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Case Report

Complete Occulusion of Left Renal Artery in Pediatric-Onset Takayasu's Arteritis

Takashi Tateyama, Shinobu Waga, Kohichi Suzuki, Kazuhiko Sugimoto, Yoshiki Kakizaki and Hiroshi Tanaka

Department of Pediatrics, Hirosaki University School of Medicine, Hirosaki 036-8562

Tateyama, T., Waga, S., Suzuki, K., Sugimoto, K., Kakizaki, Y. and Tanaka, H. *Complete Occulusion of Left Renal Artery in Pediatric-Onset Takayasu's Arteritis*. Tohoku J. Exp. Med., 2000, **190** (4), 289-294 —— A-16-year-old male adolescent with a 4-year history of protean clinical manifestations such as fever, abdominal pain, back pain, erythema nodosum and uveitis developed complete occulusion of left renal artery. Although he had been suspicious of having an autoimmune disease and treated with prednisolone, a definite diagnosis was not made. Finally, an angiography disclosed stenosis of abdominal aorta just beneath the origin of the renal arteries as well as complete occulusion of left renal artery. It has been reported that pediatric-onset Takayasu's arteritis sometimes shows protean clinical manifestations as in ours. Takayasu's arteritis should be considered as one of the underlaying disease, when a child develops protean manifestations suggesting an autoimmune disease. ———— aortitis syndrome; pediatric-onset; protean manifestations; renal artery; Takayasu's arteritis

Takayasu's arteritis (TA) is a chronic arteritis of unknown etiology involving the aorta and its major branches (Mitsuda et al. 1988; Koide 1992; Morikawa and Numano 1992; Maeda et al. 1997). Although TA is well known as pulseless disease in adult patients, the reported frequency of pediatric-onset TA is relatively rare (Maeda et al. 1997). The early manifestations in pediatric-onset cases are often non-specific, such as persistent fever, abdominal pain, arthralgia and cutaneous rash (Mitsuda et al. 1988; Maeda et al. 1997), and laboratory tests also indicate signs of active but non-specific inflammation, such as an increased level of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Hence, protean clinical manifestations sometimes prevent us from making a definite diagnosis for a long time (Vaz et al. 1988). Since the inflammatory condition gradually causes either stenosis, occlusion and/or dilatation of the involved

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Address for reprints: Hiroshi Tanaka, M.D., Department of Pediatrics, Hirosaki University School of Medicine, 5 Zaifu-cho, Hirosaki 036-8562, Japan.
e-mail: hirotana@cc.hirosaki-u.ac.jp.

arteries (Mitsuda et al. 1988; Vaz et al. 1988; Koide 1992; Morikawa and Numano 1992; Maeda et al. 1997), it is important to increase awareness of the disease, especially in the pediatric field.

We encountered a Japanese boy with protean clinical manifestations suggesting an autoimmune disease, and who finally developed left renal artery occlusion. Although he suffered from a 4-year history of non-specific inflammatory symptoms, the pulselessness or abnormal vascular murmurs did not occur during clinical course.

Case Report

A 12-year-old boy with a 2-month history of remittent fever followed by abdominal pain, erythema nodosum and uveitis was referred to our hospital in May 1990. Laboratory tests including anti-nuclear antibody (ANA), anti-DNA antibody, anti-nuclear ribonucleo protein antibodies (anti-RNP antibody) and rheumatoid factor were negative except for an increased level of the ESR and CRP. Hypocomplementemia was not observed. Repeated blood culture were negative, and an aggressive antibiotics therapy was unsuccessful. Bone marrow aspiration findings were unremarkable. He was suspicious of having a systemic autoimmune disease, and was treated with several non-steroidal anti-inflammatory drugs (NSAIDs; aspirin, ibuprofen, naproxen and sulindac), but they did not prove effective. Just before admission, he complained of upper abdominal pain with high fever follwed by an increased level of serum amylase (285 U/liter:

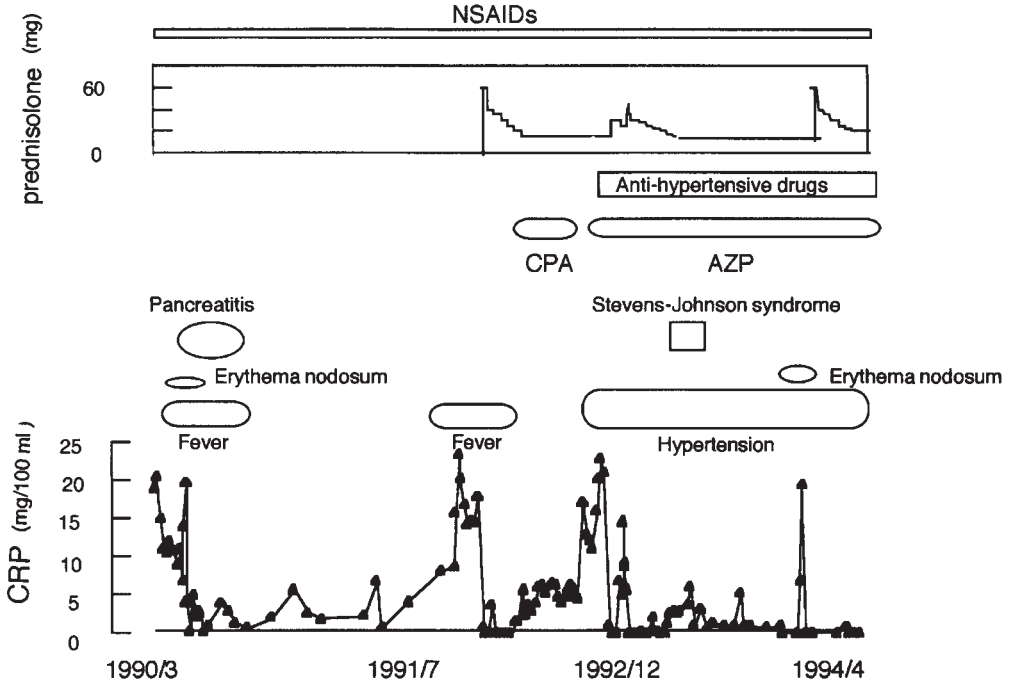

Fig. 1. Clinical course of the patient. Several clinical manifestations occurred during the course.
NSAIDs, non-steroidal anti-inflammatory drugs; CPA, cyclophosphamide; AZP, azathioprine.

normal range 50–160 U/liter). Abdominal echography revealed a swelling of the pancreas head. His clinical course is shown in Fig. 1.

On admission, his body temperature was 37.0°C, and blood pressure was 116/70 mmHg. Peripheral pulse was normal. Physical examination revealed a normotensive boy (height, 154 cm, +0.01 S.D.; body, weight 34.7 kg, −1.09 S.D.) with prominent epigastralgia. In the months ensuing the onset of his illness he had a 3-kg weight loss. No butterfly rash or enanthema was observed. The ESR was elevated to 67 mm/hour and the CRP increased to 19.7 mg/100 ml. Serum amylse was 263 U/liter. The other laboratory studies were unremarkable. His pancreatitis was successfully treated with total parental nutrition and gabexate mesilate infusion. Fever and malaise spontaneously ceased, which was followed by a decreased level of CRP.

In July 1991, recurrent episodes of transient high fever and back pain associated with an increased level of CRP occurred. Although these manifestations spontaneously ceased within a few days, the frequency gradually increased. He was suspicious of having systemic-onset juvenile rheumatoid arthritis. Then, oral prednisolone (PSL, 60 mg daily) combined with naproxen (300 mg daily) was commenced in Feburary 1992, and which resulted in rapid subsidence of fever and back pain followed by a decreased level of CRP. Thereafter the dosage of PSL was tapered. In May 1992, when he was on PSL, 15 mg daily, he experienced general malaise and severe back pain with an increased level of CRP. These manifestations successfully treated with PSL, 60 mg daily and an 8-week course of cyclophosphamide (CPA, 75 mg daily). CPA was replaced by azathioprine (75 mg daily).

In November 1992, when he was on PSL, 25 mg daily, he suddenly developed hypertension (172/104 mmHg) accompanied with generalized tonic seizure. Computed tomography (CT) of his head revealed no abnormalities. Under the diagnosis of hypertensive encephalopathy probably due to long-term steroid therapy, the administration of phenytoin sodium (PHT), a Ca-channel blocker and an angiotensin coverting enzyme (ACE) inhibitor were started, and he was transferred to our hospital. A week after the episode, Stevens-Johnson's syndrome (SJS) occurred. A lymphocyte stimulation test for PHT revealed a high index of 354%. Then, PHT administration was discontinued, and which resulted in subsidence of SJS. Although the level of CRP fluctuated from 0 mg/100 ml to 14.5 mg/100 ml, he did not complain of any disabilities. His hypertension was well controlled under the combination therapy of the Ca-channel blocker and ACE inhibitor. Serum and urinary catecholamines were within the normal values. Plasma renin activity increased to 10.0 ng/ml/hour (normal range, 0.2–2.7 ng/ml/hour). Although urinalysis did not show any abnormalities, urinary β2-microglobulin (β2-MG) gradually increased to the ranges from 1130 μg/lier to 16 200 μg/ liter (normal, <300 μg/liter) after the epidode of SJS. He was suspicious of having interstitial nephritis due to some allergic reaction. Because

of normal levels of serum urea nitrogen and creatinine, he was observed closely. An evaluation of renal arteries was not done at that time, since the family refused the proposal of angiography.

In December 1993, when he was on PSL, 15 mg daily, he experienced another episode of erythema nodosum. He was afebrile at that time. His peripheral pulse was normal. Abnormal cardiac and vascular murmurs were not found. Blood pressure was 144/85 mmHg. Serum electrolytes, urea nitrogen, creatinine, liver-function tests and urinalysis were normal. Urinary β2-MG was 170 μg/liter. Creatinine clearance decreased to 51.7 ml/minutes. Rheumatoid factor, ANA, anti-DNA antibody and anti-neutrophil cytoplasmic antibodies (proteinase 3 and myeloperoxidase) were not present. The ESR and CRP were 6 mm/hour and 0.5 mg/100 ml, respectively. Retinal examination remained normal throughout his course. Intravenous pyelography did not disclose left nephrogram. Abdominal CT showed hypotrophic left kidney and irregularity of lateral margin of abdominal aorta. He was suspicious of having TA. Digital subtraction angiography of aortic arch and its major branches were unremarkable. Thus, a selective angiography of his abdominal aorta was performed. Aortagram disclosed stenosis of abdominal aorta just beneath the origin of the renal arteries as well as complete occlusion of left renal artery (Fig. 2). The outline of the entire aortic arch and its major branches were normal.

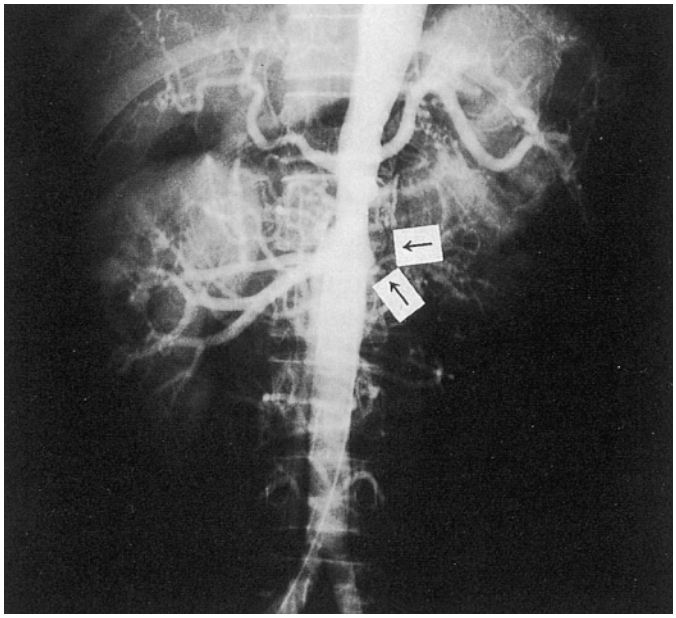

Fig. 2. Abdominal aortagram of the patient. Complete occulusion of left renal artery is shown (arrows). The segmental involvement of the abdominal aorta and the alterations of stenotic portions are also seen.

Discussion

It has been reported that TA is one of the vasculitides in childhood, however, its frequency is low (Cassidy and Petty 1995). TA is a non-specific arteritis of probable autoimmune causes, affecting predominantly young women (Koide 1992; Morikawa and Numano 1992). A striking predilection for the aortic arch and its branches is characteristic (Mitsuda et al. 1988; Koide 1992; Morikawa and Numano 1992; Maeda et al. 1997). Concerning type of arterial lesions of the disease, the abdominal aorta (without involvement of the arch) type has been reported to be relatively rare: from 5% to 18% of the patients (Koide 1992; Morikawa and Numano 1992; Maeda et al. 1997). Yamamoto et al. (1987) reported that renal artery stenosis was found in 4 (17%) of 24 patients with the disease. Hence, pediatric-onset abdominal aorta type of TA as in ours is thought to be rare.

It has been reported that pediatric-onset TA sometimes shows protean clinical manifestations with no specific abnormal signs in laboratory data, and that often prevent us from making a definite diagnosis for a long time (Vaz et al. 1988; Maeda et al. 1997). In the present patient, the long-term history of fever of unknown origin associated with several clinical manifestations, such as abdominal pain, back pain, pancreatitis, erythema nodosum, uveitis and consecutive hypertension were seen. Of these, unusual manifestations in childhood TA were pancreatitis, erythema nodosum and uveitis (Maeda et al. 1997). Although a possible vasculitic features of TA cannot be excluded, we think pancreatitis in our patient might be caused by one of the NSAIDs given at the initial presentation, since recurrent episode was not observed. Frances et al. (1990) reported that 5 (6.3%) of 80 patients with TA showed erythema nodosum as a cutaneous manifestation. Hence, recurrent episode of erythema nodosum in our patient is thought to be responsible for TA. Concerning uveitis, Rose et al. (1990) reported a case of TA associated with sarcoidosis who showed uveitis. However, to our knowledge, there is no published report to describe uveitis in TA patients without sarcoidosis to date. Further reports to describe unusual manifestations of TA is needed.

Although he had been suspicious of having an autoimmune disease, a definite diagnosis had not been made, and he finally developed complete occulusion of left renal artery. In retrospect, his abdominal pain and back pain may be the symptoms of an active lesion of the renal artery. Maeda et al. (1997) reported that abdominal pain was considered to be one of the characteristics of childhood TA. In our patient, typical manifestations suggesting TA, such as pulselessness of extremities or vascular murmurs did not occur during clinical course. Therefore an invasive diagnostic procedure, angiography was not performed in the early clinical stage. In retrospect, non-invasive diagnostic procedure, such as doppler echography of abdominal aorta or renal arteries should have been done in the early stage of the disease when an abdominal vasculitic disease was suspicious.

He had been received long-term PSL therapy combined with immunosuppressive agents during clinical course. It has been reported that corticosteroid therapy might ameliorate active lesions of the disease, and which may result in a decrease in the frequency of arterial stenosis (Vaz et al. 1988). In our patient, despite the long-term immunosuppressive treatment, the inflammatry lesion did not subside, and which finally caused consecutive occulusion of left renal artery. More aggressive therapy might be required in the early stage of the disease for the successful treatment.

We have described here a boy who presented with protean clinical manifestations due to the abdominal aorta type of TA, and that have been reported rarely in children. Despite the long-term immunosuppressive therapy, it is difficult to suppress the disease activity. TA should be considered as one of the underlaying diseases, when a child develops protean clinical manifestations suggesting an autoimmune disease.

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