Case report: Takayasu arteritis in a 3-month-old Chinese girl

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Abstract

Rationale: Takayasu arteritis is a rare large vessel systemic vasculitis that predominantly affects the aorta and its main branches in women of childbearing age. Due to nonspecific symptoms during the acute phase of disease, early diagnosis is still a challenge for pediatricians.

Patient concerns: We reported a 3-month-old girl who presented with sustained elevated levels of acute-phase reactants, which could not be explained by infectious diseases and malignant diseases.

Diagnoses: The patient’s angiography showed dilatation, stenosis, and inflammation of the aorta and its branches and was diagnosed as Takayasu arteritis.

Interventions: We prescribed glucocorticoids combined with immunosuppressive agents, which include cyclophosphamide used as an induction drug for 6 months, and mycophenolate mofetil used as a maintenance drug. Glucocorticoids gradually stopped.

Outcomes: At present, the girl went into clinical remission with normal levels of acute-phase reactants and improvement of vascular inflammation demonstrated by angiography.

Lessons: This case report illustrates that Takayasu arteritis can occur in children at a very early age after birth before apparent clinical symptoms.

Abbreviations: CMV = cytomegalovirus, CRP = C-reactive protein, CT = computed tomography, c-TA = childhood onset TA, ESR = erythrocyte sedimentation rate, EULAR = European League Against Rheumatism, Hb = hemoglobin, MRA = magnetic resonance angiography, N% = neutrophil percent, Plt = platelet, PRES = Pediatric Rheumatology European Society, PRINTO = Pediatric Rheumatology International Trials Organization, TA = Takayasu arteritis, WBC = white blood cell.

Keywords: acute-phase reactants, child, early diagnosis, Takayasu arteritis

1. Introduction

Takayasu arteritis (TA) is a rare, chronic large vessel vasculitis that predominantly affects the aorta, its major branches, and the pulmonary arteries. Segmental stenosis, occlusion, dilatation, or aneurysm formation may occur in the vessel wall during the course of the disease. The various signs and symptoms such as fever, malaise, anorexia, weight loss, extremity pain, claudication, light-headedness, bruits, absent or diminished pulses, hypertension, and loss of blood pressure can be present according to the vessel involvement.1-3 The youngest reported patient was diagnosed at 6 months after birth.2,4 Diagnosis of c-TA remains challenging because of nonspecific symptoms during the acute phase of disease and the lack of validated biomarkers to assess the activity and damage. This study reports the case of a 3-month-old girl with TA presenting with fever and elevated levels of acute-phase reactants.

2. Case presentation

On February 2015, a 3-month-old Chinese girl, from non-consanguineous parents, was admitted to the Rheumatology Department with a 1-month history of elevated levels of acute-phase reactants after cough. Both parents and her elder brother were all in good health. There were no autoimmune diseases present in the family. She was a full-term baby, with weight 4200 g, and length 54 cm. There were no significant oddities.

In January 2015, when the girl was about 2 months old, she suffered from cough after having received the Poliomyelitis vaccine. The cough was not severe, paroxysmal, gradually increased with a fever no more than 37.8°C. The laboratory examination showed a hemoglobin (Hb) level of 129 g/L (reference range 110–160 g/L), WBC count 28 × 10⁹/L (reference range 4–10 × 10⁹/L), platelet (Plt) 766 × 10⁹/L (reference range 100–300 × 10⁹/L), neutrophil percent (N%) 62.5%, and no C-reactive protein (CRP) level. After treatment with antibiotics for 1 week, the girl got better with less cough. But the repeated blood routine test showed WBC 25.38 × 10⁹/L, Plt 478 × 10⁹/L, N% 51.3%, Hb 76 g/L, CRP level was 191.6 mg/L (reference range <8 mg/L), and erythrocyte sedimentation rate (ESR) was 67 mm/h (reference range 0–20 mm/h). There were no other apparent clinical manifestations. The chest X-ray suggested pneumonia.
The local hospital gave the girl meropenem, norvancomycin plus fluconazole for more than 2 weeks, there was no significant improvement of the chest X-ray, and the levels of CRP and ESR were still high. The girl also received a bone marrow test and echocardiogram and there were no pathologic findings. The girl was transferred to the rheumatology department because of high levels of acute-phase reactants in the middle of February 2015. She was well upon admission, afebrile, no rash, no enlargement of lymph nodes, no red eyes, no strawberry tongue, no periumgal desquamation, no rales of the lung, no murmurs of the heart and the big arteries, no hepatomegaly or splenomegaly, and normotensive. Blood pressure was 85/55 mm Hg. Laboratory tests confirmed elevated levels of acute-phase reactants with CRP 89mg/L and ESR was 40mm/h and WBC count 23.8 x 10^9/L, Plt 599 x 10^9/L, N% 52.3%, Hb 133g/L.

The basic biochemistry examinations (alanine transaminase, aspartate aminotransferase, bilirubin, glycemia, cholesterol, triglycerides, albumin, amylase, ammonia) were normal. Serology (hepatitis B+C virus, toxoplasma, rubella, herpes simplex virus, cytomegalovirus, HIV, syphilis, mycoplasma, Epstein–Barr virus, parvovirus, adenovirus, respiratory syncytial virus), and immunologic tests (antinuclear antibodies, extractable nuclear antigen, rheumatoid factor, anti neutrophil cytoplasmic antibody, immunoglobins, C3, C4, total complement) were performed, with the discovery of cytomegalovirus (CMV) positivity in IgM and IgG classes, while the DNA copies of CMV were negative. Tests for basic tumor markers (neuron specific enolase, alpha fetoprotein) were negative. The TB skin test was one plus positive and T-spot test for tuberculosis was negative.

Because the chest X-ray still revealed the fixed inflammation, the patient was given chest contrast enhanced computed tomography (CT). The CT yielded a surprising finding that led us to consider TA: arteritis of the aortic arch and the branching arteries, with the dilation of aortic and pulmonary arteries and their branches, with slightly narrowing of the abdominal aorta and above the inferior mesenteric artery, with an enlargement and blurring of the walls in descending aorta, left pulmonary artery, abdominal aorta (Fig. 1). There was no apparent pneumonia.

Diagnosis of TA was confirmed and the girl was given 2 mg/kg of prednisolone daily. After 2 weeks, the patient received a revaluation, the level of CRP was 11 mg/L, and ESR was 4 mm/h. The result of the control magnetic resonance angiography (MRA) showed blurring of the walls in abdominal and descending aorta, the narrowing of abdominal aorta, slight dilation of aortic arch, no apparent pathologic findings in internal carotid and vertebral arteries and cloudiness in both renal arteries (Fig. 2). Considering the young age of onset and adverse effects of prednisolone (moon face and thrush), we therefore initiated cyclophosphamide therapy at a dose of 500 mg/m2 iv administered once monthly. Prednisolone and cyclophosphamide combination therapy was continued for 6 months, and then the patient was given mycophenolate mofetil (MMF) 25 mg/kg as maintenance treatment. A control MRA was performed again, it demonstrated abdominal aortic stenosis and aortic arch dilatation improved to near normal; there was, however, a minor narrowing of both iliac arteries (Fig. 3).

During the 6-month follow-up, prednisolone was tapered to 5 mg per day. Prednisone was stopped after 18-month treatment and with MMF only used as maintenance treatment and the acute reactants were normal.

3. Discussion

The TA is a difficult disease to deal with. Early diagnosis is difficult and requires clinical awareness and suspicion.[2,3] Clinical manifestations vary greatly depending on the affected arteries, making an early diagnosis difficult. Imaging modalities are very important for establishing the diagnosis of TA, determining the distribution of lesions and monitoring disease activity.[4] The childhood onset TA (c-TA) subset affects any age group, the youngest reported patient being diagnosed at 6 months after birth.[2] Vega-Cornejo and Meza-Beltran also reported a suspected newborn patient with TA with abnormal angiography.[5] Brunner et al reviewed 241 pediatric cases of c-TA, the most frequent presentation was hypertension (83%), and followed by headaches (31%), fever (29%), dyspnea (23%), weight loss (22%), vomiting (20%), abdominal pain (17%), and musculoskeletal symptoms (14%); in 61% (141/230) patients
had elevated ESR.\[2\] Patients with c-TA may only present with increased inflammation markers, including CRP and ESR.\[3\] In our 3-month-old patient, elevated levels of acute-phase reactants, and angiographic findings met the revised EULAR/PRINTO/PRES criteria for TA and confirmed the diagnosis of TA.\[6\]

The TA is thought to require early diagnosis for the best outcome.\[7\] Each child with sustained high levels of acute-phase reactants requires a thorough diagnostic evaluation to exclude other conditions on the differential diagnosis and angiography should be done to confirm the diagnosis of TA.\[8,9\] After 6

**Figure 2.** (2015-3-14) Magnetic resonance angiography examination showed blurring of the walls in abdominal and descending aorta, the narrowing of abdominal aorta and slightly dilation of aortic arch, no apparent pathologic findings in internal carotid and vertebral arteries, and cloudiness in both renal arteries.

**Figure 3.** (2015-8-5) Control magnetic resonance angiography demonstrated no apparent pathologic findings in thoracic and abdominal aorta.
months treatment, our patient showed improvement along the walls of arteries and normal levels of acute-phase reactants. Exposure to Mycobacterium tuberculosis may be sufficient to trigger TA inflammation,[10] other infectious stimulations inducing TA have also been suggested, including hepatitis B virus.[11] The patient had received vaccines of BCG, hepatitis B, and Poliomyelitis, she had no severe infectious factors and was only 3 months old. One can only guess the vaccines may trigger or participate in the TA inflammation process.

Glucocorticosteroids are anchor drugs for this disease, like other vasculitis.[12] Side-effects of glucocorticosteroids, especially growth retardation, osteoporosis, full moon face, and buffalo back can severely damage their quality of life. Immunosuppressive agents, including methotrexate, cyclosporine, cyclophosphamide, MMF, and tacrolimus, have been used for patients with TA. Our patient had a good reaction with the treatment of prednisolone plus cyclophosphamide and MMF.

In conclusion, TA is an inflammatory arteritis found predominantly in female patients and not rare in children. The diagnosis of infants with Takayasu arteritis is very difficult, because of the lack of typical clinical symptoms, such as hypertension, limb blood pressure asymmetry, vascular murmur, vertigo, often manifested as noninfection, nontumor inflammation. We reported a 3-month-old girl presenting with fever and elevated levels of acute-phase reactants who was diagnosed as TA. Although rare, TA must be considered in children who present with nonspecific systemic symptoms but increased acute-phase reactants. Better awareness among pediatricians of the early diagnosis of TA is necessary. MRA could be recommended as the primary investigation method in children with TA.

Author contributions

HL was responsible for the literature search and preparation of the manuscript. LS provided clinical advice regarding the management of the patient and assisted with manuscript preparation. RU, YC, and OA drafted the article and revised it. All authors approved the final copy of the manuscript.

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References

[1] Kerr GS. Takayasu’s arteritis. Rheum Dis Clin North Am 1995;21:1041–58.
[2] Brunner J, Feldman BM, Tyrrell PN, et al. Takayasu arteritis in children and adolescents. Rheumatology (Oxford) 2010;49:1806–14.
[3] Gedalia A, Cuchacovich R. Systemic vasculitis in childhood. Curr Rheumatol Rep 2009;11:402–9.
[4] Dreskenhe E, Aydin SZ, Merke PA. Assessment of disease activity and progression in Takayasu’s arteritis. Clin Exp Rheumatol 2011;29:S86–91.
[5] Vega-Corbejo G, Meza-Beltran J. Takayasu’s arteritis in the newborn: a diagnosis to suspect. Reumatol Clin 2015;11:174–6.
[6] Ruperto N, Ozen S, Pistorio A, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part I: Overall methodology and clinical characterisation. Ann Rheum Dis 2010;69:790–7.
[7] Nazareth R, Mason JC. Takayasu arteritis: severe consequences of delayed diagnosis. QJM 2011;104:797–800.
[8] Singh N, Hughes M, Sehba N, et al. Takayasu arteritis in infancy. Rheumatology (Oxford) 2013;52:2093–5.
[9] Pokrovsky T, Hladik M, Kosnovska L, et al. Takayasu arteritis in a 10-month-old boy. Vasa 2013;42:134–8.
[10] Mulhbybar C, Guilevin L, Cid MC, et al. EULAR recommendations for the management of large vessel vasculitis. Ann Rheum Dis 2009;68:318–23.
[11] Aggarwal A, Chag M, Sinha N, et al. Takayasu’s arteritis: role of Mycobacterium tuberculosis and its 65 kDa heat shock protein. Int J Cardiol 1996;55:49–55.
[12] Zaas A, Scheel P, Vehrux A, et al. Large artery vasculitis following recombinant hepatitis B vaccination: 2 cases. J Rheumatol 2001;28:1116–20.