14-YEAR-OLD GIRL was referred for evaluation of a fever of unknown origin. She was in good health until 2 months previously, when she abruptly developed an elevated temperature and back pain. A urine culture was sterile. She had an elevated white blood cell count and a Westergren erythrocyte sedimentation rate of 116 mm/h. A chest radiograph and abdominal ultrasound were normal. Sinus radiographs indicated sinusitis. She was treated with azithromycin without improvement. A radionuclide bone scan demonstrated increased tracer uptake in the calvarium, left ninth rib posteriorly, and both knees. Results from radiographs of the skull and knees were normal. Serum antinuclear antibodies were positive with a level of 1:80. Several blood and urine cultures were sterile. Results of a serologic study for Epstein-Barr virus suggested a distant infection. A cytomegalovirus serologic study was negative.

The patient had a temperature of more than 40°C daily and had migratory arthralgias, occasional frontal headaches, and intermittent nausea and anorexia. She had lost 5.85 kg during this illness. The patient lived in a metropolitan area and had not traveled recently. The family had 2 cats and the patient also reported exposure to a hamster, dogs, and a lizard. She reported multiple insect bites in the preceding several months. She denied consumption of unpasteurized milk. The family history was unremarkable.

On physical examination, the girl was pale and appeared ill. Her temperature was 38.3°C and her blood pressure was 130/75 mm Hg. The oropharynx was slightly erythematous with no exudates. The first and second heart sounds were normal. A third heart sound and intermittent gallop were audible with no cardiac murmurs noted. An epigastric bruit was present. The results from the remainder of the physical examination were normal.

The total leukocyte count was 10.9 x 10^9 L, with a normal differential. Hematocrit was 0.26 and platelet count was 725 x 10^9/L. The Westergren erythrocyte sedimentation rate was 98 mm/h. The C-reactive protein level was elevated to 149 g/L, and the serum electrolyte, blood urea nitrogen, creatinine, albumin, uric acid, and lactic dehydrogenase levels were normal. Serum alanine aminotransferase level was elevated at 69 U/L (normal, 4-46 U/L), but aspartate aminotransferase and bilirubin levels were normal. A urinalysis showed trace hemoglobin. Blood and urine cultures were sterile and stool cultures isolated only normal enteric flora. Serologic testing for coccidioidomycosis, toxoplasmosis, syphilis, hepatitis A virus, hepatitis B virus, and human immunodeficiency virus was negative. Purified protein derivative skin testing was negative, and Candida and tetanus antigen tests were positive.

A chest radiograph (Figure 1) was performed. Results of an echocardiogram showed mild aortic regurgitation. Magnetic resonance imaging of the thorax (Figure 2, left and right) followed.

From the Departments of Pediatrics and Radiology, University of Utah School of Medicine, Salt Lake City.
Denouement and Discussion

Takayasu Arteritis

Figure 1. Pulmonary artery chest radiograph demonstrates prominence and irregular contour of the descending thoracic aorta.

Figure 2. Top, T1-weighted axial magnetic resonance image demonstrates intimal thickening and saccular dilation of the transverse aortic arch. Bottom, Sagittal T1-weighted magnetic resonance image demonstrates saccular dilation of the thoracic aorta.

Takayasu arteritis (TA) is a chronic idiopathic vasculitis that involves the aorta and its main branches. First reported in 1908, it predominantly affects women and persons of Asian descent. In North America, TA is rare, occurring in an estimated 2.6 persons per million. Although a disproportionate number of patients are Asian, 75% of the patients in the United States are white and 12% are African American. The median age of onset of symptoms is 25 to 35 years, but 19% to 32% of patients are younger than 20 years at the time of diagnosis. Takayasu arteritis begins with an acute inflammatory illness in which musculoskeletal complaints and fever are common. Systemic symptoms resolve in weeks to months as symptoms and signs of vascular insufficiency evolve. Recent reports suggest that the classic triphasic presentation of TA is uncommon. Although TA was initially called “pulseless” disease because of frequent involvement of the branches of the aortic arch, the abdominal aorta and renal arteries are also affected.

The most frequent symptoms in pediatric patients are dyspnea, headache, lightheadedness, visual disturbances, and musculoskeletal complaints. Claudication is much less common in children than adults. The signs of TA in children include absent or diminished pulses (50%-100%), bruits (50%), and hypertension (35%-93%). Synovitis, lymphadenopathy, Raynaud phenomenon, and erythema nodosum–like lesions of the lower extremities may occur. In some studies, the frequency of positive purified protein derivative reactions is higher than in the normal population. Inflammatory bowel disease is present in 5% to 10% of patients with TA, and a smaller proportion have coexisting sarcoidosis. An elevated Westergren erythrocyte sedimentation rate and chronic relapsing pancreatitis are noted in more than 70% of patients, anemia in 50%, and leukocytosis in approximately 40%. The degree of elevation of acute-phase reactants does not necessarily parallel the activity of vascular disease.

Diagnosis in children is substantially delayed in comparison with adults (19 months vs 10 months from onset of symptoms).

The diagnosis of TA is based on characteristic clinical and radiologic findings. Radiographs of the chest demonstrate cardiac enlargement, prominence of the aortic arch, rib notching, diminished pulmonary vascularity, loss of the normal sharp definition of the descending aorta, mediastinal widening, or aortic calcification. Typical angiographic features of TA are occlusive changes of the aorta, its branches, or the pulmonary arteries; aneurysms; and the development of collateral vessels. Early in the disease, vessel wall thickening may be the only manifestation of vascular inflammation.

In 20% of patients, TA is a self-limited illness. Patients with ongoing, active TA are treated with immunosuppressive regimens; children seem to respond better to therapy than do adults, with a 60% response to daily corticosteroids. Patients unresponsive to corticosteroids and those who relapse on discontinuing steroids are treated with cytotoxic agents such as cyclophosphamide, methotrexate, or azathioprine. About one quarter of the patients never achieve remission of their disease.

Angioplasty and vascular bypass are helpful in the palliation of severe stenotic lesions but restenosis occurs. The 5- to 10-year survival of TA is 80% to 90%. Mortality rates are higher in children than in adults, perhaps because of delayed diagnosis and a higher incidence of congestive heart failure and severe hypertension. Most fatalities are attributable to complications of hypertension, cardiac ischemia, cerebrovascular accidents, and infectious complications of immunosuppressive therapy. Severe hypertension, cardiac disease, aneurysm formation, and functional disability predict greater mortality. Although the mortality of TA is relatively low, 75% of patients experience symptoms that interfere substantially with activities of daily living.

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Reprints: Elisabeth E. Adderson, Room 2R022, University of Utah Medical Center, 50 N Medical Dr, Salt Lake City, UT 84132.

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