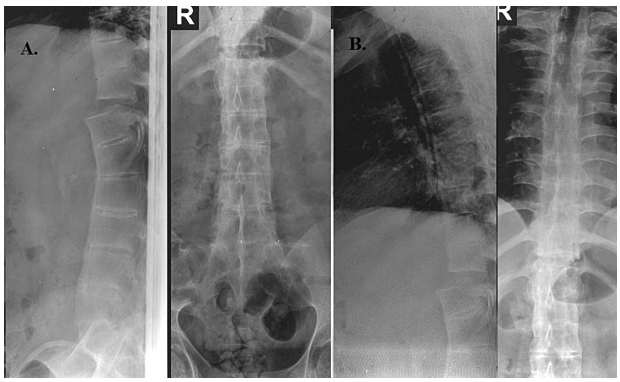


**Figure 2.** Thoracic and lumbosacral X-Rays in case 2 show diffuse bambooing of spine with a fracture-dislocation at T11-T12 level.

institution, and it showed a round slightly hyperdense prepontine lesion, without evidence of hemorrhage. No scan was performed for him in the day which the ictus happened; Figure 3). Brain MRI showed a hypointense signal in both T1- and T2-weighted images on the region of basilar artery tip, in favor of aneurysm with internal thrombosis. A T1 hypointense and T2 hyperintense region was also seen in left frontal, consistent with an old ischemia. He underwent a four vessels angiography, which showed a 9×9×19 mm saccular aneurysm projecting upward in basilar artery tip (Figure 4).

His aneurysm was first treated by endovascular Guglielmi detachable coil placement, and his thoracic fracture was managed in a different stage by posterior spinal fusion with pedicular screws. He was discharged without further deficits relating to his treatments.

## DISCUSSION

Several factors have been stated to cause cerebral aneurysms; however, the exact etiological factors for cerebral aneurysm formation need to be elucidated. Both acquired and genetic risk factors have been described to cause aneurysms. Among the most important acquired etiologies are hemodynamic factors such as atherosclerosis and hypertension, Location of proximal cerebral vessels in the subarachnoid space and lack of a firm support by surrounding and intrinsic connective tissue. Such conditions render them susceptible to hemodynamic changes, and consequently, may lead to aneurysm formation[4]. AS is a chronic inflammatory disease of the axial joint with both articular and extra-articular manifestations. One well known extra-articular vascular manifestation of AS is aneurysm formation in thoracic and abdominal aorta. Some researchers suggest that vasculitis is the underlying background for aneurysm formation in these large vessels. Miller & Maleszewsk, for instance, have described a syndrome of overabundance of IgG4-producing plasma cells, which could lead to both lymphoplasmacytic thoracic aortitis and abdominal aortic aneurysm formation[5]. Moreover, Takagi et al, have shown hyalinization of the connective tissue, numerous lymphocytic infiltrates, and absence of elastic fibers in the pathologic examination of the aneurysmal wall, which would be most compatible with aortitis. However, on studies performed in patients with concomitant AS and connective tissue disorders such as Marfan's syndrome, a process called fibrillinopathy would exist as the underlying lesion. Here, reduced fibrillin deposition into the extracellular matrix is found in ascending aorta which may render them susceptible to formation of aneurysm and dissection[6].

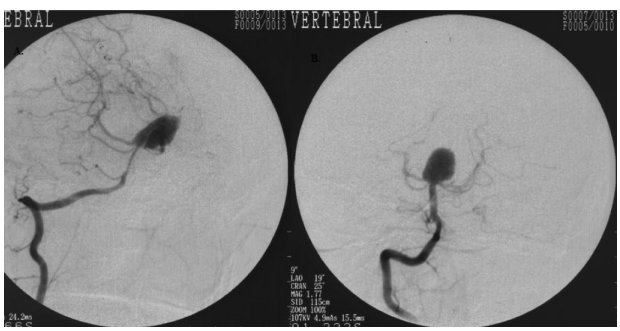


**Figure 3.** Preoperative brain CT scan in case 2 shows a hyperdense round lesion in basilar tip territory, without obvious SAH (10 days had elapsed between the CT scan and ictus).

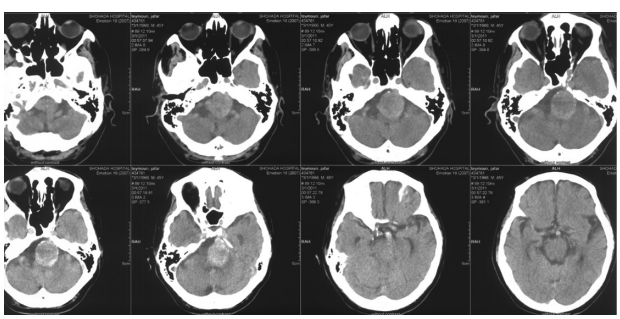

**Figure 4.** Preoperative brain 4 vessels angiography in case 2 shows an aneurysm in basilar artery tip.

Although AS is known as an etiology for aortic aneurysms, its association with cerebral aneurysms is not well recognized and reported. Lack of reports for cerebral aneurysms and AS may be due to pathologic differences between aortic and cerebral walls. Intracranial arteries are composed of the three layers of intima, media, and adventitia, like other arteries. However, unlike extracranial arteries, intracranial arteries lack the external elastic lamina[4]. Moreover, in intracranial arteries, the media has less muscle, the adventitia is thinner, and the internal elastic lamina is more prominent. However, more studies are needed to assess the pathologic changes in cerebral aneurysm wall, in cases associated with AS.

To our knowledge, our report is the second case series which describes 2 patients with concomitant AS and cerebral aneurysms. Choi et al, reported a patient suffering from long-term AS that needed surgery to treat sinus mucoceles. The patient was also diagnosed to have an incidental unruptured anterior communicating artery aneurysm. However, they also raised the possibility that the aneurysm might be caused by hemodynamic changes by an undiagnosed concomitant Takayasu's disease[3]. Both of our patients had presented with symptomatic ruptured aneurysms, leading this report the first one

which describes the association of symptomatic cerebral aneurysms and AS. Hypertension is a well-described risk factor for aneurysm formation. None of our 2 patients had a previous history of hypertension before or during hospitalization. Therefore, the formation of aneurysm could not be attributed to sole hemodynamic changes. Another possibility may be the presence of genetic disorders which would render vessels prone to malformations. Among these are mutations in collagen synthesis genes such as COL1A1, COL1A2, PTGER4, and ANTXR2. Mutations in these genes are also associated with osteogenesis imperfecta, Ehlers-Danlos syndrome, Marfan syndrome, and idiopathic osteoporosis. However, none of these phenotypes were clinically observed in our patients. Moreover, both of our cases suffered from sporadic AS, which makes the possibility of presence of genetic disorders less likely. However, this can only be confirmed by detailed genetic studies.

We could suggest that vascular changes due to AS may render these patients susceptible to aneurysm formation. Confirming this could only be feasible by obtaining tissue after surgery, possibly by cutting the aneurysm sac after clipping. However, this is not routinely performed in aneurysm surgery after clipping, as it bears some risks (for instance, clip slippage and risk of rebleeding). Moreover, in our series, only the first case underwent open surgery and the other was managed by endovascular treatment which would not provide vascular tissue.

## CONCLUSION

Although AS is a known etiology for thoracic or abdominal aorta aneurysms, it has not been reported as an etiological disease for the development of intracranial aneurysms. This manuscript is the first report of such association between AS and cerebral aneurysms. Our data may not strongly suggest vascular changes due to AS are etiological factors for developing intracranial aneurysm, due to lack of relevant histopathological studies. However, this report may raise the possibility for existence of an association between these diseases. Further studies reporting more cases and also performing genetic and pathologic studies on the patients may confirm this association.

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