Aortic dissection and ankylosing spondylitis in hypocystinemia

To the Editor:
The first author and past associates recently described aortic dissection without Marfan syndrome in ankylosing spondylitis, and coexistent ankylosing spondylitis and Marfan syndrome without aortic dissection has been reported in the literature. Reduced fibrillin deposition into the extracellular matrix is found in not only Marfan syndrome but also in a range of connective tissue disorders collectively termed fibrillinopathies, such as isolated ascending aortic aneurysm and dissection. The defective fibrillin of Marfan microfibrils and the inflammation-targeted fibrillin of ankylosing spondylitis might each lead to comparable structural phenotypes of failure. On the other hand, fibrillin-1 is rich in cysteine, and its deposition into the extracellular matrix is greatly diminished under conditions of cysteine deficiency. We here add another case, with hypocysteinemia, of coexistent aortic dissection and ankylosing spondylitis, and discuss possible roles of cyst(e)ine and fibrillin-1 in these disorders.

A 68-year-old woman with back pain was referred to our department. Computed tomographic scanning disclosed Stanford type A (DeBakey type I) acute aortic dissection (Figure 1, A), but she presented with no traits of Marfan syndrome on physical examination. Urgent replacement of the ascending aorta was successfully performed, and the pathologic examination of the aortic wall revealed neither aortitis nor cystic medial necrosis. Plasma total homocysteine concentration was normal (4.7 nmol/mL [range, 3.0-14 nmol/mL]), and cysteine concentration was decreased to 14.5 nmol/mL (range, 29-49 nmol/mL). There was a past history of ankylosing spondylitis without medication, including steroids, and abdominal radiography disclosed the characteristic deformation of the lumbar vertebrae, so-called bamboo spine (Figure 1, B). The patient had negative results for human leukocyte antigen B27 but met the European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy: inflammatory spinal pain, alternate buttock pain, and sacroiliitis.

Reduced fibrillin deposition into the extracellular matrix causes thoracic aortic aneurysm or dissection in patients without Marfan syndrome. Most sites of inflammation in patients with ankylosing spondylitis involve fibrocartilage, and fibrillin-1, a major component of the microfibrils in fibrocartilage, might be the target of this response in the aorta and the eye, as well as in bones and joints. It has been hypothesized that spondylitic inflammation might include release and activation of latent transforming growth factor β from binding sites on fibrillin-1. The hypothesis is supported by some reported cases, including the present one, of coexistent ankylosing spondylitis and Marfan syndrome without aortic dissection or coexistent aortic dissection without Marfan syndrome and ankylosing spondylitis. On the other hand, it has been demonstrated that fibrillin-1 deposition into the extracellular matrix was greatly diminished, as revealed by means of immunocytochemistry, when arterial smooth muscle cells were cultured under conditions of cysteine deficiency. When cysteine concentrations were returned to normal, the smooth muscle cells began to accumulate a matrix rich in fibrillin-1. These results indicate that a deficiency of cysteine impairs the accumulation of fibrillin-1 in the extracellular matrix and could contribute to the pathologic changes of connective tissue. Although the cause of hypocysteinemia in the present case is unclear, a possible role of fibrillin-1 affected by decreased cyst(e)ine is suggested in coexistent aortic dissection and ankylosing spondylitis.

Hisato Takagi, MD, PhD
Seishiro Sekino, MD
Takuya Umemoto, MD, PhD
Department of Cardiovascular Surgery
Shizuoka Medical Center
Shizuoka, Japan

References