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Case Report

Chronic Stanford type A aortic dissection manifesting as systemic inflammatory disorder

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ABSTRACT

Typical presentation of type A aortic dissection usually encompasses severe acute chest pain, frequently radiating to the upper back, which is seen in more than 80% of the patients, while isolated back or abdominal pain have been repeatedly reported as the first manifestation of the disease as well. Occasionally, dyspnea due to acute aortic regurgitation, syncope, or stroke, secondary to obstruction of major cerebral vessels, have also been described at presentation of type A aortic dissection. Presentation of aortic dissection as a prolonged systemic illness with a number of nonspecific clinical and laboratory findings, such as low-grade fever, fatigue, malaise, weight loss, anemia, elevated acute phase response laboratory parameters, and absence of any of typical clinical features of the dissection syndrome has been only rarely reported. We describe a patient with type A chronic aortic dissection, manifesting as a systemic inflammatory disorder in the absence of acute chest syndrome. The diagnosis was made accidentally by computed tomography, ordered in the course of the regular work up. The patient underwent emergent surgery with resection and grafting of the dissected aorta. Pathological investigation demonstrated intense acute inflammation with neutrophilic infiltration in the vicinity of the intramural hemorrhage and necrosis, as well as granulation tissue with new vessels formation and collagen deposition in the outer media. The possible pathogenic mechanisms of the phenomenon are discussed.

Keywords: Aortic dissection, Chronic, Inflammatory disease, Fever, Anemia, Weight loss

INTRODUCTION

Aortic dissection represents one of the medical emergencies. It results from separation of the aortic wall layers by the blood flow at high pressure with formation of a false lumen. A Stanford type A dissection starts usually within centimeters of the aortic valve, involves the ascending aorta, can extend to the descending aorta and has a mortality rate of 1% to 2% hourly early after symptoms onset. Typical presentation of type A aortic dissection usually encompasses severe acute chest pain, frequently radiating to the upper back, which is seen in more than 80% of the patients, while isolated back or abdominal pain have been repeatedly reported as the first manifestations of the disease as well. Occasionally, dyspnea due to acute aortic regurgitation, syncope, or stroke, secondary to obstruction of major cerebral vessels, have also been described at presentation of type A aortic dissection.[1,2] Presentation of aortic dissection as a prolonged systemic illness with a number of

nonspecific clinical and laboratory findings, such as low-grade fever, fatigue, malaise, weight loss, night sweats anemia of chronic disease, elevated acute phase response laboratory parameters, and absence of any of the typical clinical features of the dissection syndrome has been only rarely reported.[3-8] We herein describe a case of type A aortic dissection, masquerading as a systemic disease, and discuss the possible pathogenetic mechanisms of the phenomenon.

CASE REPORT

A 59-year-old man started complaining of mild shortness of breath, cough and low-grade fever about one month before his admission to the hospital. He was diagnosed with acute bronchitis and treated with amoxycyclin/clavulinic acid with complete resolution of the dyspnea. However, the patient kept complaining of low grade fever, malaise, fatigue, night sweats, and loss of appetite. Ambulatory blood tests revealed significantly accelerated erythrocyte sedimentation rate (ESR), increased serum levels of C-reactive protein (CRP) and mild normocytic anemia. The patient was referred to our hospital for further assessment of his disease. He was a heavy smoker and had a history of arterial hypertension, reasonably controlled with enalapril. On admission, he continued to complain of low grade fever, malaise, fatigue, night sweats, loss of appetite, and weight loss of 4 Kg during the last month, and denied the presence of chest or back pain.

Physical examination revealed a body temperature of 37.8°C, arterial blood pressure of 140/83 mm Hg and heart rate of 104 beats/min. Other physical findings were unremarkable. An electrocardiogram showed sinus tachycardia of 106/min, chest X-ray film revealed a mildly extended heart shadow and a small left pleural effusion. Abdominal ultrasonography was unremarkable. Laboratory studies revealed a mild normocytic anemia with hemoglobin level of 11 g/dL, leukocytosis of 13,400/mm^3 with 85% neutrophils, thrombocytosis of 532,000/mm^3 ESR of 98 mm/h, and serum level of CRP of 85 mg/dL (normal range up to 6 mg/dL). Serum level of albumin was decreased to 3.3 g/dL, while globulin level was 3.25 g/dL. Serum levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and gamma-glutamyl transpeptidase were mildly increased. Ferritin level was significantly elevated up to 965 ng/mL (normal range up to 365 ng/mL), while levels of transferrin and iron were decreased in a typical pattern for anemia of chronic disease. Diagnostic contrast enhanced computed tomography (CT) scan of the chest and abdomen revealed Stanford type A aortic dissection with dense pericardial effusion (Figure 1).

The patient underwent immediate surgical intervention with resection and replacement of the thoracic aorta by a graft. A pathological investigation of the resected aortic specimen revealed aortic dissection with hemorrhage within the media, tissue destruction, necrosis and intense inflammatory reaction, which extended to adventitia (Figure 2). Notably, these acute inflammatory changes closely neighbored with the areas of early organization, characterized by formation of granulation tissue, fibrosis and collagen deposition (Figure 3). After operation, the patient's previous symptoms completely resolved rapidly, with no recurrence over a period of six months follow-up.

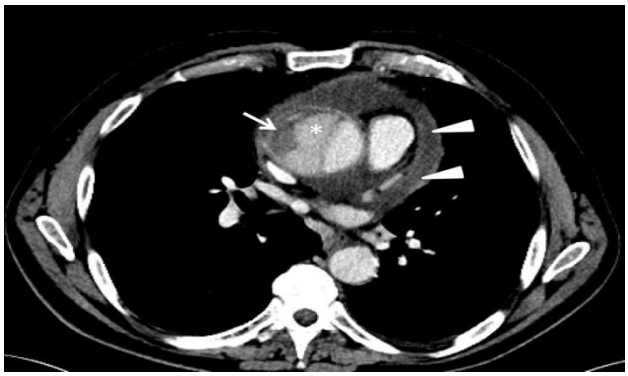

Figure 1: Computed tomography scan of the patient, showing atheroma of the ascending aorta (arrow), false lumen of the dissected aorta (star) and dense pericardial effusion (arrowheads).

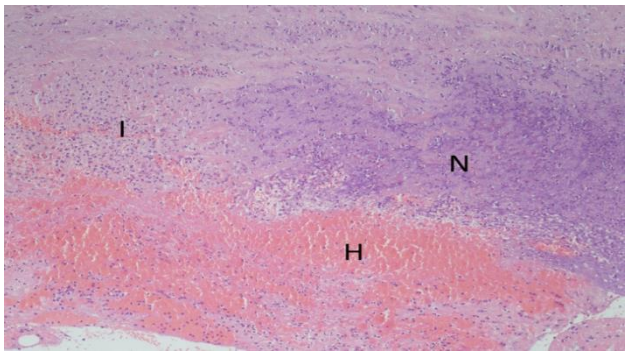

Figure 2: Histopathological changes typical for acute stage of aortic dissection. H -intramural hematoma; N – zone of necrosis; I – acute inflammatory neutrophilic infiltrate. H&A, 40X.

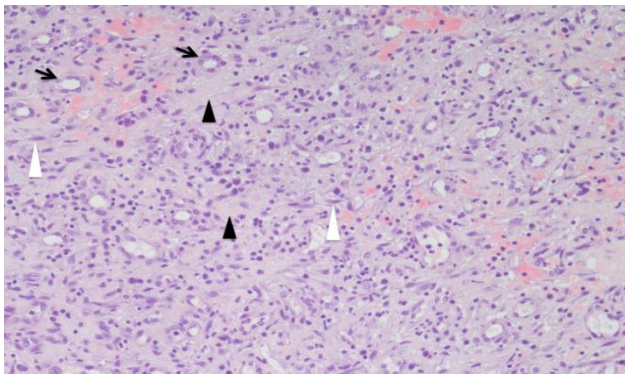

Figure 3: Early organization within the outer media: proliferating fibroblasts (white arrowheads), collagen deposition (black arrowheads) and new capillaries (arrows). H&E 100x.

DISCUSSION

The presentation of aortic dissection with features of systemic disease, such as low-grade fever, malaise, weight loss and laboratory profile consistent with nonspecific acute phase response has been rarely reported.[3-8] Of interest, while febrile reaction at presentation of acute aortic dissection is a well-known feature of the disease, chronic aortic dissection in which fever or other symptoms of systemic illness dominate the clinical picture for weeks is distinctly rare, with diagnosis usually made by imaging modalities incidentally in the course of basic investigation.[9,10] The presence of small left sided pleural effusion has been mentioned as a clue for the right diagnosis in this setting.[11,12]

The pathogenetic mechanisms of the prolonged systemic response in the course of chronic aortic dissection have not been elucidated yet. Subacute inflammatory reaction secondary to hematoma formation or to ischemic damage to the tissues, as well as Dressler's-like syndrome have been suggested as possible explanations.[5-8] Our case demonstrated that significant inflammation followed the episode of aortic dissection. Notably, two different phases of the inflammatory reaction may coexist. The first one is acute inflammation, which occurs in the vicinity of the intramural assault, with myriads of neutrophils, generating myeloperoxidase and other active enzymes, and weakening the surrounding structures. This phase is mediated as well by tumor necrosis factor-alpha, interleukin (IL)-6, IL-8 and macrophage metalloprotease-12, which participate in tissue breakdown and augment the local inflammation.[13-15] On the other hand, areas of chronic response with appearance of granulation tissue, new capillaries and collagen deposition are building up in the outer layers of media. This type of reaction can be demonstrated only days or weeks after the initial assault, and its biological significance may consist of the separation of the damaged area and strengthening of the surrounding structures.[16] Of significance, while aortic dissection from the viewpoint of a clinician is a rushing event, threatening to complicate every next minute, pathologists find pieces of evidence that, at least in some patients, aortic dissection is an ongoing process with a sequence of reactive changes weakening the adventitial wall, and gradually leading to the final event of aortic wall rupture.[16,17]

Taking into consideration all above mentioned, one can speculate that the fate of a patient who has survived the initial episode of aortic dissection depends on the balance between two types of inflammatory reactions: destructing, mostly neutrophil-mediated, and reconstructing, with collagen deposition, granulation tissue and new vessels formation. As shown in our case, the intensity and extent of neutrophilic aortic wall inflammation can be considerable and manifest with systemic clinical and laboratory features, such as low-grade fever, fatigue, malaise, anemia, and elevated ESR and CRP levels.

It should be mentioned as well that innervation of the aortic wall is limited, with nerve endings existing only in the outer media and adventitia, which may support the hypothesis that aortic dissection can be asymptomatic, particularly at its first stages, with typical excruciating chest and back pain developing in parallel with rupturing of the adventitia.[18] The described situation should be differentiated from isolated ascending aortitis, or aortitis in the course of systemic inflammatory disorder, such as giant cell arteritis.[19]

CONCLUSION

Aortic dissection can manifest as a prolonged inflammatory disease and should be thought of in patients with respective risk factors and compatible clinical presentation, even in the absence of acute chest pain syndrome.

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REFERENCES

1. Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management: Part I: from etiology to diagnostic strategies. Circulation. 2003;108:628-35.
2. Pape LA, Awais M, Woznicki EM, Suzuki T, Trimarchi S, Evangelista A, et al. Presentation, diagnosis, and outcomes of acute aortic dissection: 17-year trends from the international registry of acute aortic dissection. J Am Coll Cardiol. 2015;66:350-8.
3. Turner N, Pusey CD. Aortic dissection masquerading as systemic disease - the post dissection syndrome. QJ Med. 1990;75:525-31.
4. Schattner A, Klepfish A, Caspi A. Chronic aortic dissection presenting as a prolonged febrile disease and arterial embolization. Chest. 1996;110:1111-4.
5. Geppert AG, Mahvi A, Hainaut P, Lambert M. Chronic aortic dissection masquerading as systemic disease. Acta Clin Belg. 1998;53:19-21.
6. Gorospe L, Sendino A, Pacheco R, Alonso A, Barbado FJ, Vázquez JJ. Chronic aortic dissection as a cause of fever of unknown origin. South Med J. 2002;95:1067-70.
7. Lorenzen HP, Kurowski V, Jain D, Geist V, Richardt G. Fever and inflammatory response as principal manifestation of chronic aortic type a dissection--a case report. Angiology. 2004;55:85-8.
8. Dai MS, Cheng SM. Aortic dissection presenting as fever of unknown origin. Acta Cardiol. 2001;56:37-8.
9. Harris KM, Strauss CE, Eagle KA, Hirsch AT, Isselbacher EM, Tsai TT, et al. Correlates of delayed recognition and treatment of acute type A aortic dissection: the international registry of acute

aortic dissection (IRAD). Circulation. 2011;124:1911-8.
10. Shimada S, Nakamura H, Kurooka A, Nishioka N, Sugimura K, Ino H, et al. Fever associated with acute aortic dissection. Circ J. 2007;71:766-71.
11. Patris V, Whiteley J, Argiriou O, Lama N, Georgiou H, Constantinou C, et al. Pyrexia in patients with uncontrolled systemic hypertension: could they have an aortic dissection? J Thorac Dis. 2014;6:E246-8.
12. Schattner A, Klepfish A. Left pleural effusion and fever of unknown origin - a clue to thoracic arterial pathology. J Gen Intern Med. 2012;27:1084-7.
13. Proietta M, Tritapepe L, Cifani N, Ferri L, Taurino M, Del Porto F. MMP-12 as a new marker of Stanford-A acute aortic dissection. Ann Med. 2014;46:44-8.
14. Gu J, Hu J, Zhang HW, Xiao ZH, Fang Z, Qian H, et al. Time-dependent changes of plasma inflammatory biomarkers in type A aortic dissection patients without optimal medical management. J Cardiothorac Surg. 2015;10:3.
15. del Porto F, Proietta M, Tritapepe L, Miraldi F, Koverech A, Cardelli P, et al. Inflammation and immune response in acute aortic dissection. Ann Med. 2010;42:622-9.
16. Xu L, Burke A. Acute medial dissection of the ascending aorta: evolution of reactive histologic changes. Am J Surg Pathol. 2013;37:1275-82.
17. Schmitto JD, Popov AF, Coskun KO, Friedrich M, Sossalla S, Didilis V, et al. Morphological investigations of type A aortic dissection. Ann Thorac Cardiovasc Surg. 2010;16:331-4.
18. Slobodin G, Zeina AR, Rosner I, Boulman N, Rozenbaum M. Chronic pain of aortitis: an underestimated clinical sign? Joint Bone Spine. 2008;75:96-8.
19. Xu L, Heath J, Burke A. Ascending aortitis: a clinicopathological study of 21 cases in a series of 300 aortic repairs. Pathology. 2014;46:296-305.

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