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Ischemic Stroke in a Young Adult Female Caused by Takayasu's Arteritis: A Case Report

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Abstract
Takayasu's arteritis is one of the causes of ischemic stroke at a young age, but the occurrence is still rarely reported in Indonesia. Here we report the case of a 19-year-old Indonesian female who was admitted to the Wahidin Sudirohusodo Hospital with a sudden onset of right-sided hemiplegia. Other features of Takayasu's arteritis were observed, including a discrepancy of more than 10 mmHg between the left and right arm systolic blood pressure, claudication of the extremities, and decreased brachial artery pulse. Left hemisphere cerebral infarction was confirmed on the computed tomography (CT) scan. Angiogram abnormalities were also present, showing occlusion of the left proximal inner carotid artery after branching at the aortic arch, and occlusion of the left subclavian artery. Although no fever was observed on presentation, the patient had an elevated erythrocyte sedimentation rate (ESR) of 44 mm/hour. In conclusion, Takayasu's arteritis should be considered as a potential cause of ischemic stroke in young adults.

Keywords: Takayasu, Arteritis, Young Female, Stroke

1. Introduction

Takayasu's arteritis is an idiopathic, granulomatous arteritis that mainly involves the aorta, branches of the main arteries and (more rarely) the pulmonary arteries. It is also known as pulseless disease, aortic arch syndrome, idiopathic or stenosing aortitis, aortoarteritis, and occlusive thromboartropathy (Da Cruz et al., 2014). The condition was first described by Mikito Takayasu in 1905, when he presented the case of a visually-impaired, young female patient with peculiar changes in her central retinal vessels. Minora Nakajima was the first person to propose the name "Takayasu Disease" in 1921 when he reported several patients with symptoms resembling those described in the Takayasu report. In 1990, the American College of Rheumatology published diagnostic

criteria (ARA criteria) for the disease and since then, the name "Takayasu Arteritis" began to be accepted around the world (Espinoza et al., 2018).

Takayasu's arteritis is rare, but has been found in various parts of the world with relatively similar incidents, ranging from 0.4 to 2.6 cases per million population. It is mostly found in women, and the highest prevalence rate is in Japan (40 cases per million population), whereas in other countries it ranges from 4.7 to 8.0 per million population (de Souza & de Carvalho, 2014). And whilst the age on onset can range from infancy to middle age, references have stated the highest incidence to be in the third decade, while some report a peak incidence of 15-19 years in female patients. Despite its rarity, Takayasu's arteritis is the most common large vessel vasculitis in children with a mortality rate as high as 35% (Hwang et al., 2012).

Takayasu's arteritis may present with various neurological manifestations including headaches (50-70%), syncope (4-19%), dizziness / vertigo (24-55%), visual disturbances (15-35%) and strokes (3-22%) (Chang & Hsieh, 2015). Although cerebral ischemia is not a common complication of Takayasu's arteritis, it can cause damaging neurological symptoms and is a major cause of unwanted events and early death (Maffei et al., 2006). During the progressive phase where there is fibrosis and thickening of the arterial walls, cerebrovascular abnormalities such as transient ischemic attacks and strokes can occur in about 10% to 20% of cases. However, stroke as an initial description of Takayasu's arteritis is rarely reported in the literature (Setty et al., 2017).

2. Case Presentation

A 19 year old female was brought to the emergency department of Dr. Wahidin Sudirohusodo Hospital in Makassar, Indonesia with a chief complaint of right typical hemiplegia, with a sudden onset of 3 hours. Prior to the onset, she initially felt weakness in the left arm which improved spontaneously, followed by syncope for approximately 5 minutes. After regaining consciousness, she was unable to move her right extremity. There was no history of headache, fever, head trauma, hypertension, diabetes mellitus and heart disease. Upon measurement of the vital signs we found a difference between the blood pressure of the right arm (110/70 mmHg) and the left arm (70/40 mmHg). The right radial pulse was 86 times/minute while the left pulse felt weak on palpation. The patient had a normal respiratory frequency of 20 times per minute, and a normal temperature of 36.6° Celsius.

On the neurologic exam, the patient was fully conscious with a GCS score of E4M6V5. No meningeal signs were found. There was central paresis of the right 7^{th} and 12^{th} nerve. On motoric examination, there was a lack of movement, and a decrease of muscle tone and physiologic reflex in the right extremities. Muscle strength assessment of the right hand and leg yielded a score of zero. The Babinsky's sign was positive on the right lower extremity. There was right hipesthesia, while the autonomic nervous system was not disturbed.

On the Head computed tomography (CT) scan (Figure 1), a cerebral infarction was found in the left cerebral hemisphere around the basal ganglia accompanied with minimal edema. The MSCTA examination (Figure 2) and cerebral angiography (Figure 3) of the head and neck showed occlusion in the proximal segment of the common carotid artery after the branching of the aortic arch, and occlusion in the proximal subclavian artery, and within the collateral of the V2 segment of the vertebral artery to the subclavian artery.

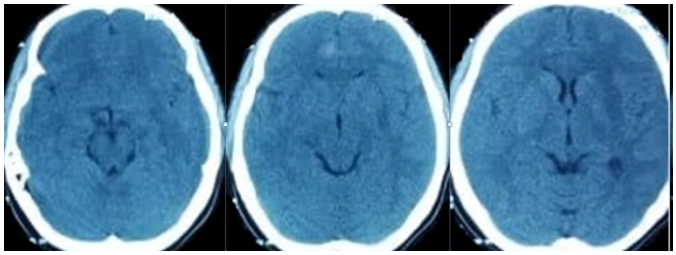

Figure 1: Head computed tomography (CT) scan results show hypodensity in the left cerebral hemisphere including the basal ganglia, internal capsule, external capsule, and frontal lobe.

The chest x-ray examination showed normal results. Echocardiographic examination showed good left and right ventricular systolic function, with an ejection fraction of 67.6%. Routine blood test showed a leukocyte count of

9200 / uL, erythrocyte count of 4.66 x 10^6 / uL, hemoglobin 11.8 mg/dL, platelet count of 400,000 mg / dl, sodium 141 mmol / L, potassium 3.7 mmol / L, chloride 108 mmol / l L, CRP 0.1 mg / l, GDS 88 mg / dl, urea 7 mg / dl, creatinine 0.73 mg / dl, prothrombin time (PT) of 10.5 seconds, INR 1.01, activated partial thromboplastin time (aPTT) of 26.2 seconds, HBsAg non reactive, anti HCV non reactive, lupus erythematosus (LE) cells are negative. An elevated erythrocyte sedimentation rate (ESR) was observed, with an ESR hour I of 44 mm, and ESR hour II of = 61 mm.

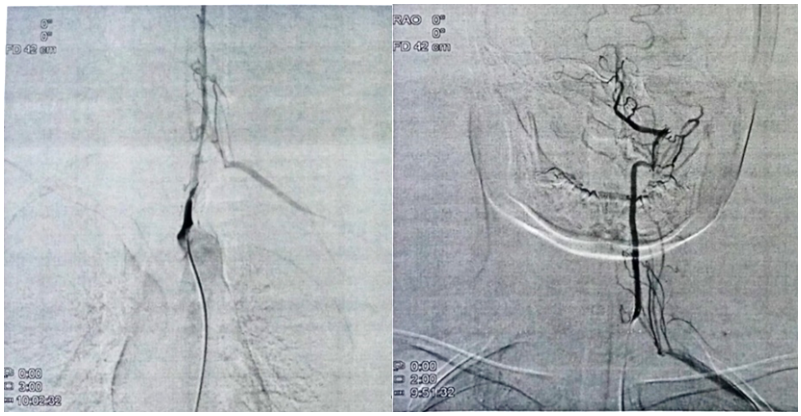

Figure 2: Multi-slice computed tomography (MSCT) angiography. Results show occlusion of the left proximal inner carotid artery after branching at the aortic arch, and occlusion of the left subclavian artery.

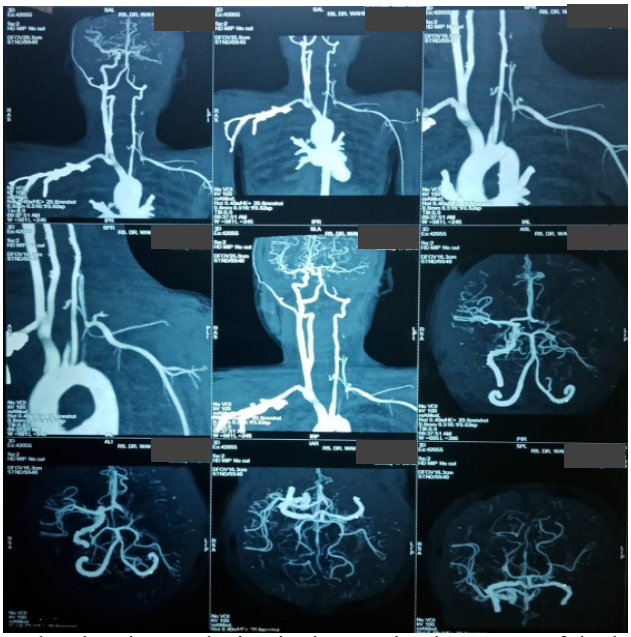

Figure 3: Cerebral angiography showing occlusion in the proximal segment of the left common carotid artery, and occlusion of the left subclavian artery. Collateral from the V2 segment of the vertebral artery to the subclavian artery can be visualized distal from the occlusion.

The patient was treated with antiplatelets and methyl-prednisolone, and was also given physical rehabilitation. After approximately 2 weeks of therapy, the patient showed slight clinical improvement in the form of increased hand motor strength. Until now the patient is still under our supervision.

3. Discussion

Takayasu's arteritis is a chronic, granulomatous, large blood vessel vasculitis, which mainly involves the aorta, its main branches or pulmonary arteries (de Souza & de Carvalho, 2014). In 1990, the American College of Rheumatology (ACR) published the six diagnostic criteria for Takayasu's arteritis, which requires a minimum of

three criterias to establish diagnosis of the condition. The ACR classification has a sensitivity of 90.5% and a specificity of 97.8% (Maffei et al., 2006). In this patient, we found 5 out of the 6 ACR criterias. First is an age of onset less than 40 years of age, wherein the patient was diagnosed at 19 years of age. Other criteria found include the presence of claudication of the extremities, decreased brachial artery pulse, a systolic blood pressure difference of > 10 mmHg between the two upper extremities, and abnormalities on arteriograms. Based on said findings, the patient was diagnosed with Takayasu's arteritis.

Although the ACR diagnostic criteria are simple and easy to use, it does not describe other clinical symptoms that may be considered for clinical diagnoses such as fever, arthralgia, weight loss, hypertension, increased erythrocyte sedimentation rate (ESR) and anemia. Therefore, in 1995 Sharma et al. modified the Ishikawa criteria by removing age and the presence of typical symptoms and signs of less than 1 month. The presence of two major criterias or one major and two minor criterias, or four minor criterias indicates a high likelihood of Takayasu's arteritis (Setty et al., 2017). In this patient, two major criterias were identified, namely lesions in the left mid-subclavian artery, typical signs and symptoms in the form of claudication of the extremities, differences in pulse and blood pressure > 10 mmHg in the arm, and one minor criterion namely left middle carotid artery lesions. Based on this, it is most likely that this patient has Takayasu's arteritis.

The etiology of Takayasu's arteritis is still unknown. Similarly, the exact pathogenesis of this disease also cannot be determined. Infection, autoimmune and genetic factors have been studied as risk factors for this disease. This disease is also associated with viral infections that may trigger vasculitis because the vascular lesions found are the same as those found in infected animals. Genetic factors that play a role in the pathogenesis of Takayasu's arteritis are mainly associated with the Human Leukocyte Antigen (HLA) complex. In Japan a clear relationship was established between arteritis and the HLA-B52 and -B39 alleles, while in Mexico and Colombia the incidence of Takayasu's arteritis was higher among carriers of the HLA-DRB1*13:01 allele and HLA-DRB1*16:02 alleles (Setty et al., 2017). Immunological mechanisms involved in the pathogenesis of Takayasu's arteritis involve cell-mediated immunity and humoral immunity that leads to inflammation and tissue damage. Dendritic cells in the tunica adventisia expresses specific HLA molecules that are activated by unknown stimuli, the activation of which may be affected by the 65kDa HSP expression in aortic tissue. These cells synthesize and release pro-inflammatory cytokines (such as IL-18) and chemokines that result in T cells recruitment in blood vessel walls and initiate a deviant T-cell response. Degenerative changes in the tunica media and adventisia, as well as intimal fibrocellular hyperplasia, eventually cause muscle weakness, aneurysm formation, vascular stenosis and thrombus formation (Da Cruz et al., 2014).

Clinically there are three different phases of Takayasu's arthritis. In the first phase, patients typically exhibit symptoms of non-specific inflammation, such as fever without a clear etiology. In the second phase, inflammation of the large blood vessel mural begins, causing carotidynia felt in the form of neck pain, sometimes accompanied by regional pain in the thoracic and dorsal regions. The third phase (advanced phase) is characterized by a decrease or absence of pulses and/or differing arterial pressure between the upper limbs, arterial bruit and intermittent claudication of the extremities (Keser et al., 2018). In this patient there were no signs of fever or carotidynia, but the patient presented with an acute onset of right-sided hemiplegia as a result of the advanced progression of the arteritis and its secondary impact. Although the exact etiology of ischemic stroke in Takayasu's arteritis remains unclear, it is speculated that a decrease in cerebral blood flow from occlusive lesions, stenosis of the aortic arch and its main branches, and accompanying heart disease such as aortic regurgitation may play a role in a number of stroke patients. Intracranial stenosis as a consequence of vasculitis involvement, or previous embolization to the blood vessels has also been hypothesized (Chang & Hsieh, 2015).

Diagnosis and monitoring of Takaysu's arteritis can be performed through blood vessel imaging. Angiography is the gold standard for evaluating vascular lesions. Digital Substraction Angiography (DSA) is a method that is not only useful for diagnosis but also to assess the level and localization of vascular involvement in Takayasu's arteritis, detect stenosis, occlusion or arterial aneurysms in the large and medium blood vessels. However, DSA can only visualize the lumen, but not the vessel wall. It is also an invasive method that poses a risk of radiation exposure, so it is not routinely used in clinical practice (Da Cruz et al., 2014). At present, some experts prefer to use Magnetic Resonance Angiography (MRA) or Computerized Tomography Angiography (CTA) to establish the diagnosis of Takayasu's arteritis. CTA can provide anatomical characteristics of structural aortic changes, but

cannot detect early-stage disease. Although MRA can show thickening and edema of the vascular wall, its correlation with clinical activity and systemic inflammation is poor and shows limitations in long-term follow-up. Color Doppler ultrasonography (CDU) is an alternative imaging modality that can help evaluate the temporal, carotid, axillary and femoral arteries. However, although CDU is inexpensive and non-invasive but it is operator-dependent and does not determine disease activity. In recent years the use of positron emission tomography (PET) with 18F-fluorodeoxyglucose (18F-FDG PET) for the diagnosis of Takayasu's arteritis has a sensitivity and specificity of up to 100% and can also detect subclinical activity, but this examination is expensive and places the patient at risk of radiation exposure (Keser et al., 2018).

Based on angiographic findings, Takayasu's arteritis is classified into five types. In Type 1, involvement is limited to the branches of the aortic arch, whilst Type 2a involves the ascending aorta, aortic arch and its main branch. Type 2b is the same as Type 2a with the additional involvement of the descending thoracic aorta. Type 3 involves the thoracic descending aorta, the abdominal aorta, and / or the renal artery. Type 4 involves the abdominal aorta and / or renal artery. Whereas type 5 is a combination of types 2b and 4 (Maffei et al., 2006). Based on the results of angiography, our patient was classified as Type 1 Takayasu arteritis.

The therapeutic aim in Takayasu's arteritis is to control acute inflammation and minimize arterial injury. Early initiation of immunosuppressive therapy is crucial to prevent further vascular complications and induce remission. Prednisolone is first-line therapy, and EULAR (European League Against Rheumatism) guidelines recommend a dose of 1 mg / kg of body weight / day for 1-3 months (maximum dose of 60 mg / day) with gradual tapering (Maffei et al., 2006). However, since only a portion of patients respond to corticosteroids, other therapeutic options include cytotoxic treatment such as cyclophosphamide (1-2 mg / kg / day), azathioprine (1-2 mg / kg / day) or methotrexate (0.3 mg / kg / day) kg / week). Vascular surgery, with either endovascular or open approaches, is predominantly used in the presence of life-threatening aneurysm or in severe organ ischemia (Mason, 2018). It is recommended to perform surgery during remission to avoid complications that may arise from inflammation, such as re-stenosis, anastomosis failure, thrombosis, bleeding and infection (Setty et al., 2017). Percutaneous transluminal angioplasty with ballooning and stenting has long been used in Takayasu's arteritis, with several studies indicating balloon angioplasty as the more efficacious option (Jeong et al., 2017). And although it provides short-term benefits, re-stenosis and aneurysm formation can occur within 1 or 2 years, thus justifying a bypass surgery (Da Cruz et al., 2014).

4. Conclusion

Takayasu's arteritis is one of the causes of ischemic stroke at a young age. Although neurological manifestations often occur after the chronic phase, acute stroke as an initial manifestation of the disease is rarely reported. Appropriate diagnosis and effective and adequate treatment can reduce patient mortality and morbidity.

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Ethics Statement

Informed consent was obtained from this patient for the publication of the report

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