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Arteriopathy of Unknown Etiology: Pathologic, Radiologic, and Cytogenetic Investigations

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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Patient: Male, 38
Final Diagnosis: Arteriopathy of unknown etiology
Symptoms: Left groin pain
Medication: —
Clinical Procedure: —
Specialty: Neurology

Objective: Unknown ethiology

Background: Dissections occur when the intima is injured and an intramural hematoma develops between the intima and the media. There are a multitude of factors which contribute to arterial aneurysms and dissections, that could be infectious, genetic, traumatic, or environmental, but there are still cases for which the etiology is not determined.

Case Report: We describe a patient who presented with arterial aneurysms and dissections that involved multiple vessels over the course of 10 years. We also reviewed the literature on possible risk factors, triggers, and genetic disorders that may predispose patients to developing arterial aneurysms and dissections.

Conclusions: To the best of our knowledge, this is the first report of this unusual pattern of presentation for idiopathic vasculopathy causing multiple dissections and aneurysms in a young patient. Idiopathic vasculopathy resulting in aneurysm and dissection is not an entirely uncommon entity; most cases of disparate dissection are not linked with a causal mechanism, although genetic influence is often heavily suspected, but it unfortunately often cannot be proven. We reviewed the available literature for a better understanding of pathologic, radiologic, and cytogenetic investigations of arteriopathy of unknown cause.

MeSH Keywords: Aneurysm, Dissecting • Aortic Aneurysm, Abdominal • Carotid Artery, Internal, Dissection

Abbreviations: **ICA** – internal carotid artery; **SMA** – superior mesenteric artery; **AAA** – abdominal aortic aneurysm; **MRA** – magnetic resonance angiography; **SAM** – segmental arterial mediolysis; **FMD** – fibromuscular dysplasia; **CT** – computed tomography; **PET** – positron emission tomography; **FDG** – fluorodeoxyglucose; **ABI** – ankle brachial index; **CRP** – C-reactive protein; **CAD** – cervical arterial dissections; **TGFBR2** – TGF-beta receptor 2; **vEDS** – vascular Ehlers-Danlos syndrome; **TAAD** – familial thoracic aortic aneurysm disorder; **SMA** – segmental mediolytic arteriopathy

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/917353

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Background

Arterial aneurysms and dissections are major causes of morbidity and mortality. True aneurysms are an abnormal dilatation of a vessel due to a week arterial wall [1], while false aneurysms (i.e., pseudoaneurysms) are caused by blood leaking from a vessel, forming a hematoma outside the artery, which is contained by the surrounding tissues [2].

Dissections occur when the intima is injured and an intramural hematoma develops between the intima and the media [3]. There are many factors that can contribute to arterial aneurysms and dissections, including infectious, genetic, traumatic, or environmental factors, but there are still cases for which the etiology is unclear.

We describe a patient who presented with arterial aneurysms and dissections that involved multiple vessels on the course of 10 years. We also reviewed the literature on possible risk factors, triggers, and genetic disorders that can predispose to developing arterial aneurysms and dissections.

Case Report

A 38-year-old male presented to our hospital for follow-up of a recent left ICA dissection. Past medical history was significant for arteriopathy of unknown etiology with multiple aneurysms and dissections over the previous 11 years, including right ICA dissection, SMA aneurysm, AAA, and bilateral iliac aneurysms, which were operatively repaired. He was admitted with a left ICA dissection and was conservatively managed with anti-coagulation and anti-hypertensive optimization. MRA, as depicted in Figure 1, showed a known dissection of the left internal carotid artery beginning approximately 1 cm above the bifurcation and extending into the distal cervical segment, where there is decreased but still preserved flow. There was also a 4-mm pseudoaneurysm of the distal cervical segment of the right internal carotid artery.

This was unfortunately not the first arterial dissection in this patient, the first of which occurred at age 27, when the patient had a ruptured left common iliac artery aneurysm. At that time, he presented with 2 weeks of left groin pain, an episode of pre-syncope, and reduced ejaculatory volume. Pathology showed acute medial dissection with local pseudoaneurysm, but no evidence of arteritis.

At age 29, he had an episode of severe headache and dizziness. MRA showed poor flow void within the right ICA, which was worrisome for dissection, along with a punctate focus of restricted diffusion compatible with a small right parietal infarct (Figure 2). The patient was administered aspirin, with no surgical options pursued. At that time, inflammatory markers were normal. A broad differential diagnosis was considered, including Loeys-Dietz syndrome; mutations in genes TGFBR1/2 were tested but came back negative. Another condition to be ruled out was vascular Ehlers-Danlos syndrome, so testing for COL3A1 was done, with no mutations detected. Testing also was performed to detect mutations in fibrillin 1, MYH11, and MYLK genes and all were negative.

At age 30, he developed mesenteric aneurysms presenting as abdominal pain, nausea, and vomiting. A CT angiogram (Figure 3) demonstrated an 11-mm saccular aneurysm of the proximal SMA, with crescentic wall thickening and segmental

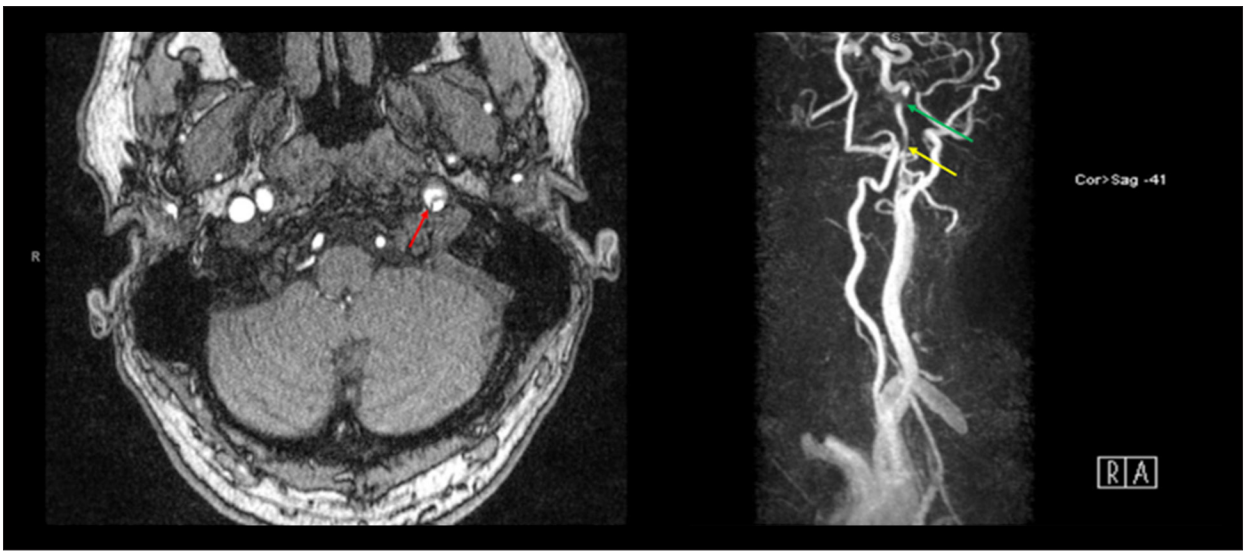

Figure 1. MRA showing a dissection of the left internal carotid artery (red arrow) beginning approximately 1 cm above the bifurcation (yellow arrow) and extending into the distal cervical segment where there is decreased, but preserved, flow (green arrow).

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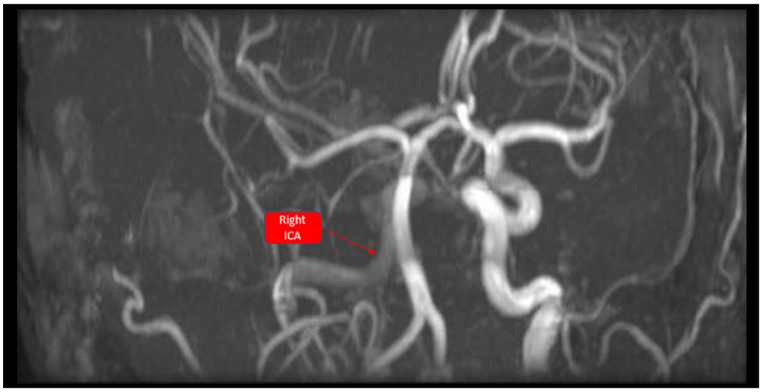

Figure 2. MRA showing poor flow void within the right ICA, which was worrisome for dissection (red arrow).

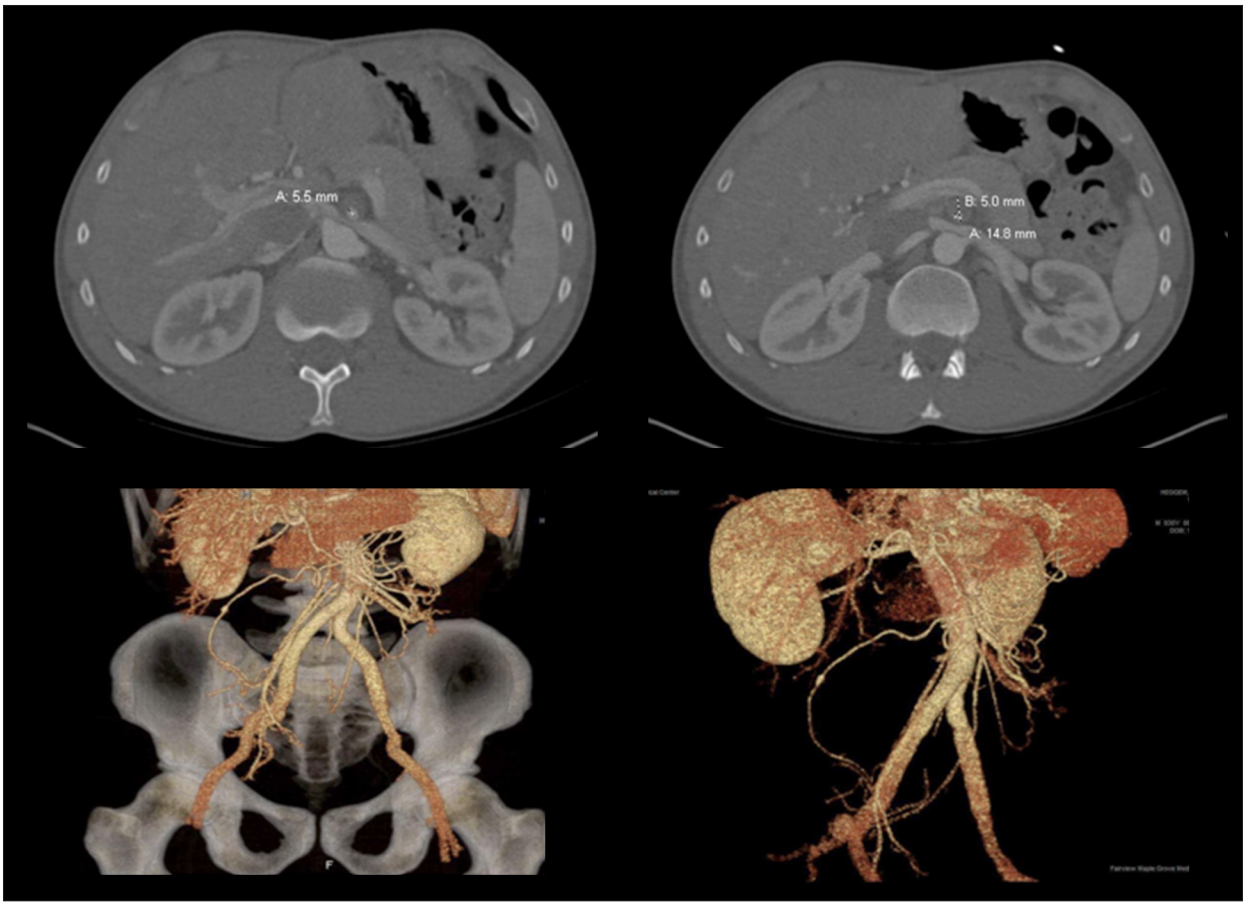

Figure 3. The superior mesenteric artery is pathologic, with crescentic wall thickening along the anterior lateral aspect of the vessel. The SMA, including the thickened portion of the wall, measures approximately 15 mm in diameter, while the lumen of the SMA measures 5 mm in diameter. Approximately 5.7 cm from the origin of the SMA there is an 11-mm aneurysm extending anteriorly. A branch vessel, likely the middle colic artery, arises from the aneurysm itself. Distal to the level of the aneurysm, several of the jejunal branches appear well-preserved. However, there is segmental occlusion of the ileocolic artery. Several tubular soft tissues structures extending along the expected location of SMA branch vessels are likely massively inflamed/thrombosed portions of the SMA.

occlusions. Thus, we sought to determine if this was segmental arterial mediolysis (SAM), FMD, or mesenteric vasculitis suspicious for polyarteritis nodosa. To investigate for the latter, hepatitis B serology was performed and turned out to be negative. PET scan showed moderate FDG uptake in the left common iliac artery compared to the aorta and great vessels, which was thought to be atypical for segmental arterial mediolysis. He was started on a prednisone taper 40 mg daily and

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the plan was to follow up in 3 months with repeat PET. Follow-up took place at a tertiary center where specialists evaluated the patient: CT angiogram of the abdomen and pelvis showed a new dissection extending form the distal abdominal aorta to involve the right common iliac artery, the right internal iliac artery, and the proximal right external iliac artery. Additionally, there was a 15-mm aneurysm of the right internal iliac artery at the level of the divisional bifurcation. There was near-complete resolution of the SMA dissection and pseudoaneurysm.

Out of a strong suspicion for vascular angiopathy, permission was obtained to talk to the patient's mother (father was estranged); she agreed to have a CT angiogram, which was normal. A maternal sample was evaluated for the MYH11 genetic mutation and she was negative. Given that there was no strong evidence suggesting vasculitis as SMA normalized, the steroid therapy was tapered off. Follow-up with imaging 3 months later showed an increasing dilatation of dissected right common and external iliac arteries.

At age 31, he underwent a surveillance exercise ABI measurement, despite the absence of claudication symptoms: At rest, ABI values were right 1.02 and left 1.09, and these remained normal at 1.08 and 1.05, respectively, with ambulation. He was evaluated by a rheumatology consultant who did not think he had a defined rheumatological illness. Several months later, normal values were documented for CRP, myeloperoxidase Ab, and proteinase (PR3). Duplex artery US of the right iliac artery was stable.

At age 33, he underwent repair of the right common iliac artery aneurysm and internal iliac artery aneurysm due to increasing discomfort in the right iliac fossa. He underwent extensive adhesiolysis, omentoplasty, rigid colonoscopy, placement of right and left whistle-tip ureteral stents, and repair of a jejunal enterotomy.

A follow-up CT angiogram was performed after less than a year, which demonstrated patency of the right distal aorta to external iliac graft. The internal iliac artery graft was compressed in its mid-segment against the vertebral body and occluded. There was, however, robust distal flow into the distal right internal iliac artery, as well as at the left iliac artery, which was ligated at the initial repair. Collateral flow was provided by large distal aortic lumbar branches, as well as via the inferior mesenteric artery. The appearance of the SMA was unchanged. There was occlusion of the distal iliac branches, as well as a first-order renal branch with an infarction in the upper pole of the left kidney.

Subsequently, he developed left ICA dissection beginning approximately 1 cm above the bifurcation and extending into the distal cervical segment. The patient presented symptomatically with a low-grade occipital headache and was evaluated for stroke via vessel imaging and MRI. He did not have stroke, but he was found to have an extra-cranial ICA dissection. After discussion with the patient, he was started on anti-coagulation with follow-up in 3 months. His course was uncomplicated, and his headache resolved. Follow-up imaging revealed a healing dissection with proximal formation of a pseudoaneurysm. His anti-coagulation was discontinued, and he was placed on high-dose aspirin for the foreseeable future.

Discussion

We describe the case of a 38-year-old man who developed arterial aneurysms and dissections that involved multiple arterial blood vessels. Over the course of 11years, the patient suffered from a ruptured left common iliac artery aneurysm, right ICA dissection, and SMA aneurysm. He also developed an aortic dissection that also involved the right common iliac artery, the right internal iliac artery, and the proximal right external iliac artery. Lastly, he presented with left ICA dissection along with right ICA pseudoaneurysm.

The exact etiology of arterial dissections is sometimes unclear. Many factors have been suggested as possible triggers for cervical arterial dissections (CAD), although the majority develop spontaneously or due to minor trauma. These triggers include recent infections [4], sports activities and minor sports injuries [5–8], roller coaster rides [9], coughing or sneezing [10], and chiropractic neck manipulation [11].

A different set of risk factors predispose to aortic disease. Aortic dissection is most commonly caused by hypertension, which is responsible for 72% of cases [12]. Having a preexisting aortic aneurysm accounts for 13–19% of cases [13]. Other factors that increase the risk of aortic dissections are conditions that cause inflammation in the aorta, including, but not limited to, giant cell arteritis, Takayasu arteritis, and syphilitic aortitis [14]. Aortic aneurysms, on the other hand, are mainly related to aging, male sex, white race, smoking, and atherosclerosis [15].

Genetics play an important role in the risk of developing an arterial aneurysm or dissection. Family history of CAD increases the risk of developing the disease, even in the absence of a well-defined connective tissue or vascular disorder in the patient's family [16,17]. The same is true for abdominal aortic aneurysms and thoracic aortic aneurysms [18,19].

Connective tissue and vascular disorders explain only a minority of CAD cases [20]. The most commonly found vascular disorder is fibromuscular dysplasia (FMD), which accounts for 15–20% of CAD cases [21]. It is a non-inflammatory disease

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that leads to aneurysms and dissections in the renal and cervical arteries, and, less frequently, the iliac and abdominal visceral arteries [22]. The diagnosis is usually confirmed with duplex ultrasound, CT angiogram, or angiography [23].

Marfan syndrome plays a more important role in young patients with aortic dissection, accounting for about 50% of cases [13]. It is an autosomal dominant disorder caused by a mutation in the fibrillin 1 or, least commonly, by a mutation in the TGF-beta receptor 2 (TGFBR2) or TGFBR1 [24]. It is characterized by aortic root dilatation and dissection, mitral valve abnormalities, and ocular and musculoskeletal findings [25].

Ehlers-Danlos syndrome type IV (vascular EDS) is rarely responsible for CAD, accounting only for 1–2% of cases [20,26]. However, it is more commonly associated with aortic root dilatation and spontaneous rupture of the abdominal aorta, usually without dissection [27]. The vascular type of EDS (vEDS) is an autosomal dominant disease caused by a mutation in the COL3A1 gene [28]. Patients usually present with variable clinical features that include thin translucent skin, easy bruising, characteristic faces, and rupture of arteries, uterus, or bowel [26], features which our patient did not have.

Other genetic disorders are rarely identified in arterial aneurysms and dissections. Loeys-Dietz syndrome is a newly described autosomal dominant disease that is caused by mutations in TGFBR1 and TGFBR2 [29]. It is marked by dysmorphic facies along with aggressive aortic aneurysms and dissections [30].

Familial thoracic aortic aneurysm disorder (TAAD) is another genetic disease that results in thoracic aortic aneurysms and dissections [18]. Many genes have been associated with TAAD, including TGFBR2, MYH11, and ACTA2 [31–33].

Segmental mediolytic arteriopathy (SMA) is in extremely rare vascular disease of unknown pathophysiology. Most commonly, it causes aneurysms and dissections in the abdominal visceral arteries, but other arteries may be involved, including the intracranial and coronary arteries [34–36]. Angiography may suggest the diagnosis, but SMA is usually confirmed by histopathology, which remains the criterion standard for diagnosis [37].

Various other genetic disorders have been associated with arterial aneurysms and dissections. These include osteogenesis imperfecta [38], homocystinuria [39], autosomal dominant polycystic kidney disease [40], and alpha-1 antitrypsin deficiency [41]. However, the association of these disorders with vascular pathology lacks definitive evidence.

Our patient was evaluated for all of the conditions that can predispose to arterial aneurysms and dissection. He was a young patient who had normal blood pressure and never smoked. He did not have any recent or past infections, nor had he experienced any traumas. None of his family members had similar complaints. He was tested for FMD, Marfan, vEDS, Loeys-Dietz syndrome, TAAD, and SMA; all of the tests came back negative. The patient's condition might be explained by a yet to be identified vascular disorder.

Conclusions

To the best of our knowledge, this is the first case report of this unusual pattern of presentation of idiopathic vasculopathy causing multiple dissections and aneurysms in a young patient. Idiopathic vasculopathy resulting in aneurysm and dissection is not an entirely uncommon entity; most cases of disparate dissection are not linked with a causal mechanism, and although a genetic influence is heavily suspected, it often cannot be proven. We reviewed the available literature for a better understanding of pathologic, radiologic, and cytogenetic investigations of arteriopathy of unknown cause.

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Conflict of interest

None.

References:

1. McPhee JT, Hill JS, Eslami MH: The impact of gender on presentation, therapy, and mortality of abdominal aortic aneurysm in the United States, 2001–2004. J Vasc Surg, 2007; 45(5): 891–99
2. Kalapatapu VR, Shelton KR, Ali AT et al: Pseudoaneurysm: A review. Curr Treat Options Cardiovasc Med, 2008; 10(2): 173–83
3. Criado FJ: Aortic dissection: A 250-year perspective. Tex Heart Inst J, 2011; 38(6): 694–700
4. Guillon B, Berthet K, Benslamia L et al: Infection and the risk of spontaneous cervical artery dissection: A case-control study. Stroke, 2003; 34(7): e79–81
5. Mas Rodriguez MF, Berrios RA, Ramos E: Spontaneous bilateral vertebral artery dissection during a basketball game: A case report. Sports Health, 2016; 8(1): 53–56
6. Abe A, Nishiyama Y, Kamiyama H et al: Symptomatic middle cerebral artery dissection in a young tennis player. J Nippon Med Sch, 2009; 76(4): 209–11
7. Karnik R, Rothmund T, Bonner G et al: Inline skating as a possible cause of consecutive bilateral vertebral artery dissection. Acta Neurol Scand, 2000; 101(1): 70–71

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8. Slankamenac P, Jesic A, Avramov P et al: Multiple cervical artery dissection in a volleyball player. Arch Neurol, 2010; 67(8): 1024
9. Biousse V, Chabriat H, Amarenco P, Bousser MG: Roller-coaster-induced vertebral artery dissection. Lancet, 1995; 346(8977): 767
10. Caso V, Paciaroni M, Bogousslavsky J: Environmental factors and cervical artery dissection. Front Neurol Neurosci, 2005; 20: 44–53
11. Reuter U, Hamling M, Kavuk I et al: Vertebral artery dissections after chiropractic neck manipulation in Germany over three years. J Neurol, 2006; 253(6): 724–30
12. Hagan PG, Nienaber CA, Isselbacher EM et al: The International Registry of Acute Aortic Dissection (IRAD): New insights into an old disease. JAMA, 2000; 283(7): 897–903
13. Januzzi JL, Isselbacher EM, Fattori R et al: Characterizing the young patient with aortic dissection: Results from the International Registry of Aortic Dissection (IRAD). J Am Coll Cardiol, 2004; 43(4): 665–69
14. Gornik HL Creager MA: Aortitis. Circulation, 2008; 117(23): 3039–51
15. Kent KC, Zwolak RM, Egorova NN et al: Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals. J Vasc Surg, 2010; 52(3): 539–48
16. Schievink WI, Mokri B, Piepgras DG, Kuiper JD: Recurrent spontaneous arterial dissections: Risk in familial versus nonfamilial disease. Stroke, 1996; 27(4): 622–24
17. Martin JJ, Hausser I, Lyrer P et al: Familial cervical artery dissections: Clinical, morphologic, and genetic studies. Stroke, 2006; 37(12): 2924–29
18. Coady MA, Davies RR, Roberts M et al: Familial patterns of thoracic aortic aneurysms. Arch Surg, 1999; 134(4): 361–67
19. Lederle FA, Johnson GR, Wilson SE et al: The aneurysm detection and management study screening program: validation cohort and final results. Aneurysm Detection and Management Veterans Affairs Cooperative Study Investigators. Arch Intern Med, 2000; 160(10): 1425–30
20. Grond-Ginsbach C, Debette S: The association of connective tissue disorders with cervical artery dissections. Curr Mol Med, 2009; 9(2): 210–14
21. Schievink WI: Spontaneous dissection of the carotid and vertebral arteries. N Engl J Med, 2001; 344(12): 898–906
22. de Bray JM, Marc G, Pautot V et al: Fibromuscular dysplasia may herald symptomatic recurrence of cervical artery dissection. Cerebrovasc Dis, 2007; 23(5–6): 448–52
23. Slovut DP, Olin JW: Fibromuscular dysplasia. N Engl J Med, 2004; 350(18): 1862–71
24. Ramirez F, Dietz HC: Marfan syndrome: From molecular pathogenesis to clinical treatment. Curr Opin Genet Dev, 2007; 17(3): 252–58
25. De Paepe A, Devereux RB, Dietz HC et al: Revised diagnostic criteria for the Marfan syndrome. Am J Med Genet, 1996; 62(4): 417–26
26. Pepin M, Schwarze U, Superti-Furga A, Byers PH: Clinical and genetic features of Ehlers-Danlos syndrome type IV, the vascular type. N Engl J Med, 2000; 342(10): 673–80
27. Wenstrup RJ, Meyer RA, Lyle JS et al: Prevalence of aortic root dilation in the Ehlers-Danlos syndrome. Genet Med, 2002; 4(3): 112–17
28. Schwarze U, Schievink WI, Petty E et al: Haploinsufficiency for one COL3A1 allele of type III procollagen results in a phenotype similar to the vascular form of Ehlers-Danlos syndrome, Ehlers-Danlos syndrome type IV. Am J Hum Genet, 2001; 69(5): 989–1001
29. Loeys BL, Chen J, Neptune ER et al: A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in TGFBR1 or TGFBR2. Nat Genet, 2005; 37(3): 275–81
30. Loeys BL, Schwarze U, Holm T et al: Aneurysm syndromes caused by mutations in the TGF-beta receptor. N Engl J Med, 2006; 355(8): 788–98
31. Vaughan CJ, Casey M, He J et al: Identification of a chromosome 11q23.2-q24 locus for familial aortic aneurysm disease, a genetically heterogeneous disorder. Circulation, 2001; 103(20): 2469–75
32. Pannu H, Avidan N, Tran-Fadulu V, Milewicz DM: Genetic basis of thoracic aortic aneurysms and dissections: Potential relevance to abdominal aortic aneurysms. Ann NY Acad Sci, 2006; 1085: 242–55
33. Zhu L, Vranckx R, Khau Van Kien P et al: Mutations in myosin heavy chain 11 cause a syndrome associating thoracic aortic aneurysm/aortic dissection and patent ductus arteriosus. Nat Genet, 2006; 38(3): 343–49
34. Slavin RE: Segmental arterial mediolysis: Course, sequelae, prognosis, and pathologic-radiologic correlation. Cardiovasc Pathol, 2009; 18(6): 352–60
35. Ro A, Kageyama N, Takatsu A, Fukunaga T: Segmental arterial mediolysis of varying phases affecting both the intra-abdominal and intracranial vertebral arteries: An autopsy case report. Cardiovasc Pathol, 2010; 19(4): 248–51
36. Lie JT, Berg KK: Isolated fibromuscular dysplasia of the coronary arteries with spontaneous dissection and myocardial infarction. Hum Pathol, 1987; 18(6): 654–56
37. Baker-LePain JC, Stone DH, Mattis AN et al: Clinical diagnosis of segmental arterial mediolysis: Differentiation from vasculitis and other mimics. Arthritis Care Res (Hoboken), 2010; 62(11): 1655–60
38. Rouviere S, Michelini R, Sarda P, Pages M: Spontaneous carotid artery dissection in two siblings with osteogenesis imperfecta. Cerebrovasc Dis, 2004; 17(2–3): 270–72
39. Weiss N, Demeret S, Sonneville R et al: Bilateral internal carotid artery dissection in cystathionine beta-synthase deficiency. Eur Neurol, 2006; 55(3): 177–78
40. Larranaga J, Rutecki GW, Whittier FC: Spontaneous vertebral artery dissection as a complication of autosomal dominant polycystic kidney disease. Am J Kidney Dis, 1995; 25(1): 70–74
41. Vila N, Millan M, Ferrer X et al: Levels of alpha1-antitrypsin in plasma and risk of spontaneous cervical artery dissections: A case-control study. Stroke, 2003; 34(9): E168–69

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