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Case Report

Transcatheter thrombolysis in children with Takayasu's arteritis complicated by acute cerebral infarction: a case report

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Abstract: Background: Takayasu arteritis (TA), a rare systemic macrovasculitis in children, affects multiple arteries, causing necrosis, remodeling, stenosis, or dilatation. Due to nonspecific symptoms, early diagnosis is challenging, and it is often missed until organ dysfunction occurs. TA poses a significant health threat, with few reports on acute cerebral infarction in pediatric cases. Case presentation: An 11-year-old girl presented with TA-induced thrombosis in the right middle cerebral artery's upper trunk. Despite prompt thrombolysis restoring blood flow, brain tissue necrosis and dysfunction persisted. Pre-intervention MRA showed occlusion and stenosis in relevant arteries. Subsequent angiography confirmed multiple-artery acute stroke, supported by imaging, serology, and cerebrospinal fluid tests. Timely rehabilitation, hormone treatment, and early diagnosis led to a favorable outcome. Conclusions: Early diagnosis and treatment of pediatric TA are crucial to prevent organ damage. Transcatheter thrombolysis effectively restores brain perfusion in acute infarction cases.

Keywords: Takayasu arteritis, children, acute cerebral infarction, transcatheter contact thrombolysis, case report

Introduction

Takayasu arteritis (TA), also known as polyarteritis, is a chronic, progressive, nonspecific macrovasculitis that affects the aorta and its principal branches, with the carotid artery frequently being the primary segment involved [1-3]. The etiology and pathogenesis of this condition remain unknown and intricate, encompassing factors such as infections, genetic predispositions, cellular and humoral immunity, and other mechanisms [4]. Patients often experience persistent illness, with recurrent episodes being commonplace. In severe cases, complications may include arterial lumen stenosis or occlusion, cerebral infarction, reduced blood flow to the extremities, and ischemia of vital organs. Consequently, timely evaluation and management of the disease are of paramount importance. However, the incidence of Takayasu arteritis is poorly understood, specific clinical manifestations are often absent, and early diagnosis poses significant challenges, thereby endangering patient life and health. Historically, few cases of intracranial large vessel occlusion secondary to Takayasu arteritis have been reported, with most therapeutic strategies focused on mechanical thrombectomy, stent placement, and balloon angioplasty. To date, there are no documented cases of catheter-directed thrombolysis as a treatment modality.

This paper presents the case of an 11-year-old girl diagnosed with Takayasu arteritis by magnetic resonance angiography (MRA) and digital subtraction angiography (DSA). MRA indicated occlusion of the superior trunk of the right middle cerebral artery and stenosis of the right anterior cerebral artery, while DSA confirmed thrombotic obstruction at the origin of the superior trunk of the right middle cerebral artery. The comprehensive diagnosis and treatment process is detailed to serve as a reference for managing similar clinical cases.

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Case presentation

The patient is an 11-year-old girl, a first-year senior high school student, who presented to the emergency department following a sudden onset of headache accompanied by left limb weakness and impaired speech after returning to the classroom following a 40-minute run. Upon admission, the initial physical examination indicated that her left upper limb exhibited a muscle strength of 0, her left lower limb strength was assessed at 2, and she was unable to articulate speech.

The patient had no significant medical history, with no prior occurrences of hypertension, hyperlipidemia, or diabetes. She reported no adverse habits, including tobacco, alcohol, or drug use. There were no additional contributing factors in her personal or family history. Vital signs were as follows: temperature 36.2°C; pulse 77 beats/min; respiration 10 breaths/min; blood pressure 130/78 mmHg; peripheral oxygen saturation 94%. Neurological examination revealed lethargy, dysarthria, and the absence of pathological reflexes. The National Institutes of Health Stroke Scale (NIHSS) score was 15 points (2 points for consciousness, 1 point for gaze deviation, 2 points for dysarthria, 2 points for partial facial paralysis, and 8 points for limb weakness). The modified Rankin Scale score was 4.

Postoperative routine blood examinations indicated decreased values of RBC (3.70), Hb (102.0), and Lymph% (15.1), alongside an elevated Neut% (78.3), while WBC, PLT, and other relevant parameters remained within normal limits. Although this information is pertinent for general health assessment, it is not critical for the specific diagnosis of Takayasu arteritis.

Serological analysis revealed elevated levels of IL-8 (34.95, normal value ≤ 15.71 pg/mL), while levels of IL-2, -4, -5, -6, -10, -12P70, -17A, -17F, -22, and TNF-β remained within normal ranges. Detailed cerebrospinal fluid (CSF) analysis, including IgGcsf, ALBc, 24IgG8.75, IgG, ALBs, IgCSZ, and IgGhczs, along with gkI, is generally unnecessary for diagnosing Takayasu arteritis specifically.

Emergency computed tomography (CT) scans demonstrated no abnormal findings, and magnetic resonance imaging (MRI) T1 and T2 sequences also revealed no significant irregularities. However, diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) sequences showed patchy abnormal signals in the right insular lobe, consistent with acute cerebral infarction (**Figure 1**). MRI-enhanced SPACE arterial wall imaging indicated centripetal thickening of the vascular wall, essential for the diagnosis of Takayasu arteritis.

Magnetic resonance angiography (MRA) displayed an absence of development in the superior trunk of the right middle cerebral artery and narrowing of the A1 segment of the right anterior cerebral artery (**Figure 2A**). The procedural course is illustrated in the digital subtraction angiography images obtained during the operation (**Figures 2B**, **3A**). On the first postoperative day, MR images of the head revealed patchy abnormal signals in the right frontal lobe, paraventricular nucleus, and basal ganglia, consistent with a diagnosis of subacute cerebral infarction, with no change in the extent compared to preoperative imaging.

Based on the preoperative imaging findings, the physician initially diagnosed the patient with acute cerebral infarction secondary to childhood Takayasu arteritis. Further imaging focused on arterial wall alterations was conducted postoperatively, ultimately confirming the diagnosis of acute cerebral infarction caused by childhood Takayasu arteritis (**Figure 3B**, **3C**).

Treatment

Following the acquisition of informed consent from the patient's family, cerebral angiography was promptly conducted. Whole brain angiography, performed through the right femoral artery approach under local anesthesia, revealed occlusion of the superior trunk of the right middle cerebral artery, characterized by truncation at the occluded segment. The distal vessels of the A1 segment of the right anterior cerebral artery exhibited thinning (**Figure 2B**), with slow passage of the contrast medium. The remaining arteries displayed no abnormalities, and no irregularities were detected during the venous phase.

During the procedure, the clinical manifestations of left limb weakness attributable to thromboembolism in the upper trunk of the right middle cerebral artery were deliberated. The consulting physicians unanimously recom-

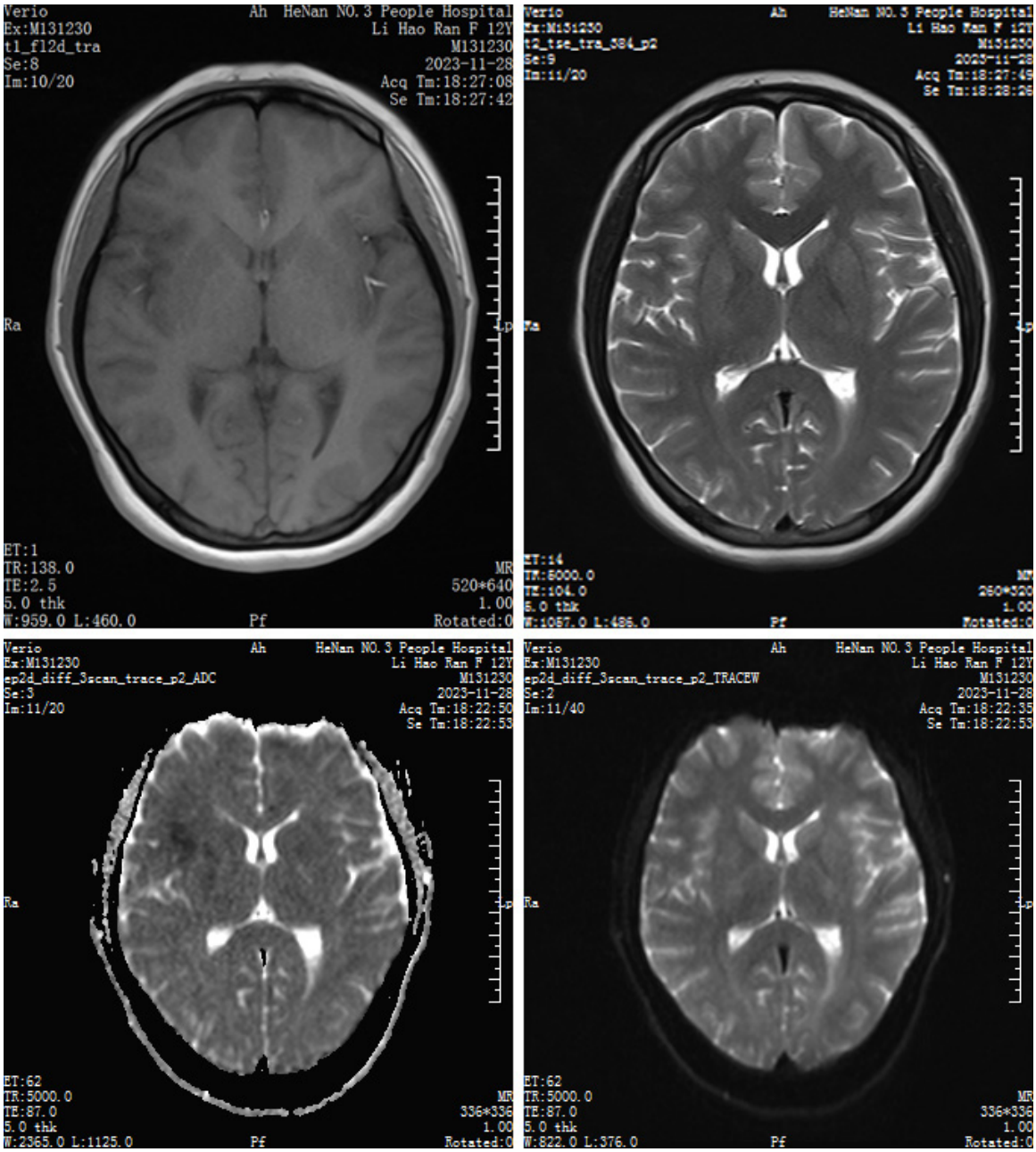

Figure 1. Nuclear magnetic resonance imaging. No abnormal signs were found on T1 or T2 MR images, but patchy abnormal signals were observed in the right insular lobe on DWI and ADC imaging equences, which was consistent with the diagnosis of acute cerebral infarction.

mended immediate transcatheter contact thrombolysis, thrombectomy, or stent thrombectomy to promptly restore cerebral blood supply. The patient's condition was communicated to the family, and additional signatures were obtained.

Under intravenous general anesthesia, a 6F guiding catheter was introduced into the right internal carotid artery with the assistance of a guide wire. A Synchro-14-200 microwire was navigated through the guiding catheter to direct a Rebar-18 Micro Catheter to the thrombus located in the upper trunk of the right middle cerebral artery. A total of 300,000 units of urokinase (100,000 units per branch, with urokinase dissolved in 5 mL saline; Nanjing Nanda Pharmaceutical Co., Ltd.) was administered through the catheter. Five minutes post-injection, angiography revealed unobstructed

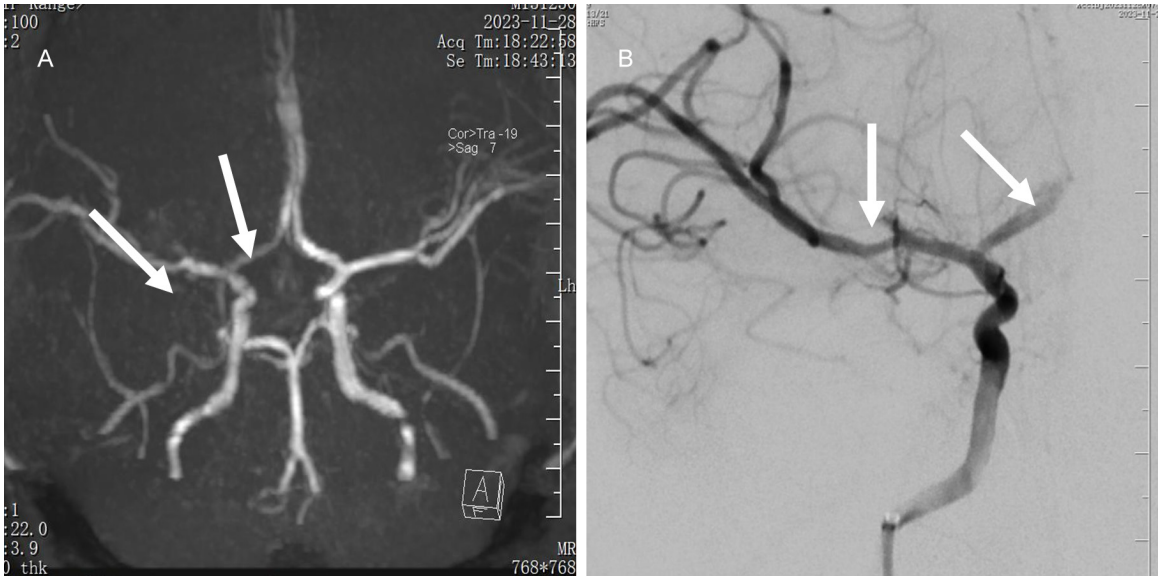

Figure 2. Magnetic resonance angiography and digital subtraction angiography. A. The upper trunk of the right middle cerebral artery was not visible, and the A1 segment of the right anterior cerebral artery was narrowed. B. The occluded end of the upper trunk of the right middle cerebral artery was "truncated", and the right anterior cerebral artery showed thinning.

blood flow within the vessel (**Figure 3A**), with forward flow assessed at mTICI grade 3 (mTICI grades range from 0 to 3, indicating varying degrees of blood flow stagnation to normal flow).

Following the procedure, 8 mL of tilofiban hydrochloride sodium chloride (Xinweining Yuanda Pharmaceutical Co., Ltd., China) was administered intravenously through a continuous micropump at a rate of 5 mL/h for 24 hours. The anesthesia reversal was uneventful, the femoral artery sheath was preserved, and the patient was transferred to the intensive care unit for monitoring. One hundred milligrams of aspirin and 75 mg of clopidogrel were administered orally 2 hours prior to the cessation of tilofiban hydrochloride sodium chloride infusion, continuing daily for 6 months to mitigate the risk of thrombosis. The patient's postoperative NIHSS score was 6, her mTICI score was 3, the DPT (time from admission to femoral artery puncture) was 62 minutes, and her DRT (door-to-recanalization time, time from admission to vascular recanalization) was 102 minutes.

Outcome and follow-up

On the first postoperative day, the patient was alert but exhibited impaired speech fluency. Her left upper limb demonstrated a muscle strength of grade 1, while her lower limb strength was assessed at grade 4. Additionally, her mouth was slightly deviated to the right. Magnetic resonance imaging of the head and laboratory evaluations were conducted (refer to imaging examination). By the third postoperative day, she was transferred to the rehabilitation department, where she simultaneously commenced treatment with oral prednisone.

During the 15-day follow-up post-surgery, the child remained conscious, displayed fluent speech, demonstrated normal cognitive function, and was able to ambulate independently. Her modified Rankin Scale (mRS) score was recorded as 2, with left upper limb muscle strength at grade 2 and lower limb strength at grade 4; her mouth continued to show slight rightward deviation. The patient continued to receive ongoing rehabilitation in the rehabilitation department.

Discussion

Takayasu arteritis (TA) represents the most prevalent form of systemic macrovasculitis, characterized by granulomatous inflammation affecting the primary artery and its major branches, which may ultimately result in segmental stenosis, occlusion, dilation, and/or

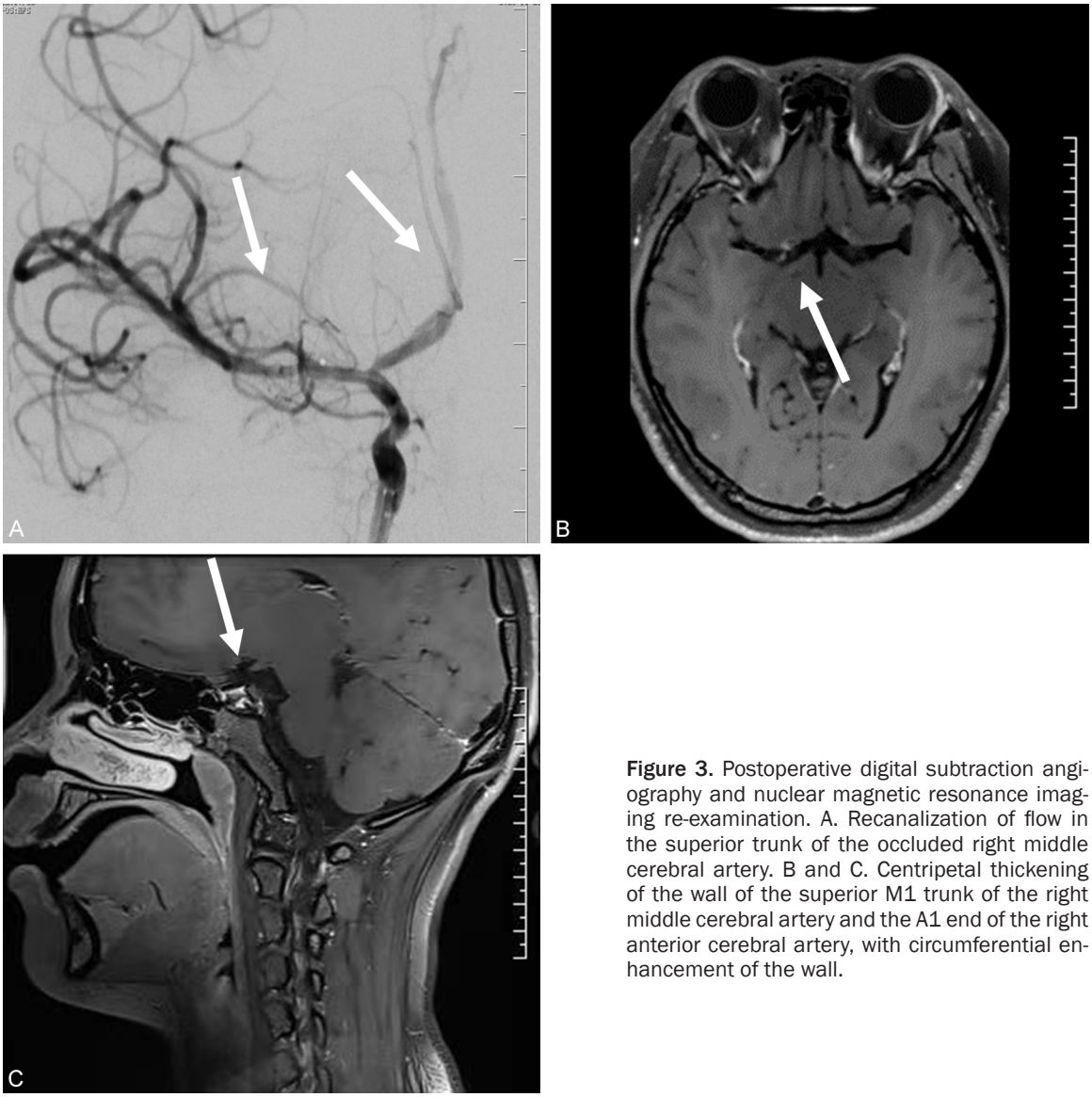

Figure 3. Postoperative digital subtraction angiography and nuclear magnetic resonance imaging re-examination. A. Recanalization of flow in the superior trunk of the occluded right middle cerebral artery. B and C. Centripetal thickening of the wall of the superior M1 trunk of the right middle cerebral artery and the A1 end of the right anterior cerebral artery, with circumferential enhancement of the wall.

aneurysms [5]. In pediatric patients diagnosed with TA, the male-to-female ratio ranges from 1:2.5 to 1:3.0. TA can manifest at any age, with a mean onset age of approximately 12 years. To date, reports of intracranial large vessel occlusion attributable to TA remain relatively scarce, with treatments primarily consisting of mechanical thrombectomy, stenting, and balloon angioplasty. Among these cases, instances of intracranial large vessel occlusion due to Takayasu arteritis in children are particularly rare (**Table 1**).

Currently, the majority of research concerning the pathogenesis of TA focuses predominantly on adults or animal models of macrovasculitis. Both innate and adaptive immunity play significant roles in the pathophysiological processes associated with TA. Histopathologic examinations reveal that inflammation typically occurs outside the adventitia and media, though it can involve all layers of the blood vessel, resulting in vascular wall injury, laminar necrosis, rupture of elastic fibers, fibrosis, and arterial remodeling. The inflammatory cells infiltrating the arterial wall include macrophages and lymphocytes (αβ CD4+, CD8+, and γδ T cells, natural killer cells, and B cells). Various pro-inflammatory cytokines are implicated in the pathogenesis of TA.

Most cases of TA exhibit a subacute onset, which often leads to diagnostic delays ranging from several months to several years; TA may

Table 1. Reported cases of severe cerebral ischemia resulting from Takayasu arteritis

Case	Age/Gender	Occlusive blood vessel	Treatment	Outcome
Shinya Miyamoto et al. 2012 [6]	32/female	LCCA	Single stage multiple stenting	Survival
Kiron Varghese et al. 2016 [7]	40/female	MCA	Balloon angioplasty and stent implantation	Survival
Kiron Varghese et al. 2016 [7]	15/female	MCA	Balloon angioplasty and stent implantation	Survival
Shan L et al. 2018 [8]	15/female	MCA	Intracranial revascularization	Survival
Kentaro Tatsuno et al. 2020 [9]	25/female	MCA/ICA	Mechanical thrombectomy	Survival
Kamble Jayaprakash Harsha et al. 2022 [10]	32/female	SCA/MCA	Balloon guide catheter assisted mechanical thrombectomy	Survival
Marilena Mangiardi et al. 2022 [11]	40-50/male	MCA/ICA/ACA	Stenting and Thrombectomy	Survival

gradually progress to arteritis obliterans and vascular disease-related symptoms [12]. Up to 25% of children with TA may experience irreversible vascular damage by the time of diagnosis. The most frequently involved arteries in TA include the aortic arch, thoracic aorta, and abdominal aorta, followed by the renal artery, subclavian artery, carotid artery, and visceral artery. Compared to adults, children with TA more commonly exhibit involvement of the aortic arch, entire aorta, inferior phrenic renal artery, and mesenteric artery. Vascular lesions are often characterized by stenosis, occlusion, thickening of the vascular wall, and aneurysms, typically located near the origin of the aortic branches, displaying segmental and plaque-like distribution.

The diagnosis of TA primarily relies on clinical features and vascular imaging; acute-phase reactants (such as ESR and CRP) can further corroborate systemic inflammation, although normal ESR or CRP values do not exclude TA [13-15]. Imaging studies are crucial for diagnosing TA and assessing the extent of vascular lesions [16]. Patients suspected of having TA should undergo arterial magnetic resonance angiography (MRA) or CT angiography (CTA) to evaluate the arterial lumen [17, 18].

In this case, the patient's RBC, Hb, and Lymph% indices were decreased, while her Neut% index was elevated. Serological examinations indicated an increased concentration of IL-8. Additionally, the cerebrospinal fluid exhibited elevated levels of IgG CSF (CSF immunoglobulin), ALBc (CSF albumin), and 24IgG8.75, consistent with findings documented in clinical literature. However, the erythrocyte sedimentation rate (ESR), procalcitonin (PCT), and C-reactive protein (CRP) values remained within normal ranges.

Conclusions

Timely diagnosis and prompt treatment of childhood Takayasu arteritis are crucial in preventing significant organ dysfunction. Transcatheter thrombolysis utilizing urokinase can facilitate rapid restoration of cerebral perfusion in pediatric patients experiencing acute cerebral infarction.

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Disclosure of conflict of interest

None.

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