We report a very rare case of Williams syndrome accompanying moyamoya disease in whom postoperative global cerebral infarction occurred unpredictably, despite of conventional postoperative management of moyamoya disease.

CASE REPORT

A 9-year-old boy was presented with right hemiparesis after second operation for coarctation of aorta. He was diagnosed as having Williams syndrome at the age of 1 year. Brain MRI showed left cerebral cortical infarction, and angiography showed severe stenosis of bilateral internal carotid arteries and moyamoya vessels. To reduce the risk of furthermore cerebral infarction, we performed indirect anastomosis successfully. Postoperatively, the patient recovered well, but at postoperative third day, without any unusual predictive abnormal findings the patient’s pupils were suddenly dilated. Brain CT showed the global cerebral infarction. Despite of vigorous treatment, the patient was not recovered and fell in brain death one week later. We suggest that in this kind of labile patient with Williams syndrome accompanying moyamoya disease, postoperative sedation should be done with more thorough strict patient monitoring than usual moyamoya patients. Also, we should decide the revascularization surgery more cautiously than usual moyamoya disease. The possibility of unpredictable postoperative ischemic complication should be kept in mind.

Key Words : Moyamoya disease · Williams syndrome · Postoperative infarction · Ischemic complication.

INTRODUCTION

Williams syndrome is a rare neurodevelopmental disorder caused by a deletion of about 26 genes from the long arm of chromosome 7\(^\text{12}\). It is known to occur approximately 1 in 10,000 births\(^\text{5}\). It is characterized by a distinctive, "elfin" facial appearance, along with a low nasal bridge, an unusually cheerful demeanor and ease with strangers, developmental delay coupled with unusual language skills, and cardiovascular problems such as supravalvular aortic stenosis and transient hypercalcemia\(^\text{5,8,9}\).

In moyamoya disease, normocapnia, normotension, postoperative sedation and pain control are strictly controlled to prevent postoperative ischemic complications\(^\text{2,6,7,13}\). However, postoperative ischemic complications sometimes occur despite of maximum efforts to stabilize the hemodynamic states such as above\(^\text{2,6,7,13}\).

We report a very rare case of Williams syndrome accompanying moyamoya disease in whom postoperative global cerebral infarction occurred unpredictably, despite of conventional postoperative management of moyamoya disease.

CASE REPORT

A 9-year-old boy was presented with right hemiparesis after the second operation for coarctation of aorta. The patient was diagnosed as Williams syndrome at the age of one year due to supravalvular aortic stenosis. Chromosome study by FISH (Fluorescence In Situ Hybridization) confirmed that the deletion of genetic material from the region q 11.23 of chromosome 7. Also, he had a family history that his grandfather had been diagnosed as Williams syndrome. He underwent patch dilatation of aortic valve. After the surgery, he was followed up through pediatric department. Two months prior to this admission, he underwent second surgery for coarctation of aorta. Four days after that surgery, he suddenly experienced right hemiparesis.

Brain MR images showed infarction involving left frontal lobe, left putamen, right caudate nucleus and right frontal periventricular white matter (Fig. 1) Cerebral angiogram showed...
severe stenosis of bilateral internal carotid arteries and moyamoya vessels. (Fig. 2) Brain SPECT study at resting state showed decreased cerebral perfusion in the involved right periventricular white matter, left frontal cortex and left basal ganglia. And, brain SPECT study by Diamox injection showed that more decreased cerebral perfusion in the same lesions (Fig. 3). For one month after cardiac surgery, he experienced three recurrent attacks of right hemiparesis. Followed brain MRI showed newly appeared cerebral infarction involving left frontal lobe.

Surgical intervention was considered to be necessary to prevent development of additional cerebral infarction. Two months after surgery for coarctation of aorta, we performed encephalo-duro-arterio-synangiosis (EDAS) at the left temporal area and encephalo-galeo-synangiosis at the both frontal area successfully.

Postoperatively, the patient recovered well without neurological deterioration, and postoperative brain CT images revealed small left frontal cortical infarction (Fig. 4). The patient's clinical condition was same as preoperative status, but he was a little bit irritable. For this reason, we sedated the patient slightly and kept the blood pressures in normotensive state.

However, at postoperative third day, the patient's pupils were suddenly dilated without any unusual predictive abnormal findings. Brain CT performed one hour after the incident showed the global cerebral infarction (Fig. 5).

The patient was not recovered and fell in brain death one week later, despite of vigorous treatments.

**DISCUSSION**

Williams syndromes is caused by the deletion of genetic material from the region q 11.23 of chromosome 7[12]. The deleted region included more than 25 genes, and researchers believe that the loss of several of these genes probably contributes to the characteristic features of this disorder[2]. CLIP2, ELN, GTF2I, GTF2IRD1, and LIMK1 are among the genes that are typically deleted in people with Williams syndrome[5,9,12]. Researchers have found that loss of the ELN gene, which codes for the protein elastin, is associated with the connective tissue abnormalities and cardiovascular disease[5,9,12]

Because of the multiple genes that are missing in people with Williams syndrome, there are many effects on the cardiovascular abnormalities and brain.

Arterial narrowing may be isolated or may occur simultaneously in numerous locations, including the aortic arch, the descending aorta, pulmonary, coronary, renal, mesenteric, and intracranial arteries. In the literature reviews, brain MRI revealed an overall 10 to 15% reduction in cerebral volume, with preserved cerebellar volume[3,5,9,12].

To our knowledge, there was only one case report of moyamoya disease with Williams syndrome by the autopsy of the patient who suddenly died due to bilateral intraventricular hemorrhage[9]. In that first reported case, autopsy revealed an abnormal complicated cerebrovascular network in the cerebral arteries[9]. The narrowed vessels of the circle of Willis showed intimal thickening with an extremely wavy internal elastic lamina and marked thinning of the media[9].

Reports in the literature suggest that the histopathology of arterial stenosis associated with Williams syndrome are characterized by a prominent medial hyperplasia with variable degrees of intimal hyperplasia[1,9]. An increased intima-media thickness of carotid arteries, consistent with a generalized elastin arteriopathy, is present in all cases[3,9].

It is difficult to confirm the etiological relationship of postoperative global cerebral infarction between Williams syndrome and moyamoya disease.

Despite the best efforts of neurosurgeons including measures such as normocapnia, normotension, and proper postoperative interventions, surgical intervention was considered to be necessary to prevent development of additional cerebral infarction. Two months after surgery for coarctation of aorta, we performed encephalo-duro-arterio-synangiosis (EDAS) at the left temporal area and encephalo-galeo-synangiosis at the both frontal area successfully.

Postoperatively, the patient recovered well without neurological deterioration, and postoperative brain CT images revealed small left frontal cortical infarction (Fig. 4). The patient's clinical condition was same as preoperative status, but he was a little bit irritable. For this reason, we sedated the patient slightly and kept the blood pressures in normotensive state.

However, at postoperative third day, the patient's pupils were suddenly dilated without any unusual predictive abnormal findings. Brain CT performed one hour after the incident showed the global cerebral infarction (Fig. 5).

The patient was not recovered and fell in brain death one week later, despite of vigorous treatments.
sedation, children with moyamoya disease can experience serious postoperative ischemic attacks.\(^2,13\)

In fact, postoperative ischemic complications are closely related to hemodynamic instability in moyamoya disease. Many researchers have found that several factors such as hypercapnia, hypocapnia, hypotension and inadequate hematocrit level can increase the postoperative ischemic risks.\(^2,4,6,7,10,13\)

The incidence of postoperative ischemic complications had been reported to range from 3.7 to 22.2%.\(^2\) For preventing these ischemic complications, neurosurgeons have tried to maintain sustained normocapnia [\(\text{PaCO}_2\) (35-45 mmHg)], normotension [MABP (100-120 mmHg)], adequate hematocrit level (>30%) and postoperative sedation.\(^2,4,7,10,13\)

As previously described, we performed successful indirect revascularization surgery and kept sustained normocapnia, normotension, adequate hematocrit level and postoperative sedation due to irritability. The patient had favorable postoperative recovery, but the patient had whole brain infarction of unknown cause on the third day after the surgery.

The cause of unpredictable postoperative ischemia in this case is uncertain, but, endovascular problems of Williams syndrome such as medial and intimal hyperplasia were thought to played some roles in this incident. We thought that this vascular abnormality of Williams syndrome could be correlated with hemodynamic instability. Postoperative ischemic complication might be exacerbated by complex effects, between endovascular problems of Williams syndrome and unstable hemodynamic state of Moyamoya disease.

We thought that in this kind of labile patient of moyamoya disease with Williams syndrome, postoperative sedation should be done more cautiously through strict patient monitoring such as brain oximeter monitoring, frequent examination of neurological state with more shorter interval than usual. And, postoperative patient monitoring such

---

**Fig. 3.** Brain SPECT at resting state (A and B) shows decreased cerebral perfusion in the involved right periventricular white matter, left frontal cortex and left basal ganglia. Brain SPECT study by Diamox injection (C and D) shows that more decreased cerebral perfusion in the same lesions.
as measurement of arterial blood pressure via an arterial catheter, measurement of cardiac filling pressures via a flow-directed pulmonary artery catheter, and continuous assessment of arterial and mixed venous oxygen saturation via pulse oximetry and an oximetric pulmonary artery catheter, are needed for stable hemodynamic state with regard to coartation of aorta.

In reviewed literature, surgery within 6 weeks after the last ischemic attack of infarction showed a higher incidence of postoperative ischemic complications. But, in this case, the patient experienced three recurrent attacks of right hemiparesis for a month after the cardiac surgery. Therefore, we thought that early surgical intervention was inevitable to prevent development of additional cerebral infarction.

But in this labile patient who have cardiovascular abnormalities such as Williams syndrome, the surgeons should recognize the possibility of these unpredictable postoperative ischemic complications, and decide the revascularization surgery more carefully with consideration of benefits and risks.

CONCLUSION

Williams syndrome is a rare disease which includes cerebrovascular abnormalities, and cardiovascular complications are the major cause of death in patients with Williams syndrome. Our case is second report for Williams syndrome accompanying moyamoya disease.

It is difficult to confirm the etiological relationship of unpredictable postoperative ischemic complication between Williams syndrome and moyamoya disease.

But, we suggest that in this kind of labile patient of moyamoya disease, the perioperative treatment should be done more carefully through more strict patient monitoring.

In treatment of moyamoya disease, preoperative detailed evaluation for other combined cerebrovascular abnormalities should be needed, because of the possibility of unpredictable postoperative complications such as our case. In the clinical setting with the patient having other cerebrovascular abnormalities such as Williams syndrome, the neurosurgeons should carefully consider the benefits and risks of surgery related to these underlying problems. Also, when the revascularization surgery in this kind of labile patient is decided, surgeons should be more kept in mind for possibility of unpredictable postoperative complication than usual moyamoya patients.

• Acknowledgements

This work was supported by Chungbuk National University Grant in 2009.

References