A Review of Vertebrobasilar Dolichoectasia

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Abstract: Vertebrobasilar dolichoectasia (VBD) is an uncommon vasculopathy of unclear aetiology affecting the arterial wall of vertebral and/or basilar arteries, which is easily misdiagnosed. The review summarizes research datas of VBD in recent years respectively from epidemiology, etiology and pathology, diagnosis, clinical manifestation and mechanism, treatment and prognosis, aiming to provide basis for the further study of VBD.
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Vertebrobasilar dolichoectasia (VBD) is an arteriopathy characterized by distinct dilatation, elongation and tortuosity of the basilar artery (BA) and the vertebral artery (VA). In 1986, Smoker(Smoker, Corbett et al. 1986) firstly proposed the concept of VBD. In 2005, Caplan (Caplan 2005) amended the concept of VBD, which replacing the previous name of 'Vertebrobasilar system tortuosity', 'Vertebrobasilar prolonged expansion', 'Huge extended aneurysm malformation', 'Arterial variation and fusiform aneurysm' and others.

Epidemiology

The incidence of VBD in the general population is 0.06% to 5.8% (Yu, Moseley et al. 1982, Dziewasa, Freund et al. 2003). For different study populations, the incidence of VBD exists difference as well. While the incidence of asymptomatic VBD is 1.3 % by the conventional MRI and MRA examination (Ikeda, Nakamura et al. 2010). The incidence of VBD is approximately 2.06% for the first stroke population (Ince, Petty et al. 1998), the incidence is 3.7% for the patients with posterior circulation infarction (Kumral, Kisabay et al. 2005),while the incidence of VBD is 6% by autopsy for the patients with fatal stroke (Pico, Labreuche et al. 2007).However, the overall incidence is 12 % for the ischemic stroke patients with intracranial arterial dolichoectasia (Pico, Labreuche et al. 2005). The Asian studies show that the incidence of VBD is 7.7% in stroke patients in Japan, of which the incidence of ischemic stroke is 6.4%, hemorrhagic stroke is 12.1% (Nakamura, Hirayama et al. 2012). Korean data suggests that the incidence of VBD is 18.8% in patients with pontine infarction(Kwon, Kim et al. 2009).

Etiology and pathology

Etiology

The research on VBD etiology are inconclusive, the results are even conflicting. The occurrence of VBD may be the result of the congenital factors, immune factors and degenerative disease interacting. VBD may be related to some congenital diseases, the study of Schievink (Schievink, Torres et al. 1997) has shown that the VBD incidence of polycystic kidney, a kind of autosomal recessive genetic disease, is much higher than those without this disease. In addition, there are also some case reports of VBD associated with Sickle-cell anemia, Marfan syndrome, pompe disease, Fabry disease, Ehlers-Danlos syndrome, abdominal aortic aneurysm and coronary dilatation. Toyoshima (Toyoshima, Emura et al. 2012) states that VBD may be a related 194 autoimmune diseases. VBD may also be the result of progression of fusiform aneurysm and arteries dissection(Anson, Lawton et al. 1996).In the past the atherosclerosis is considered to be the main risk factor of VBD, because some acquired risk factors of VBD are similar with atherosclerosis (Gutierrez, Sacco et al. 2011), such as female, hypertension, myocardial infarction, lacunar infarction (Pico, Labreuche et al. 2003) and smoking (Nakamura, Hirayama et al. 2012). But now research suggests that atherosclerosis is not likely to be the major risk factor of VBD. Because atherosclerosis and hypertension are common, the VBD incidence is very low. Pico(Pico, Labreuche et al. 2003) even proposed that expansion of intracranial artery is irrelevant to the atherosclerosis. Furthermore the early pathology of VBD and atherosclerosis is different, atherosclerosis is based on lipid infiltration and intimal hyperplasia, while the main pathology of VBD is crushing and thinning of elastic layer, so they are different diseases (Nakatomi, Segawa et al. 2000). So far, there is no evidence to suggest that VBD has inevitable relation with intracranial artery atherosclerosis (Pico, Labreuche et al. 2007, Vasovic, Trandafilovic et al. 2012).

Pathology

The blood vessels of VBD patient lack of middle layer elastic tissue and the inner elastic layer is degenerated under the microscope, which result in the

artery wall dolichoectasia in long-term impact of blood flow, hypertension can accelerate this process. The arterial tree of VBD patients is prone to be abnormal, such as the aortic arch plaques, basilar artery plaques, thoracic aortic diameter enlarged, abdominal aortic aneurysm and coronary artery dilation(Pico, Labreuche et al. 2004, Pico, Biron et al. 2005). One study finds that the MMP-3 levels of plasma decrease in VBD patients (Pico, Jacob et al. 2010).MMP can break internal elastic layer of artery, damaging the mesh of fiber connecting with protein on the walls of blood vessels, then promote smooth muscle cells to migrate to the middle layer under pressure and further results in destruction of the internal elastic layer and intima, finally the blood vessel walls tend to expand (Rosenberg, Sullivan et al. 2001). Compared to the anterior circulation, posterior circulation is easier to be involved in VBD. It may be related to the distribution of neurotrophic support. There is less sympathetic innervation in posterior circulation than anterior circulation and the asymmetry of innervation on the walls of blood vessels expose the the vessels of posterior circulation to high pressure of blood flow, which making vessels more easily to be deformed.

Diagnosis

Some studies show that the basilar artery and vertebral artery diameter are different for Chinese male and female. The basilar artery and vertebral artery diameter of Chinese male are respectively 2.2 ~ 4.2 mm and 2.0 ~ 4.0 mm, while Chinese female are 1.4 ~ 3.4 mm and 1.1 ~ 3.1mm (Deng, Cheng et al. 2012). However an autopsy study abroad showed that the basilar artery diameter is 3.51 ~ 8.92 mm and vertebral artery diameter is 0.67~5.91mm(Vasovic, Trandafilovic et al. 2012). So vertebrobasilar shape, length and diameter are discrepant for different populations and gender (Deng, Cheng et al. 2012). There were no uniform diagnostic criteria for VBD so far, VBD diagnosis mainly according to imaging and the common diagnostic criteria used now are the following two.

CT

It often indicates the presence of VBD if CT scan finds the basilar artery calcification, but CT cannot fully demonstrate the changes of thrombosis of the blood vessel walls.

CT criteria proposed by Smoker et al(Smoker, Price et al. 1986): If the basilar artery is beyond the slope or saddle back, or basilar artery bifurcation point is beyond the suprasellar cistern, and the basilar artery diameter at any point is greater than 4.5 mm, then it can be diagnosed as VBD.

MRA

MRA is not only capable of displaying brainstem compression derived from vertebrobasilar, but also can be more clearly to show thrombosis and the decrease of blood flow speed. The criteria were proposed by Ubogu and Zaidat (Ubogu and Zaidat 2004).

MRA criteria: ectasia of the vertebrobasilar system was defined as arterial diameter>4.5 mm in any location along its course. For the basilar artery (BA), bifurcation above the suprasellar cistern or evidence of any portion lateral to the margin of the clivus or dorsum sellae was considered elongated (Smoker, Corbett et al. 1986, Giang, Perlin et al. 1988). Measurements on the MRA source images using the above neuroanatomical landmarks, prior to 3 dimensional TOF arterial reconstruction and direct MRA measurements, revealed that a length>29.5 mm or lateral deviation >10 mm perpendicular to a straight line joining the BA origin to its bifurcation on MRA was abnormal. Using the aforementioned technique, VA on intracranial MRA were considered elongated if the length was>23.5 mm. Any portion of the VA with deviation >10 mm perpendicular to a straight line joining its intracranial entry point to the BA origin was considered abnormal.

Other imaging diagnosis

Currently more imaging technologies are used for VBD diagnosis (Ubogu and Zaidat 2004, Kumral, Kisabay et al. 2005, El-Ghandour 2010, Lou and Caplan 2010). CTA can clearly show the relationship between vessels route and bone structure, but cannot reveal structures of peripheral nerve and hemodynamics. As the gold standard for the diagnosis of cerebrovascular disease, DSA can not only show the lesion clearly, but also can be used as a method of treatments, although it means greater trauma and high-risk. Transcranial doppler sonography (TCD) can reveal the attenuation of blood flow of anterior and posterior circulation and the pathology of abnormal vessels.

Clinical manifestations

Clinical manifestations are various and non-specific. Ischemic stroke is the most common, followed by brain stem and cranial nerve compression, hydrocephalus, cerebral hemorrhage(Flemming, Wiebers et al. 2005, Passero and Rossi 2008). Severity of symptoms depends on the patient's age and the location of lesions. Previous studies suggest that cases charactered by the diameter expansion of blood vessels are more likely to occur stroke, while compression symptoms can be found more common in cases featured by tortuous expansion(Passero and Rossi 2008).

Stroke

Ischemic stroke

The most common clinical symptoms of

VBD is ischemic stroke, the incidence is about 48%, mainly charactered by posterior circulation ischemia (Levine, Turski et al. 1995) . From large vessels to deep perforating branches could all be involved, which may occur in the cerebellum, pons, medulla oblongata and thalamus. Cerebral hemisphere infarction is not uncommon. VBD is also the most common cause of death in patients with posterior circulation ischemia (Flemming, Wiebers et al. 2005, Passero and Rossi 2008), and risk of ischemia recurrence is high. Flemming et al. found that annual recurrence of ischemic stroke was 6.7 %. Passero (Passero and Filosomi 1998) studied 40 VBD cases with infarction and 40 cases without infarction, and found 60% located in infratentorial area, 40% located in supratentorial area. These patients clinically manifested as lacunar infarction syndrome, paralysis, partial anesthesia, Weber syndrome, Raymard syndrome, Wallenberg syndrome, occipital headache, sudden tinnitus etc. The pathogenesis includes the following aspects (Flemming, Wiebers et al. 2005, Kumral, Kisabay et al. 2005, Passero and Rossi 2008): (1) Blood flow of vertebrobasilar artery in VBD cases is bidirectional, leading to reduction of forward blood flow. Although the peak flow rate is relatively constant, the average flow velocity reduced, resulting in hypoperfusion of its blood supply area. (2) The blood flow velocity decrease of the expanded artery can cause thrombosis, and blood clots move with the blood flow into the distal vessels or occlude opening of perforating artery, which causing infarction. (3) Hemodynamic changes of the vertebrobasilar artery result in endothelial injury and the formation of atherosclerotic which could block blood vessels after falling off. (4)The artery of VBD pulls and twists the branch vessels, especially the branch of the basilar artery, decreasing the blood flow of these perforating arteries.

Hemorrhagic stroke:

Cerebral hemorrhage of VBD patients primarily results from the dolichoectasia of vessels, intimal damage and rupture of the vascular wall (Passero, Rossi et al. 2001).Arterial dissection and fusiform aneurysms are also important causes of hemorrhage, including cerebral hemorrhage and subarachnoid hemorrhage. Passero (Passero, Calchetti et al. 2005) conducted a prospective study of 156 VBD patients with an average follow-up of 9.35 years. 28 cases occurred in patients with intracerebral hemorrhage (6 cases of subarachnoid hemorrhage), including 4cases of rebleeding, of which the most common type is thalamic hemorrhage, followed by occipital lobes, brainstem and cerebellum. Subarachnoid hemorrhage often occurs around mesencephalon(Passero, Calchetti et al. 2005). Multivariate analysis revealed that intracranial hemorrhage is associated with vascular diameter, the extent of basilar artery excursion, hypertension, anticoagulation, antiplatelet and female.

GENIC (Pico, Labreuche et al. 2006) found that stroke mortality hazard ratio increased 1.23, as basilar artery diameter increases for additional 1mm. If the diameter is greater than 4.3mm, stroke mortality hazard ratio was 3.69. If the score of the basilar artery bifurcation height is greater than 1, the hazard ratio was 2.08. However, the risk seems to be no relationship with the lateral displacement of the basilar artery. So the degree of extension and dilation of basilar artery are directly related to the prognosis of stroke.

Compression symptoms

Brainstem in compression:

Because VBD brainstem oppression is gradually progress, the course of the disease is slow. Sometimes expansion is serious and mass effect is very obvious, but the patients don't show obvious clinical symptoms because the brain stem can gradually tolerate to the situation(Pereira-Filho, Faria et al. 2008). Therefore, the clinical manifestations are not entirely consistent with the severity of compression. Expansion of the basilar artery can directly oppress medulla oblongata and pons, causing transient or persistent symptoms in movement, like weakness, dizziness, ataxia, tingling, tinnitus, hoarseness, dysphagia, slurred speech, headache, etc. It can also be performance of apnea, cerebellar ataxia (Savitz, Ronthal et al. 2006). If the basilar artery bifurcates is above the saddle compartment and violates the third ventricle, then hydrocephalus is more likely to occur (Siddiqui, Chew et al. 2008).

Cranial nerve compression:

The facial nerve and the trigeminal nerve are most likely to be involved, mainly manifest as trigeminal neuralgia and hemifacial spasm(Noma, Kobayashi et al. 2009, Jimenez Caballero and Casado Naranjo 2012), followed by auditory nerve and oculomotor nerve involved. The probability occurrence of cranial nerve compression caused by VBD is not consistent. For example, some studies show that only 0.7% of the patients with hemifacial spasm is caused by VBD oppression(Han, Chang et al. 2009). Multiple cranial nerve involvement is not uncommon, especially nerves associated with the eye movement.

Obstructive hydrocephalus:

Levine (Levine, Turski et al. 1995) (31%) indicated that this symptom was mainly due to the cerebrospinal fluid circulation disorder by VBD which directly or indirectly oppresses Monro hole, the bottom of the third ventricle or the cerebral aqueduct(Jamjoom, Rawlinson et al. 1990, Siddiqui, Chew et al. 2008, Kansal, Mahore et al. 2011). Hydrocephalus caused by directly oppression of VBD is showed obvious

obstruction on imaging. Siddiqui et al reported one case of this obstructive hydrocephalus. Another kind of hydrocephalus has no obstruction on imaging. Breig indicated that this kind is mostly functional. The mechanism is the basilar artery produces a 'water hammer' effect in the bottom of the third ventricle, offsetting or interfering with the pump pressure of cerebrospinal fluid from the third ventricle. That causes the slow progress and the normal pressure hydrocephalus of the third ventricle and the lateral ventricles, which is non-communicating nor obstructive

Treatment and prognosis

The treatment of VBD includes medical and surgical treatment. VBD usually occurs in the deep part of brain and often involves the entire vertebral basilar artery, besides there are a lot of important blood vessels throughout vertebrobasilar artery, so it's very difficult for treating VBD. There is no systematic large-scale study for the treatment of VBD by drugs, surgery or interventional operation. It's lack of large-scale randomized controlled trial for anticoagulation and antiplatelet therapy. There are some reports (Ferreira, Walcott et al. 2011) on the VBD compressing cranial nerve by bypass surgery or decompressive surgery, while there is no reports to confirm whether this method can be used for VBD compressing brain stem. In spite of some case reports by effective interventional operation when drugs don't work are reported (Wu, Xu et al. 2013), but there is still a long way to go for interventional operation. The treatment principles of the acute phase of VBD haven't been reported, while the precautionary principle of the chronic phase of VBD is similar with atherosclerotic disease. VBD patients are prone to have cerebrovascular disease, so the secondary prevention of cerebrovascular disease should be focused on for VBD patients. At present symptomatic treatment is mainly practiced. The benefits of surgery is still needed to be defined further, especially more evidence is needed to support the decision whether to do surgery before making clinical decision, since there may be potential complications and uncertain clinical prognosis after surgery. VBD patients should be promptly tracking imaging changes and closely observed the occurrence of vascular events.

Several studies indicate that VBD is progressive disease. 43% of VBD patients exacerbate during follow-up and the mortality is high, especially those patients with rapid expansion. The most common cause of death is stroke (Passero and Rossi 2008). Unfortunately, the factors leading to exacerbate is not clear and the VBD prognosis is not optimistic. 50 % of Patients with vertebrobasilar artery continuing to expand have bleeding artery walls. Another study suggests that about 20% of VBD patients with compression symptom occur compression symptom again during the study period, while 15.8% of patients with no compression symptom at first occur compression symptom later(Rosenberg, Sullivan et al. 2001). The 1-year, 5 -year and 10-year incidence of stroke are respectively 2.7%, 11.3% and 15.9% (Flemming, Wiebers et al. 2005).

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