Rapid Resolution Of Symptoms After Transient Ischemic Attack And The Circle Of Willis.
S Furukawa, A Takaya, T Nakagawa, I Sakaguchi, K Nishi

Abstract
A case of a transient ischemic attack is reported in which the focal neurological symptoms and signs resolved within 2 hours. The patient’s symptoms appeared suddenly and were in a vascular territory, suggesting an ischemic vascular event. Magnetic resonance imaging (MRI) revealed an infarct on the right side of the corona radiata and internal carotid artery stenosis. The circle of Willis was completely formed. The circle of Willis is considered an important collateral pathway in maintaining adequate cerebral blood flow. To investigate the anatomic variation of the circle of Willis, 200 subjects underwent magnetic resonance angiography (MRA) and the morphology of the circle of Willis was compared with autopsy data from 55 individuals. This study illustrates the prevalence of anatomical variations of the circle of Willis, with only 7% of the individuals studied by MRA and only 33% of the subjects studied at autopsy having an entirely complete circle of Willis. The important results of the study is that only few brains examined possessed a normal complete circle of Willis. The relationship between the circle of Willis and the remission time of symptoms was investigated.

INTRODUCTION
A transient ischemic attack (TIA) is a syndrome characterized by the sudden onset of discrete neurological symptoms which resolve completely within 24 hours. A patient presenting with a TIA is at high risk of subsequent adverse events. The 90-day risk of stroke has been reported to be greater than 10%, with the highest risk occurring in the first 2 days [1]. If small vessel disease, brainstem events, or transient symptoms are suspected, MRI especially with diffusion-weighted images (DWIs) would be superior for defining the ischemic site and topography. Diffusion-weighted imaging (DWI) can reveal focal ischemia within 30 minutes to 1 hour after symptom onset and may show abnormalities in patients with transient symptoms [2]. MR angiography (MRA) has evolved notably during the past 10 years with improved sensitivity and specificity for identifying stenoses and types of pathology. The sensitivity and specificity of MRA to detect a greater than 50% stenosis of the intracranial arteries is approximately 88% and 96%, respectively. A 66-year-old man, presented to the emergency department after experiencing the sudden onset of slurred speech associated with left hemiplegia. Diffusion-weighted MRI revealed an acute infarct in the right corona radiata, and MRA showed an occlusion of the internal carotid artery (ICA). (Fig.1, Fig.2) However, the symptoms only lasted about 2 hours and had completely resolved by the time of examination so that he patient did not qualify for treatment with tissue plasminogen activator (tPA). (Fig.3) The blood pressure was 130/80 mmHg. Initial CT of the head was normal. The results of laboratory tests, including complete blood count (CBC), electrolytes, prothrombin time, and erythrocyte sedimentation rate, were normal and an electrocardiogram (ECG) revealed normal sinus rhythm. The patient was a non-smoker, and did not use drugs except for antihypertension or alcohol. There was no history of diabetes, coronary artery disease or hyperlipidemia. The afferent blood supply travels into the brain through the left and right common
carotid arteries (CCAs) and through the left and right vertebral arteries (VAs). Linking these arteries are the efferent arteries, the anterior communicating artery and the two posterior communicating arteries. These so-called collateral-arteries essentially form a structure known as the circle of Willis (CW), which is named after the seventeenth century physician Thomas Willis (1621–1675) and is best known for his description and configuration of the CW [3,4,5,6].

In patients with obstruction of the ICA, numerous collateral pathways redistribute blood to the deprived side and maintain adequate cerebral blood flow. The development of such detour routes depends on individual morphological and hemodynamic factors. The anterior communicating artery (ACoA) and the bilateral posterior communicating arteries (PCoAs) are component vessels of the CW and are designated as the primary collateral pathways.

There is considerable variation in the presence and morphology of the arterial segments of the CW. On the anterior side, the anterior communicating artery or one of the A1 (proximal) segments of the anterior carotid arteries (ACA) can be missing or hypoplastic and on the posterior side, the PCoA can be unilaterally- or bilaterally absent. Arterial abnormalities of the adult CW are associated with morphological variations [7,8,9,10]. The risk of cerebral ischemia is increased in a patient with an incomplete, nonfunctioning circle [11,12]. MRA can give reliable data about the intracranial circulation, thus making it possible to assess collateral flow. Previous studies have shown that MRA is well-suited to investigate the CW as it is able to provide accurate morphological and hemodynamic information concerning blood flow direction in individual vessels [13,14].

The aim of this study was to evaluate the prevalence of anatomical variations of the CW. The study is based on the data obtained from postmortem autopsy and the MRA of the cerebral arteries, and focuses especially on the anatomy of the CW.

**MATERIALS AND METHODS**

The study population consisted of 107 males and 93 females (mean age 61.9 years, age range 20-89 years) who were referred to the magnetic resonance (MR) unit. Patients were excluded if they had severe vertebral or basilar artery lesions (as detected by intra-arterial digital subtraction contrast angiography) or had been diagnosed with a dissection. All subjects gave signed informed consent and approval was obtained from the institution’s ethics committee on scientific research on human subjects. The procedures followed were in accordance with institutional guidelines. The autopsy data of 55 individuals (mean age of 68.9 years, age range 37-96 years, 31 males and 24 females) were collected as a part of normal forensic medical autopsies. The subjects had died of natural or traumatic causes and were candidates for autopsy because of medico-legal reasons. The study was approved by the ethical committee of the university and hospital, but the ethics committee waived the need for consent from the patients’ next of kin because the autopsy was dictated by law.

The following vessels, which form part of the CW, were examined in the study: the anterior communicating artery (ACoA), the precommunicating part of the anterior cerebral arteries (A1), the precommunicating part of the posterior cerebral arteries (P1), and the posterior communicating arteries (PCoAs). Whether the P1 segment (a small connection between the carotid system and the vertebrobasilar system) is present or absent is important. Hypoplastic vessels are defined as vessels with an external diameter of less than 1 mm [13]. The parts of the circle of Willis were classified as deficient if one of the component vessel segments was absent or hypoplastic (i.e., having a diameter measuring less than 1mm). Diameter measurements were
performed on transverse slices of the 3-dimensional time-of-flight (3D TOF) MRA data set for the ACoA, the A1 segments of the ACAs, the PCoAs, and the P1 segments of the posterior cerebral arteries (PCAs). The computer software Osiris (downloadable for free from the World Wide Web) was used to measure the external diameter of the vessels, according to the metric scales placed along the plane of the vessels. These measurements were done on multiple images of the circle of each patient. For classification purposes in this study, segments without hypoplasia were considered normal segments. The percentage of complete circle parts was calculated. Segmental variations were also studied, performed on cadaveric brains during autopsy and performed on living individuals using MRA.

Table 1. The morphology of the circle of Willis (CW).

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<thead>
<tr>
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<th>Complete</th>
<th>Incomplete</th>
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<tr>
<td><strong>Anterior part of the CW</strong></td>
<td>MRA study (N = 200)</td>
<td>91 (45.5%)</td>
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<td>Autopsy study (N = 55)</td>
<td>45 (81.8%)</td>
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<tr>
<td><strong>Posterior part of the CW</strong></td>
<td>MRA study (N = 200)</td>
<td>21 (10.5%)</td>
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<tr>
<td></td>
<td>Autopsy study (N = 55)</td>
<td>25 (81.8%)</td>
</tr>
<tr>
<td><strong>All parts of the CW</strong></td>
<td>MRA study (N = 200)</td>
<td>14 (7.0%)</td>
</tr>
<tr>
<td></td>
<td>Autopsy study (N = 55)</td>
<td>18 (32.7%)</td>
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**Figure 2**
Fig. 1. Diffusion-weighted MRI showing an acute infarct in the right corona radiata.

**Figure 3**
Fig. 2. MR angiogram (MRA) shows the right internal carotid artery (ICA) occlusion.

**Figure 4**
Fig. 3. MRA taken 2 hours after the sudden onset of the symptoms revealing that a collateral pathway has developed.

**Figure 5**
Fig. 4. Image of an incomplete cerebral arterial circle with a hypoplastic right PCoA (autopsy).
Figure 6
Fig. 5. MRA with absent or hypoplastic bilateral PCoAs.

RESULTS AND DISCUSSION
This study illustrates the prevalence of anatomical variations of the CW, with only 7% of the individuals studied by MRA and only 33% of the subjects studied at autopsy having an entirely complete CW. (Table. 1)

Figure 4 (autopsy study) shows an example of an incomplete cerebral arterial circle with a hypoplastic right PCoA and Fig. 5 (MRA study) shows an example with absent bilateral PCoAs. The important results of this study is that only a few brains examined possessed a normal complete CW.

CASE STUDY
A 66-year-old man was admitted to hospital 1 hours after suffering weakness of the left arm and leg, and slurring of speech due to a right-hemisphere transient ischemic attack (TIA). On examination the symptoms had completely resolved and only 2 hours later there was no weakness or sensory impairment.

Normal cerebral blood flow in humans is approximately 50-60mL/100g of brain tissue per minute. When flow decreases to less than 10-15mL/100g per minute, irreversible tissue damage occurs. Because of extensive collateral blood flow in the brain, there is variability in perfusion changes within an ischemic lesion. In cases of unilateral absence of the ICA, the collateral circulation is sufficient to maintain cerebral function with little or no neurological damage.

The results of the present study were influenced by at least three factors. Firstly, the subjects were not age- and sex-matched (the autopsy group had a mean age of 68.9 years and was 56.4% male, the MRA group had a mean age 61.9 years and was 53.5% male), secondly, 3D TOF MRA has a lower sensitivity for detecting low or turbulent flow and thirdly, the so-called hypoplastic vessels may change to vessels having a diameter larger than 1mm over time. This study gives a snapshot of the circle using the arbitrary definition of 1mm as the criterion for differentiating hypoplastic segments. As the mean age difference between the autopsy and MRA subjects was only 7.0 years in this study, a mismatch in the mean age of these populations cannot account for the large differences in the mean diameter of the vessels.

A second important aspect of the present study is related to the use of 3D TOF MRA in evaluating the presence of small intracranial arteries. It is well known that the sensitivity of 3D TOF MRA decreases when the blood flow velocity decreases, therefore the prevalence of complete CW configurations in the MRA study subjects may have been underestimated because of the impaired visualization of functional communicating vessels [15]. Some vessel segments are consequently classified as hypoplastic or absent. As a result, a complete circle of Willis was only visualized in a low percentage in the MRA study, relative to the autopsy study. The symptoms of the MRA group subjects (n=200) included headache (n=14), vertigo (n=11), depression (n=4), and epilepsy (n=2). Therefore, it remains unclear whether collateral cross-flow leads to an overestimation or to an underestimation of the vessel diameters on MR angiograms.

Fisher [16] and many others believe that a 1mm diameter may be adequate for an artery to carry collateral flow to a small territory of the brain.
Some authors have criticized this threshold and suggest that the term hypoplasia should be reserved for those vessels which cannot supply a collateral flow [17]. The cases in this study were selected from autopsies carried out on subjects for whom the apparent cause of death was either natural or traumatic and it is uncertain whether the postmortem measurements are similar to those in living people. Some technical considerations may minimize the potential sources of error. The measured diameters of collapsed vessels may be less precise than, or different from, the diameters measured after the removal of the circles and compressing them between glass plates, subjecting them to formalin fixation, or using injection techniques. Macchi et al. [18] in a MRA study of 100 healthy subjects (involving 50 men and 50 women) found no statistically significant difference in the frequency of variation between the two genders. Alpers and Berry [19] reported that at autopsy only 33% of brains with cerebral softening demonstrated a normal configuration of the CW. Riggs and Rupp [20] investigated brains after autopsy taken from adults who had shown evidence of neurological dysfunction before death and classified 21% of the subjects as having a normal arterial CW. There is also some evidence that patients who suffer ischemic stroke in the anterior circulation have an even higher incidence of collateral deficient circle of Willis than patients with atherosclerotic disease without ischemic cerebrovascular disease [21]. The percentage of complete circles in living patients with an ICA obstruction compared with the autopsy population (as described by Alpers and Berry [19] and Riggs and Rupp [20]) is likely due to the use of 3D TOF MRA and to differences among the patient populations being studied. Miralles et al. [22] concluded in their study that the relative risk of hypoperfusion infarction is significantly higher in patients with a non-functioning ACoA. Schomer et al. [23], however, concluded that the presence of a large unilateral PCoA was the only feature that correlated significantly with the absence of a watershed infarct and that the role of the PCoA appears to be more important in preventing cerebral ischemia. In patients with bilateral ICA occlusion, the vertebrobasilar arteries supply a significantly larger part of the MCA and ACA flow territories [24]. In functionally independent patients with symptomatic ICA occlusion, the middle cerebral artery flow territory ipsilateral to the occluded ICA is mainly supplied by the vertebrobasilar arteries, whereas the anterior cerebral artery flow territory on the occluded side is mainly supplied by the contralateral ICA [24]. The variation in the flow territories of the contralateral ICA and vertebrobasilar arteries in patients with unilateral ICA occlusion is partly caused by differences in the collateral flow pattern in the circle of Willis [24]. From this case report and our study of circle of Willis, we think that the complete circle of Willis increase collateral blood flow and shorten the remission time of the symptoms.

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