PAI-1 4G/4G polimorfizminin ME ile ilişkili olduğuna dair çok sayıda rapor bildirilmişken 4G/5G polimorfizmi ile ilgili çelişkili raporlar mevcuttur (6). Salas ve ark. larının (1) yaptıkları çalışmada kırk beş yaş ve altı ST elevasyonlu akut MI (STEMI) geçiren hastalarda PAI-1 4G allelinin bağımsız risk faktörü olduğunu bildirmişlerdir. Bu çalışmada PAI-1 plazma konsantrasyonu 4G/4G polimorfizmi olanlarda en yüksek, 5G/5G polimorfizmi olanlarda en az ve heterozigotlarda orta düzeyde bulunmuştur. Yakın zamanda yapılan bir başka çalışmada STEMI nedeniyle trombolitik tedavi uygulanan hastaların anjiyografik incelemesinde, PAI-1 4G/5G mutasyonuna sahip olanlarda bu mutasyonun olmadığı bireylere göre no-reflow riskinin artmış olduğu bildirilmiştir (7).

PAİ-1 polimorfizminin yanı sıra t-PA Alu repeat I/D polimorfizminin de tromboz gelişiminde rol oynadığına dair çelişkili veriler mevcuttur. Gong ve ark. (8) tarafından yapılan metaanalizde PAI-1 4G allelinin ME için risk faktörü olduğu ancak tPA Alu repeat I/D polimorfizmin ME ile ilişkili bulunmadığı bildirilmiştir.

PAI-1 polimorfizmi ve t-PA Alu repeat I/D polimorfizmi sıklığı etnik gruplara ve cinsiyete göre de farklılık göstermektedir. Türk popülasyonunda PAI-1 genotipinin sağlıklı ve hasta bireyler arasındaki dağılımına ilişkin veriler sınırlıdır. Önalan ve ark. (9) tarafından yapılan bir araştırmada PAI-1 4G/4G genotipi sıklığı sağlıklı bireylerde %26, akut ME ile prezante olanlarda %32,7 olarak saptanmış olup 4G/4G polimorfizminin aterosklerotik lezyonu olan olgularda ME gelişimi için risk faktörü olduğu bildirilmiştir. Bir başka çalışmada elli beş yaş altı MI geçiren erkeklerin çocuklarında PAI-1 seviyesinin yüksek olduğu bildirilmiştir (10). Bu tespit diğer risk faktörleri ile birlikte 4G allelini taşıyan bireylerin kardiyovasküler yönden primer korumasında faydalı olabilir.

Sonuç

Genç yaşta görülen, tekrarlayan veya geleneksel risk faktörleri ile açıklanamayan MI olgularında, PAI-1 polimorfizmi olasılığının akılda tutulması, trombolitik tedavi uygulanacaksa PAI-1'e dirençli fibrinolitik ajanların tercih edilmesi ve genetik inceleme yapılması yönünden önemlidir.

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Video 1. Selektif sol koroner anjiyografide sol ön inen arterde birinci diyagonal arter sonrasında stent içi trombüs imajı izlendi
Video 2. Selektif sağ koroner anjiyografide, sağ koroner arterde proksimalde %70 darlığa yol açan trombüslü lezyon saptandı

Kaynaklar

1. Isordia-Salas I, Leanos-Miranda A, Sainz IM, Reyes-Maldonado E, Borrayo-Sanchez G. Association of the plasminogen activator inhibitor-1 Gene 4G/5G polymorphism with ST elevation acute myocardial infarction in young patients. Rev Esp Cardiol 2009; 62: 365-72. [CrossRef]
2. Dawson S, Henney A. The status of PAI-1 as a risk factor for arterial and thrombotic disease: a review. Atherosclerosis 1992; 95: 105-17. [CrossRef]
3. Huber K. Plasminogen activator inhibitor type-1 (part two): role for failure of thrombolytic therapy. PAI-1 resistance as a potential benefit for new fibrinolytic agents. J Thromb Thrombolysis 2001; 11: 195-202. [CrossRef]
4. Sayer JW, Gutteridge C, Syndercombe-Court D, Wilkinson P, Timmis AD. Circadian activity of the endogenous fibrinolytic system in stable coronary artery disease: effects of beta-adrenoreceptor blockers and angiotensin-converting enzyme inhibitors. J Am Coll Cardiol 1998 ;32: 1962-8. [CrossRef]
5. Dawson SJ, Wiman B, Hamsten A, Green F, Humphries S, Henney AM. The two allele sequences of a common polymorphism in the promoter of the plasminogen activator inhbitor-1 (PAI-1) gene respond differently to interleukin-I HepG2 cells. J Biol Chem 1993; 268: 10739-45.
6. Lima LM, Carvalho MD, Fonseca Neto CP, Garcia JC, Sousa MO. PAI-1 4G/5G polymorphism and plasma levels association in patients with coronary artery disease. Arq Bras Cardiol 2011; 97: 389-462.
7. Özkan B, Çağlıyan CE, Elbasan Z, Uysal OK, Kalkan GY, Bozkurt M, et al. PAI-1 4G/5G gene polymorphism is associated with angiographic patency in ST-elevation myocardial infarction patients treated with thrombolytic therapy. Coron Artery Dis 2012; 23: 400-3. [CrossRef]
8. Gong LL, Peng JH, Han FF, Zhu J, Fan LH, Wang YH, et al. Association of tissue plasminogen activator and plasminogen activator inhibitor polymorphism with myocardial infarction: a meta-analysis. Thromb Res 2012; 130: e43-51. [CrossRef]
9. Rallidis LS, Megalou AA, Papageorgakis NH, Trikas AG, Chatzidimitriou GI, Tsitouris GK. Plasminogen activator inhibitor-1 is elevated in the children of men with premature myocardial infarction. Thromb Haemost 1996; 76: 417-21.
10. Önalan O, Balta G, Oto A, Kabakçı G, Tokgözoğlu L, Aytemir K, et al. Plasminogen activator inhibitor-1 4G4G genotype is associated with myocardial infarction but not with stable coronary artery disease. J Thromb Thrombolysis 2008; 26: 211-7. [CrossRef]

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An acute coronary syndrome patient: is this atherosclerosis?

Bir akut koroner sendrom vakası: Bu ateroskleroz mudur?

Introduction

Atherosclerosis is the most common cause of cardiovascular diseases manifesting frequently as stenotic coronary artery lesions or aortic aneurysm formation. Although other causes such as coronary artery emboli, dissection, cocaine toxicity, congenital coronary anomalies, systemic vasculitis, metabolic and hematologic disorders are rare, they should be envisaged in the differential diagnosis in patients with systemic symptoms or atypical involvement of the vessels and in young patients. We present herein a patient with chest pain and multiple aneurysms of the coronary arteries, aorta and its main branches.

Case Report

This is a 55-year old male with new onset angina and ST segment depression on the electrocardiography who was referred for possible operation of the ascending aortic aneurysm. On his transthoracic echocardiography (TTE); aneurysmal dilatation of the aortic root was detected starting from just above the ostia of the coronary arteries (Fig. 1A, Video 1. See corresponding video/movie images at www.anakarder.com). The ostium of the left main coronary artery (LMCA), was also prominent. During

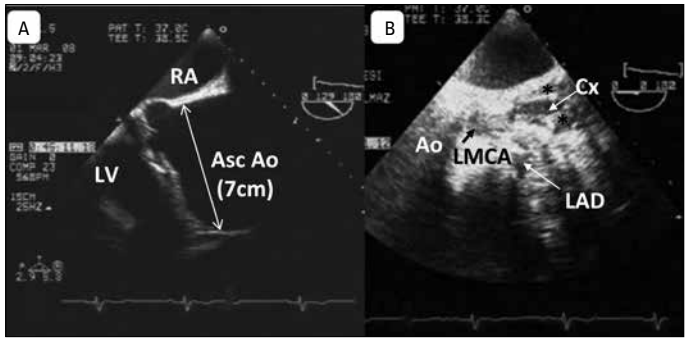

Figure 1. Parasternal long axis view showing aneurysmal dilatation of the aortic root (A), transesophageal short axis view showing proximal left main, left anterior descending and circumflex coronary arteries with partial thrombosis (asterisks) of the lumen (B)

Ao - aorta, Asc - ascendant, Cx - circumflex, LAD - left anterior descending, LV - left ventricle, RA - right atrium

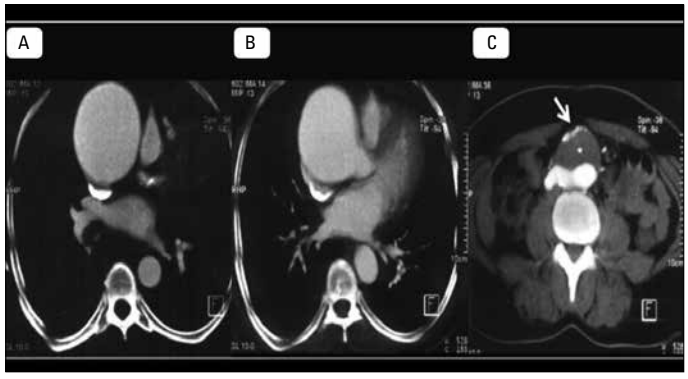

Figure 2. Thoraco-abdominal computerized tomography angiography showing dilated ascending aorta but normally calibrated descending thoracic aorta (A), dilated left main coronary artery (arrow) (B), and dilated and partially thrombosed (asterisk) abdominal aorta with thickened wall and contrast enhancement (arrow) (C)

the TTE examination the remaining portions of the aorta were also visualized: the aortic arch and thoracic aorta were of normal calibration, but the abdominal aorta was severely dilated and partially thrombosed (Video 2. See corresponding video/movie images at www.anakarder.com). Transesophageal echocardiography (TEE) was performed to better visualize the aorta and revealed multiple aneurysms in the LMCA and the proximal portions of the left anterior descending and circumflex arteries that were partially thrombosed (Fig. 1B, Video 3A-C. See corresponding video/movie images at www.anakarder.com). Therefore the patient underwent thoraco-abdominal computerized tomography (CT). CT images confirmed the aneurysmatic dilatations in the ascending and abdominal aorta. Also segmental wall thickening was detected despite aneurysmal dilatations (Fig. 2A-C). No dissection was detected. In addition, CT revealed aneurysms of the carotid arteries at the level of bulbus extending into the internal and external carotid arteries on both sides. Coronary angiography showed aneurysms of all proximal coronary arteries with no stenotic lesions (Fig. 3A, B). The patient had normal renal and liver function tests, normal blood glucose and lipid levels. However erythrocyte sedimentation rate and C-reactive protein (66 mm/h and 9.4 mg/L, respectively) were elevated. Additional immunological serologic tests including p-ANCA, c-ANCA, VRDL were negative. Coronary artery bypass graft surgery and aortic root replacement were performed. Biopsy specimen revealed inflammation with dense lymphoplasmocytes, histiocytes and

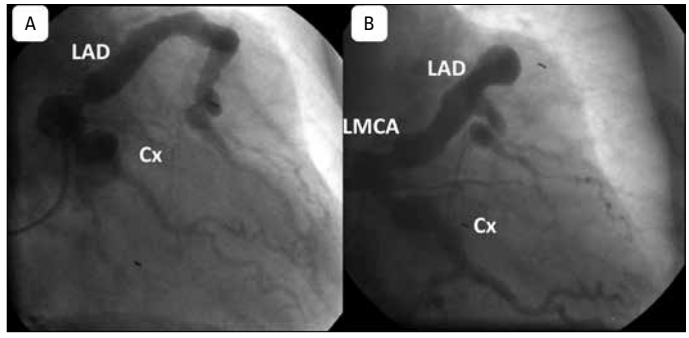

Figure 3. Coronary angiography showing aneurysmal dilatation of the left main coronary artery (LMCA) and proximal portions of the left anterior descending (LAD) and circumflex (Cx) coronary arteries (A, B)

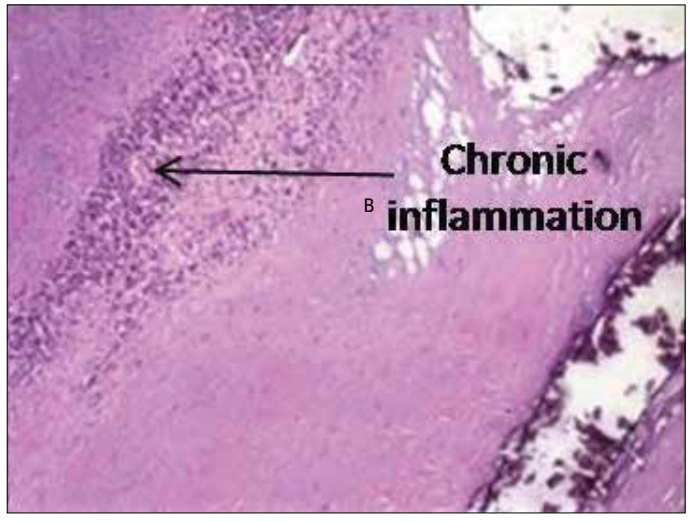

Figure 4. Biopsy specimen from the coronary artery wall showing inflammation with dense aggregates lymphocytes and histiocytes (arrow)

lymphoid aggregations suggesting giant cell arteritis (Fig. 4). The patient was discharged on steroid treatment. Three months later the patient was in good condition without any complaints, had normal acute phase reactant levels and was still on low dose corticosteroid.

Discussion

Atherosclerosis is the most common cause of cardiovascular diseases. Atherosclerosis is a diffuse disease causing severe morbidity mostly due to cerebrovascular, coronary artery and peripheral arterial involvement. The present case came in with typical chest pain and multiple aneurysms were detected in the coronary arteries, aorta and its main branches. Although atherosclerosis leads to stenotic lesions most of the time, aneurysms instead of stenotic lesions may be the main manifestation in some cases. Multiple aneurysms and the unexpected absence of stenotic lesions urged us to consider alternative diagnoses in this case. Moreover our patient had high levels of acute phase reactants at presentation which subsided under corticosteroid treatment. Vasculitis must be considered among the causes of ischemic heart disease, which may be as high as 8-14% under the age of 35 (1, 2). In the differential diagnosis; giant cell arteritis (GCA) and other non atherosclerotic large vessel vasculitides should be discussed. Differentiation from other large cell vasculitides are summarized in the Table 1 (3-5).

Table 1. Differential features of other large cell vasculitides

Large cell vasculitis	Differential features
Kawasaki disease	Fever, diffuse mucosal inflammation and dysmorphic skin rashes
Cogan's syndrome	Interstitial keratitis and acute onset of sensorineural hearing loss and several other neurological manifestations
Syphilitic aortitis	Skin, mucous membranes manifestations, Negative VDRL
Rheumatoid arthritis	Joint manifestations
Ankylosing spondylitis	Sacroilitis
Retroperitoneal fibrosis	Periaortic and aortic inflammation associated with retroperitoneal and mediastinal fibrosis
Behçet's disease	Genital and oral aphthous ulcers, uveitis
Sarcoidosis	Interstitial lung diseases

Our patient was not young, however in the elderly GCA can mimic atherosclerosis (6). GCA has a typical acute onset of new headache with constitutional symptoms and thickened, tender temporal arteries. Elevation of acute phase reactants is useful for the diagnosis and for defining disease activity (6). Involvement of the coronary arteries is less than 5%, however involvement of the aorta and its branches can be seen in 1/3 to 2/5 of the patients with GCA (6-8). In a multicenter study of 788 patients, who were operated for aneurysms or dissection, the diagnosis of GCA was as high as 4.9% (1). Patients with involvement of the aorta are usually free of typical symptoms related to vessel involvement but may have constitutional symptoms until complications occur (6, 8). Temporal artery biopsy confirms the diagnosis of GCA but in patients with involvement of the aorta and its branches, symptoms and signs of temporal artery involvement are rare and the biopsy is usually non-diagnostic (8). The biopsy specimen obtained during the by-pass surgery revealed inflammation with dense lymphoid aggregates and histiocytes. Temporal arteritis is a granulomatous vasculitis and the presence of lymphocyte infiltration and giant cells with fragmentation of internal elastic lamina are characteristic findings on biopsy (9). In our case, although we could not demonstrate granulomatous reaction, the presence of lymphocytic aggregates and hystiocytes are supporting the diagnosis of GCA. Segmental involvement of vessels which is characteristic for GCA and severely damaged artery walls due to aneurysm formation may be the reasons for the lack of typical diagnostic histopathological features in our patient. Steroids are the mainstay therapy of GCA and clinical improvement shortly after steroid treatment is characteristic (6). Our patient did well under corticosteroid treatment. With these features it is plausible to consider GCA in the differential diagnosis of this patient. Thickened aortic wall on CT or magnetic resonance angiography with contrast enhancement are supportive findings for the diagnosis of GCA (10). In our case there was also thickening of aortic wall. Positron Emission Tomography-CT is another useful tool for the differential diagnosis of vasculitis and atherosclerosis (10).

Conclusion

Vigilant imaging in patients admitted for chest pain syndromes is of importance. Echocardiography is a good screening test but should not be confined to wall motion abnormalities in patients presenting with chest pain syndromes. Echocardiographic imaging of the aorta and proximal coronary arteries may provide useful and quick information for initial patient management. The differential diagnosis of atherosclerotic heart disease should include GCA in patients with multiple aneurysms in the aorta and its main branches.

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Video 1. Transthoracic echocardiography, parasternal long axis view showing dilated aortic root
Video 2. Transthoracic echocardiography, transverse section of the abdominal aorta with aneurysm and partial thrombosis
Video 3. Transesophageal echocardiography, short axis view from the high esophagus showing aneurysm of the aortic root (A), aneurysmal dilatation of the left main and circumflex coronary arteries with partial thrombosis of the lumen (B), and aneurysmatic dilatation of the left main, circumflex and anterior descending coronary arteries with partial thrombosis of the lumen (C)

References

1. Pacini D, Leone O, Turci S, Camurri N, Giunchi F, Martinelli GN, et al. Incidence, etiology, histologic findings, and course of thoracic inflammatory aortopathies. Ann Thorac Surg 2008; 86: 1518-23. [CrossRef]
2. Carroll SC, Gaskin BJ, Danesh-Meyer HV. Giant cell arteritis. Clin Experiment Ophthalmol 2006; 34: 159-73. [CrossRef]
3. Antonios N, Silliman S. Cogan syndrome: an analysis of reported neurological manifestations. Neurologis 2012; 18: 55-63. [CrossRef]
4. Miller DV, Maleszewski JJ. The pathology of large-vessel vasculitides. Clin Exp Rheumatol 2011; 29: S92-8.
5. Luqmani R. Large vessel vasculitides: update for the cardiologist. Curr Opin Cardiol 2012; 27: 578-84. [CrossRef]
6. Weyand CM, Goronzy JJ. Giant-cell arteritis and polymyalgia rheumatica. Ann Intern Med 2003; 139: 505-15. [CrossRef]
7. Prieto-González S, Arguis P, García-Martínez A, Espígol-Frigolé G, Tavera-Bahillo I, Butjosa M, et al. Large vessel involvement in biopsy-proven giant cell arteritis: prospective study in 40 newly diagnosed patients using CT angiography. Ann Rheum Dis 2012; 71: 1170-6. [CrossRef]
8. Bossert M, Prati C, Balblanc JC, Lohse A, Wendling D. Aortic involvement in giant cell arteritis: current data. Joint Bone Spine 2011; 78: 246-51. [CrossRef]
9. Hunder GG, Bloch DA, Michel BA, Stevens MB, Arend WP, Calabrese LH, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum 1990; 33: 1122-8. [CrossRef]
10. Blockmans D. Diagnosis and extension of giant cell arteritis. Contribution of imaging techniques. Presse Med 2012; 41: 948-54. [CrossRef]

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