Adventitial Cystic Disease

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Adventitial cystic disease (ACD) is an unusual cystic tumor of blood vessels characterized by the accumulation of mucinous substance in the adventitia of the non-axial blood vessels adjacent to joints. Patients with ACD often suffer from intermittent claudication and/or limb pain, mostly involving the popliteal artery. We report a 30-year-old male who presented with intermittent claudication in his left leg. Angiography showed an obstructive lesion in the left popliteal artery. The lesion was treated successfully by surgical excision followed by graft vessel replacement. ACD involving the popliteal artery was diagnosed by pathologic findings of multiple cysts of the adventitia with external compression and focal narrowing of the vascular lumen. The cysts contained acid mucin and were partially lined by multiple rows of cytologically bland, synovium-like cells with positive immunoreactivity to vimentin and CD68 but negative immunoreactivity to cytokeratin. The histopathologic findings in this case suggest that it was caused by the developmental rests of mucin-secreting mesenchymal cells derived from the knee joint. [J Formos Med Assoc 2006; 105(12):1017–1021]

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Adventitial cystic disease (ACD), also known as cystic adventitial disease, is a rare condition characterized by cystic lesions of the non-axial blood vessels adjacent to joints. ACD was first described by Atkins and Key in 1947. Since that time, about 350 cases of ACD have been reported in the English literature. ACD usually involves the popliteal artery, but other great arteries and veins of the lower and upper extremities can also be involved. Intermittent claudication of the legs and limb pain are the main clinical presenting symptoms. Here, we report a 30-year-old male with ACD who was successfully treated by total excision of the lesion and graft replacement. The histopathologic findings and possible pathogenesis of this disease are discussed.

Case Report

A 30-year-old male truck driver presented with a 1-month history of weakness of the left leg and a 2-week history of pain in the left leg. These symptoms were relieved by rest. He had a 7–8-year history of smoking one pack of cigarettes per day, but had no other known risk factors for peripheral arterial occlusive disease or systemic disease. A slightly lower temperature on the left lower leg than on the right lower leg was found on physical examination. Pulsation was absent in the left posterior tibial artery and dorsal pedis. Pulse–volume recording showed an ankle/brachial pressure index of 5.5. Arteriography via the right femoral artery demonstrated an abrupt filling defect in the left popliteal...
artery with slow blood flow compared with the right side (Figure 1). No other systemic disease was noted.

Peripheral arterial occlusive disease was diagnosed and the patient underwent bypass surgery. The left popliteal fossa was approached posteriorly, and an enlarged and tortuous segment with a fusiform appearance measuring 3.4 cm in length was noted at the left popliteal artery. The external surface of the adventitia of the fusiform segment was smooth and without connection to the adjacent knee joint. The fusiform segment of the popliteal artery was resected, followed by graft replacement. The patient recovered uneventfully and there was no evidence of recurrence 5 months after surgery.

On gross examination, the excised arterial segment was dilated and tortuous, and enclosed by a multilocular cyst containing sticky jelly-like mucoid material at the adventitia (Figure 2A). The vascular lumen was compressed and the tunica intima was smooth and glistening. Pathologically, the tunica adventitia was highly collagenized with multiple cystic spaces encroaching on the tunica media (Figure 2B). The cyst contained acid mucin as demonstrated by positive mucicarmine and alcian blue staining, but was negative for periodic acid-Schiff (PAS) staining. Some cystic spaces were partially lined by multiple rows of synovium-like cells (Figure 2C). The cells lining the inner cyst wall were polygonal in shape with abundant eosinophilic or clear and vacuolated cytoplasm; the vacuolated cytoplasm was positive on mucicarmine and alcian blue staining (Figure 2D). The nuclei of these cells were bland and round to ovoid in shape. These cells were strongly positive for vimentin and CD68, and negative for cytokeratin (AE1/AE3) (Figures 2E, 2F) by immunohistochemistry. Some foci of myxoid degeneration with accumulation of mucoid material and a large amount of floating synovium-like cells in the connective tissue of the cystic wall were also noted.

Discussion

ACD was first described by Atkins and Key in 1947.3 Flanigan et al4 and Ishikawa5 reported a series of 115 cases and 129 cases, respectively, and summarized their clinical presentations, pathologic features, treatment modalities, possible etiologies and pathogenesis. ACD accounts for only 0.1% of vascular disease and approximately 1 in 1200 cases presenting with claudication.6,7 ACD is a well-known cause of intermittent claudication in middle-aged patients who are not at risk for peripheral arterial occlusive disease. There is a male predominance with a male-to-female ratio of 5:1.8 The age at presentation ranges from 11 to 72 years, and the mean age is about 42 years.9 More than 80% of ACD involves the popliteal artery, followed by the iliofemoral artery, radial/ulnar arteries, and brachial and axillary arteries.2,8,10 Solitary lesions are seen in most patients; synchronous and metachronous lesions have never been reported. About 5% of ACD cases involve either the common femoral vein or the external iliac vein,6,11 although rare cases involving the saphenous vein, the popliteal vein, and veins of the wrist area have been reported.11,12 Venous involvement in ACD presents as a gradually progressive

Figure 1. Arteriography of both legs demonstrates an abrupt filling defect in the left popliteal artery near the knee joint (arrow).
edema of the lower limb, a palpable tumorous lesion, pain, or even deep vein thrombosis.11,12

The treatment of choice for ACD is surgical evacuation of the cyst with preservation of native artery. If preservation of native artery is not feasible, resection of the affected arterial segment with a vascular graft is required. Percutaneous cyst aspiration and percutaneous transluminal angioplasty with stenting have been reported with poor results and high rate of recurrence.6,13–15 Recurrence is always associated with incomplete excision of the cyst.

Figure 2. Adventitial cystic disease (ACD) of the popliteal artery. (A) Gross appearance of ACD. The cystic lesion is mainly at the adventitia with external compression and focal narrowing of the vascular lumen (arrows). The tunica intima is intact and smooth. (B) Histology of arterial wall (arrow) and adjacent adventitial cyst (asterisks). (C) The cyst is partially lined by multiple rows of synovium-like cells (arrow) (hematoxylin and eosin, 200x). (D) The cytoplasm of lining cells shows alcin blue-positive material (arrow). The lining cells are positive for: (E) vimentin and (F) CD68. (Immunohistochemical stain colorized by diaminobenzidine [DAB] and hematoxylin counterstained, 400x).
Morphologically, ACD is characterized by unilocular or multilocular cysts in the adventitia of the involved blood vessel with accumulation of mucinous substance in the cysts. The mucoid substances in the cysts are mucopolysaccharides with high concentration of hyaluronic acid.\textsuperscript{16–18} The inner surface of the cysts may be partially lined by mucin-secreting, synovium-like cells with negative reactivity to markers for synovial cells and endothelial cells.\textsuperscript{8,16,19}

The pathogenesis of ACD is not known. Four hypotheses of the pathogenesis of ACD have been proposed, including: (1) repeated microtrauma; (2) ectopic ganglion cyst migrating from adjacent joint; (3) systemic myxomatous degeneration; and (4) developmental rests of mucin-secreting mesenchymal cells derived from adjacent joint.\textsuperscript{2,6,8}

The theory of repeated microtrauma suggests that repeated flexing of the joint results in mucoid and cystic degeneration of the adventitia of the adjacent vessel.\textsuperscript{2} However, this hypothesis is not supported by several findings, including the following: (1) the very rare incidence of ACD; (2) most patients lack a history of recurrent trauma; (3) the frequency of this condition is lower in laborers and athletes, who sustain more mechanical stress than people in the general population; and (4) none of the case reports involving children support this hypothesis.\textsuperscript{1,8,20–22}

The morphologic similarity of ACD to ganglion cyst of the joint has been noted. Furthermore, communication between ACD and the adjacent joint capsule is sometimes encountered during surgery.\textsuperscript{1,8,16,23,24} The ectopic ganglion cyst theory postulates that ACD arises from synovial cysts migrating along vascular branches into the adventitia of the adjacent major vessel.\textsuperscript{14,18,19,23} This theory is supported by the proximity of ACD to the joints and connections in some cases.\textsuperscript{1,8,16,23,24} Some authors have demonstrated the biochemical similarity between ACD and ganglion cysts.\textsuperscript{14,19,24} However, the cystic lining cells in some ACD cases were not positive to immunohistochemical markers of synovial cells, such as cytokeratin 4, 8 and 12, which does not support this theory.\textsuperscript{8,16} There are also arguments about the origin of the cystic lining and the biochemical features of mucin, including how to explain the higher concentration in ACD cysts than in synovial fluid.\textsuperscript{16–18,22,23,25}

The systemic myxomatous degeneration theory is unlikely because no cases of ACD in association with initial or long-term systemic manifestations have been reported.

Levien and Benn reviewed the literature concerning the theories on the formation of ACD and embryology of limb vessels.\textsuperscript{8} They proposed that ACD cysts are caused by incorporation of developmental rests of mucin-secreting mesenchymal cells derived from the adjacent joint into the developing non-axial vessels. This hypothesis is based on findings that the development of non-axial vessels and limb bud formation occurs in the same period, and ACD almost always occurs in close proximity to the adjacent joint. This theory presumes the mesenchymal origin of the cystic linings of ACD, and provides a reasonable explanation of the immunohistochemical features of these lining cells and the biochemical features of the mucin content.

In our patient, ACD involved the left popliteal artery without communication with the knee joint. The cyst was multilocular, enclosed the involved artery, occupied the tunica adventitia, and encroached on the tunica media with collagenization of the stroma. The cyst contained acid mucin as demonstrated by positive mucicarmine and alcian blue staining but negative PAS staining, indicative of connective tissue instead of epithelial cell origin. The cyst was partially lined by multiple rows of cytologically bland, synovium-like cells. These cells also contained acid mucin and showed strong immunoreactivity to vimentin and CD68 but negative immunoreactivity to cytokeratin (AE1/AE3). These biochemical and immunohistochemical results suggest a mesenchymal/histiocytic origin of the cystic lining cells. The overall histopathologic findings of this case support the theory that ACD may be caused by the developmental rests of mucin-secreting mesenchymal cells derived from the adjacent joint.
References
