Giant Serpentine Aneurysm in a Patient with Multiple Endocrine Neoplasia Type 1 Syndrome

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Summary

Giant serpentine aneurysms (GSA) are a rare, distinct group of giant intracerebral aneurysms. Multiple endocrine neoplasia type 1 (MEN 1) syndrome is characterised by tumours of the parathyroid glands, pancreatic islets and the pituitary.

We report a case of a GSA in a diabetic patient diagnosed with MEN 1 syndrome.

Introduction

Giant serpentine aneurysms (GSA) comprise a rarely seen group of giant intracerebral aneurysms. These aneurysms usually have a poor prognosis, and the patients either neurologically deteriorate or die from mass effect or less frequently because of haemorrhage.

Prompt diagnosis and treatment of this rare condition, especially in young patients, is of paramount importance.

The main therapeutic goal is to exclude the aneurysm from the circulation, thus stopping the mass effect. This can be done by occlusion of the parent vessel, following a balloon occlusion test.

MEN 1 syndrome is a familial disease characterised by tumours of the parathyroid glands, pancreatic islets and the pituitary.

Case Report

A 47-year-old man was diagnosed with multiple endocrine neoplasia type 1 (MEN 1) in 1998 when he was found to be hypercalcaemic due to parathyroid tumour. At the time of the initial investigations for his primary disease, in 1998, an aneurysmal dilatation of the carotid bifurcation was identified. He underwent cerebral angiography which revealed a giant serpentine aneurysm affecting mainly the proximal M1 and A1 segments of the middle and anterior cerebral arteries on the right (figure 1). No active treatment was suggested at that time.

Over the years, there was a definite deterioration in the radiological appearance, in terms of the size of the thrombus mass and also the extent to which the carotid branches were involved. The patient remained asymptomatic and received no treatment. In July of 2004 (six years after the initial angiogram), he noticed increased lacrimation in the right eye, associated with retro-orbital pain and since September 2004 experienced right-sided ptosis.

MRI scan in October 2004 revealed a heterogeneous, hyperdense mass within the right frontal lobe, which was causing a midline shift of approximately 10 mm and slight impingement of the right midbrain. The post-contrast

Figure 1 R ICA angiogram (AP view) shows a giant serpentine aneurysm affecting mainly the proximal M1 and A1 segments of the middle and anterior cerebral artery.

scan showed that the entire length of both A1 and M1 segments, and one of the M2 branches were involved (figure 2).

He attended the Institute of Neurological Sciences, Glasgow, in November of 2004 for a balloon occlusion test, with the plan to proceed to a permanent right internal carotid occlusion. The angiogram that preceded the balloon occlusion test failed to demonstrate any cross-flow from the left or posterior circulations (figure 3).

The balloon occlusion test was performed with a 7x7 mm Hyperform balloon (MTI/ev3). He was unable to tolerate occlusion distal to the level of the ophthalmic artery, as he became dysphasic and developed an immediate left-sided weakness. Subsequently, the balloon was inflated proximal to the ophthalmic artery and the patient tolerated this proximal occlusion (during 20 minutes of inflation) with the whole hemisphere being supplied retrogradely via the right ophthalmic artery.

We decided however that this was inadequate to sustain the hemisphere, under more normal conditions and occlusion was therefore not undertaken. It was decided to improve the blood supply to the right hemisphere by an extracranial/intracranial anastomosis (ECA-ICA by-pass).

He was readmitted in January 2005 for a combined definitive treatment. During those three last months since his previous admission,

he was feeling more tired and had a tendency to sleep more. He underwent a superficial temporal to middle cerebral arterial anastomosis. Two days later, an endovascular balloon occlusion was performed, using two detachable latex balloons (Goldvalve no 16, Nycomed, Paris, France), one across the ophthalmic artery and one in the cervical carotid (figure 4A,B). He was kept on a Heparin infusion for 48 hours and nursed flat in the High Dependency Unit for three days. He was gradually allowed to sit up in bed, before mobilising over the next few days. Initial postural hypotension and fainting episodes were treated with rehydration and he was discharged from hospital 12 days after the balloon occlusion.

A post-procedural CTA showed excellent patency of the ECA/ICA by-pass with marked reduction of the MCA when compared to the pre-operative investigation. Over the short period of follow-up (five months) there was an almost complete resolution of the right ptosis.

The 20-month CT Angiography at the University Hospital of Patras where he is being followed up, showed that the ECA/ICA by-pass was patent while there was a retrograde filling of the entire right M1 and A1 lumen, from the by-pass. The vessel lumens were now of normal calibre although the heterogeneous mass had not regressed, and the patient remained in excellent condition (figure 5A-C).

Discussion

Giant serpentine aneurysms (GSA) were first described as a different entity from saccular aneurysms in 1977¹. They are giant, usually partially thrombosed aneurysms, affecting the middle cerebral artery (MCA) or its main branches in more than half of the cases. The anterior cerebral artery (ACA) is rarely affected². These aneurysms are characterised by separate entrance and outflow pathway and absence of a discrete identifiable neck, in contrast to the saccular aneurysms.

They follow the normal orientation and location of the parent vessel, while the parent lumen is surrounded by a larger mass which in most cases represents an organised blood clot of different ages³. Previous pathological reports showed that these aneurysms contain numerous small vessels similar to vasa vasorum⁴. In our case the serpentine aneurysm involved the right MCA as well as the ACA and had an

irregular channel which continued into normal distal branches.

Giant serpentine aneurysms usually present as an intracranial mass rather than intracranial haemorrhage. Symptoms are dependent on the location and the predominant signs and symptoms include headaches, hemiparesis, visual disturbances, cranial nerve palsies, etc. In our case, the aneurysm was incidentally discovered, while the patient remained asymptomatic for almost six years thereafter, in spite of its large size. Only one other case of asymptomatic incidental SGA has been described, in a 14-year-old boy².

The exact cause and pathogenesis of giant serpentine aneurysms is unclear. Several theories and hypotheses have been described in recent years; none of them is yet proven. Until now, the most attractive theory proposed recurrent episodes of localized eccentric haemorrhage (possibly due to microdissections of the vessel wall), which then become organised into mature clots. Other authors have implicated haemodynamic reasons for the aneurysm formation⁵⁻⁷.

An alternative pathogenesis has recently been proposed by Lasjaunias⁸. According to this theory which could apply for GSA, aneurysm formation is the result of an inflammatory process, where the endothelial cells of vasa vasorum and the 5-LO (lipoxygenase) pathway play an important role by releasing ECM-degrading factors which break down the elastic lamina of the vascular wall and lead to the formation of the aneurysm. This would be similar to the formation of aortic aneurysms⁹. Our case may offer support for this theory for two reasons with regard to his co-morbidity factors. Our patient suffered from diabetes and was found to have MEN 1 syndrome.

Recently, new pathogenic links have been reported between hyperglycaemia and adventitial inflammation and neovascularization of vasa vasorum¹⁰. This could be the initial trigger point for aneurysm formation, as described above, or it could contribute to the progress of the disease.

Furthermore, MEN 1 syndrome is a condition where several hormonal and metabolic events are present and hypercalcaemia is profound¹¹. Interestingly enough there are reports in the literature describing the presence of a GSA in patients with hypercalcaemia¹².

Figure 2 MRI scan (T1 Weighted image, Post Gd) reveals a mass within the right frontal lobe causing a midline shift of approximately 10 mm and slight impingement of the right midbrain. The scan also shows that the entire length of both A1 and M1 segments, and one of the M2 branches were involved.

Figure 3 L ICA angiogram (AP view) shows no cross-flow to the right hemisphere.

Figure 4 A) Post balloon occlusion angiogram (common carotid injection, early arterial phase) shows the superficial temporal to middle cerebral arterial anastomosis (black arrow). B) Post balloon occlusion angiogram (common carotid injection, late arterial phase) shows the retrograde flow to the aneurysmal sac (black arrowhead).

GSA and MEN 1 syndrome are exceptionally rare entities. Their co-existence has never been described in the literature and could be coincidental or imply a metabolic relationship that could trigger the cascade.

Our case was interesting from the therapeutic point of view as well. Untreated aneurysms have an unpredictable course, but many of them have a relatively poor prognosis (neurological deterioration, death). Therefore treatment of this rare condition is of crucial importance. The aim is to eliminate the mass effect by obliteration of the vascular channel and its exclusion from the intracranial circulation. The most effective way of doing that is the permanent occlusion of the parent vessel with surgical (carotid ligation) or endovascular procedures (detachable balloons or coils).

Other alternative therapeutic methods, such as endovascular trapping of the aneurysm or ECA/ICA by-pass only, have also been performed^{2,13,14}. Prior to this procedure, a balloon occlusion test is required to evaluate intracranial haemodynamics. If the test occlusion is not tolerated, then an ECA/ICA by-pass is performed prior to the embolization to improve the blood supply to the affected hemisphere.

In our case, we did not proceed with the balloon occlusion of the carotid, although our patient clinically passed the test, when the balloon was inflated proximal to the ophthalmic artery. The reason was twofold.

a) He was unable to tolerate the occlusion distal to the level of ophthalmic artery, as he became dysphasic and developed an immediate left-sided weakness and

b) there was an angiographic failure of the test, as there was no filling from the contralateral side, or the posterior circulation. It has been reported that the angiographic testing for tolerance to therapeutic occlusion of the carotid artery, with synchronous opacification of the hemispheric cortical cerebral veins, proved to be the most reliable factor, predicting tolerance to the occlusion¹⁵.

For the balloon occlusion we used a Gold-valve balloon which actually caused a problem during its detachment. We used the same balloon for the balloon occlusion test prior to the final detachment and permanent balloon occlusion. We had planned to detach the balloon proximal to the right ophthalmic artery (the one major collateral route that had worked prior to the by-pass) since in the initial test the patient did not tolerate the occlusion at the level of the ophthalmic artery. Therefore, we tried to deflate it and re-position it at a lower level after the second balloon occlusion test (performed prior to the final treatment and after

Figure 5 A) CT Angiography (VRT algorithm) shows good patency of the ECA/ICA by-pass (white arrow). B) CT Angiography (VRT algorithm) reveals a retrograde filling of the entire right M1 and A1 lumen from the by-pass (white arrow). The lumen is of normal calibre. C) MRI (T1 weighted scan) again shows the mass within the right frontal lobe causing a midline shift of approximately 10 mm and slight impingement of the right midbrain.

the ECA/ICA by-pass), but due to malfunction of the balloon it was impossible to deflate it and we had no choice other than to detach it at the level of the ophthalmic artery. This unfortunate event which did not have any clinical sequel (thanks to the ECA/ICA by-pass) but could potentially have led to stroke, queries the usefulness of a non-detachable balloon for any occlusion test. Of course we have to remember that the advantage of using the same detachable balloon is that you do not need to deflate it at the end of the procedure, just detach it. On the other hand, in cases of non-detachable balloon, the static column of blood proximal to the balloon could develop a thrombus which could

embolize distally on deflation. This is probably very rare, but so is failure to deflate. Where does the balance lie? Probably it is a matter of opinion.

The 20-month clinical and radiological follow-up revealed that there was significant improvement of the 3rd nerve palsy, although the mass was still present. It is known that in such cases, removal of the pulsation pressure that the aneurysm produces on the adjacent brain, by occlusion of the parent artery, can lead to improvement of the clinical sequel even though the mass is still there. There was no evidence of further growth although it has been reported that recurrence can occur, even two years after

a successful ECA/ICA by-pass and ligation of the parent vessel, while in another case the aneurysm form changed variously over a ten year period^{16,17}.

Our case is interesting, not only because there is co-existence of two rare medical condi-

tions, which might imply a connection at the molecular level: a generalised metabolic upset that could trigger aneurysmal formation, but also emphasized the usefulness of the angiographic failure of the balloon occlusion test, even in the presence of a clinical success.

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