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REVIEW

New Perspectives in the Management of Aortic Intramural Hematoma – a literature review

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Aortic intramural hematoma frequently appear in elderly hypertensive patients who suffered a vasa vasorum rupture into the media, presenting clinical symptoms similar to aortic dissection. The current available data suggest a similar treatment strategy as in aortic dissection, although intramural hematoma is a different pathophysiological entity.

The issue of the vulnerable contact of the intraaortic plaque, which is prone to rupture and to trigger the formation of an intramural hematoma, has not been elucidated so far. We present a brief literature review regarding complex plaque analysis, which opens a new area in identification of vulnerable patients with intramural hematoma, important for management of these patients and optimization of their treatment in order to avoid complications.

Keywords: Intramural hematoma, Ulcer-like projection, Penetrating atherosclerotic ulcer

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Pathophysiological concept of intramural hematoma

The acute aortic syndrome (AAS) traditionally includes: aortic dissection (AD), intramural hematoma (IMH), and penetrating atherosclerotic ulcer (PAU). Recent reports indicate that aortic rupture due to trauma and intimal laceration should also be listed between these urgent features [1,2].

IMH is represented by a hemorrhage into the medial layer which can propagate longitudinally or circumferentially, without rupture into the lumen, dissection flap, tear or longitudinal flow in the false lumen. There are different points of view regarding the pathophysiology of this disease: some authors suggested that IMH is caused by a rupture of vasa vasorum, whereas other claim that hematoma is caused by microscopic tears in the aortic intima [3]. The rupture commonly occurs at the level of the right lateral wall of the ascending aorta, few centimeters below the aortic valve, due to asymmetric hydraulic stress of the aorta [4]. Lansman et al. assumed that aortic wall layers disintegration and hematoma propagation or flow depends by 2 factors: magnitude of the source (vasa vasorum or an intimal tear) and resistance to flow in the media, which could be affected by a multitude of factors leading to degenerative changes in the media, such as atherosclerosis, pathological neovascularization, local response to blood flow in the media or generalized inflammatory disease [1,5-9]. All these factors could lead to development of an ulcer-like projection (ULP) or a penetrating atherosclerotic ulceration (PAU), which could progress to intramural hematoma. The differences between these two entities are presented in Table 1. A complete understanding of these entities (ULP/PAU) and of the differecnces between them is still missing. While ulcer-like projection are mainly localized on ascendant aorta, representing an early complication of IMH, PAU usually involves descendent aorta, as a consequence of a rupture of an atherosclerotic plaque. Nathan et al. suggest to use the same term: PAU, to include both entities: penetrating atherosclerotic ulcer and ulcer-like projection [10].

The relationship between PAU and IMH is also unclear. Some authors has identified PAUs as a cause of IMHs, whereas others have considered PAUs and IMHs distinct entities [11]. A study which included 388 patients revealed that isolated PAU disease is more frequent (57.7%), while PAU with IMH appear in 14,4% of both types having a high prevalence in descending thoracic aorta (isolated PAU -55,6% and PAU with IMH – 89,3%) [12].

Patel et al reported that a significant limitations of the current imaging modalities is the possibility to identify an intimal tear without flow communication to the aorta, while it cannot be defined exactly whether intimal tear exists or not at the moment of symptoms onset [10].

Identifying the vulnerable patient with aortic intramural hematoma

IMH appears in 5-20% of hypertensive patients who present symptoms and signs suggestive for acute aortic syndrome: chest pain, back pain, diminished carotid pulse, acute renal insufficiency, or neurological symptoms such as: syncope, anterior spinal syndrome or hoarseness [13]. The localization of the pain can help to guide the examiner to 2 types of IMH in analogy to the Stanford classification of aortic dissections: Type A (proximal, involving ascendent aorta) and Type B (distal, without ascending

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Table1. Differences between PAU and IMH.

	PAU	IMH/ ulcerlike projection (intimal tear)
Described	Shennan,1934. Stanson et al. In 1986 showed its presence as a separate clinical and pathological entity	Krukenberg, 1920
Gender	male	male
Average age	63 years	>65 years
Prevalence	2,3-7,6%	10-30%
Definition	Ulceration of an aortic atherosclerotic lesion penetrates the internal elastic lamina into media, distinct pathological variant of classic false-lumen aortic dissection	Functional definition: blood collection within the aortic wall, not freely communicating with the lumen, with restricted flow
Description	Out pouching of the lumen with jagged edges, presence of aortic atheroma, mushroom-like	Bleeding into the outer layers of the aortic media
Without	Intimal flap, fals,branch vessel affection lumen	
Symptoms	Painless or low intensity pain, pain located in back or abdomen, high blood pressure	Chest (in type A) or back (in type B) pain, tends to be more of a segmental process, therefore radiating pain to leg or to head is uncommon, rarely any malperfusion
Risk factors	Hypertension (92%), tobacco use (77%), hyperlipidaemia, coronary artery disease (46%) (Mayo Clinic database)	Hypertension (75%), required and genetic disorders with alterated connective tissue function, smoking, direct blunt trauma, use of illicit drugs
Co-mordities	Diffuse atherosclerosis, hypertension, diabetes, COPD, cardiac and renal failure	
Paucity of specific sign	No: pulse deficit, aortic regurgitation, stoke, visceral vessel compromise (because is a localized lesion, in contrast with aortic dissection, were this features are present)	
Localisation	mostly isolated, localized	
AAA	42,10%	29,40%
Descending Ao	90%	71%
Complication	Intramural haemorrhage(mainly remanding localized near the PAU lesion, in contrast to IMH which is diffuse extended),(pseudo) aneurysm or whiteout rupture, pleural effusion	Type A- pericardial effusion, pleural effusion, aortic insufficiency
Imaging	Focal, crater-like with contrast-material fill lesion, thickened aortic wall, calcified intima displaced with IMH +/- pleural, pericardial fluid	Crescent-shaped or concentric, circular thickening of the aortic wall >5-7mm
Treatment	Ascending aorta	Thoracic aorta
Surgical treatment	Early	Early, if are sign for progression (pain, increasing aortic wall thickness, PAU greater than 20mm x10mm, increasing pleural effusion, or IMH associated with PAU)
Medical	Ineffective	Acceptable
Endovascular treatment	Indicated because of isolated, localized location, but with technique and anatomical restriction	
TAAR - early	Rupture, pain	
TAAR- in chronic cases	Recurrent pain, aortic diameter > 55mm, depth > 10mm/year	
Progression	Remain unchanged over time	Reabsorption under medical treatment (19-67%), progress to AD
Predictors to progression	Sustained or recurrent pain (P< .0001),increasing pleural effusion (P= .0003), maximum PAU diameter (>20mm)(P = .004), maximum PAU depth (> 10mm)(P=.003)	Recurrent or persisting pain (the most important), presence of penetrating aortic ulcer. Progression to AD, increasing IMH thickness, increasing aortic diameter, increasing pericardial/pleural effusion or tamponade, no regression
Follow-up	Asymptomatic: repeat CT at 6 months, 12 months, and then every 2 years	
Indication for intervention	Aortic diameter exceeding 55mm, and increase in diameter exceeding 10 mm per year or development of any other complication: dissection, saccular aneurysm	

aorta). In cases of atypical clinical presentation, a complex imagistic assessment is necessary for an early diagnosis and establishment of a correct treatment strategy. Classical noninvasive investigations such as transesophageal echocardiography or transthoracic echocardiography from the suprasternal view have been recently replaced by computed tomography (CT) and magnetic resonance (MR). The echocardiography, especially the transesophageal, is still useful in emergency department to evaluate unstable patients and to assess the function of the aortic valves, but the widespread, first choice investigation method is the CT examination, which presents a high sensibility and specificity (95-98%) for diagnostic of different types of aortic dissection.

Cardiac CT examination could be useful in these cases to:

- diagnose an aortic intramural hematoma (diagnostic criteria being represented by an aortic wall maximal thickness greater or equal to 7 mm), differentiating from aortic dissection, which have same clinical manifestation but exhibiting an intimal flap which separates the two lumens: the true and the false lumen.
- define the exact location and extension of the disease,
- evaluate the prognosis of hematoma, because an decreased attenuation has been associated with a longer duration of the hematoma,

– identify the associated complications: pericardial or pleural effusion, involvement of coronary arteries or visceral organs
– identify the possible congenital comorbidities: right-sided arch, vascular ring or coarctation.

Magnetic resonance imaging can also be used for a complex diagnosis of this disease, however it could be less practical in the acute settings due to the longer exmination times.

Fluorodeoxyglucose-positron emission tomography (FDG-PET) [14], and micro-OCT are the future investigation methods, that could help for a superior understanding of the pathological pathway of this disease, providing complementary information related to inflammatory status that precedes subsequent Ca deposition and lead to active micro calcifications [14,15,16].

Several biomarkers have been recently suggested for ruling-out the presence AAS, such as smooth muscle myosin heavy chains or soluble elastin fragments [17].

New perspectives in approaching patients with IMH

There is no agreement on the management of IMH in the absence of a definite clinical algorithm. Initial medical therapy hint heart rate control and blood pressure reduction with target values of 100-120 mmHg for systolic blood pressure and 60-80 bpm for heart rate. First line medication is represented by beta-blockers and analgesia should be prescribed in order to reduce catecholamine-induced tachycardia and hypertension [1].

At present, the criteria used to guide disease specific treatment varies according to the anatomic features of the lesion, presence or absence of PAU, clinical presentation and patient comorbidities, being similar to the criteria used for aortic dissection in the corresponding segments of the aorta [3].

The treatment strategy for type A IMH remains Controversial. The approaches recommended so far include surgery, endovascular grafts (TEVAR) or hybrid interventions. A meta-analysis of 12 studies (primarily Asians centers) involving 328 patients reported no significant difference in early mortality between those medically managed and those surgically treated (14.4% vs 10.1%, p= 0,36) [18]. Another meta-analysis comparing Eastern versus Western studies indicated a lower mortality with surgically treatment in Japan/Korea (7,8%) Western as compared to medical treatment (NA/Europe) (7.8% vs 33.3%, $p < .0001$) [19]. These significant differences indicated a less severe evolution in European population as compared to Asian one, observation that has not been explained yet. Furthermore a recent report in the literature describes an Asian ethnicity case with full resolution of type A IMH [20]. For type B IMH, general agreement exist that it should be treated with B-blockers and other vasodilator drugs in order to control the blood pressure, and that it should be closely followed with imagining techniques, presenting better outcomes as compared to type A IMH or aortic dissection [3,7,21, 22].

Some studies suggested that PAU located in the ascending aorta or aortic arch progress more frequently to complications. Eggebrecht et al. suggested that if PAU is identifiable, it should be considered as a target lesion for urgent endovascular treatment [2,3]. Because an intimal tear could be subtle whereas the imagistic identification remains a challenging task, some authors suggested to consider the enlargement of the aortic diameter (greater than 4,8 cm) or the progression of the maximal aortic wall thickness (greater than 11mm) as critical issues for the decision of medical care. On the contrary, Patel et al. demonstrated that neither aortic nor PAU size-related criteria can help in predicting PAU progression and the need for urgent surgery [10].

However, the indication of urgent or delayed surgical management of ascending aorta IMH, as compared with medical treatment only, has not been established so far, while the investigation algorithm needs to be updated.

Sueyoshi et al observed that one-third of patients with IMH type A were found to have ulcer-like projection, than patients with intramural hematom (type B). This was developed mostly within the first 3 months of follow-up, similarly with the development of the intimal tear in early stages of aortic dissection with thrombosed false lumen, due to great mechanical stress. The same group showed that IMH associated with ulcer-like projection at ascendent aorta and aortic arch do more often progress to complications than other types of IMH [23].

Another researchers group showed that IMH involving the entry aorta is frequently associated with small atherosclerotic plaque rupture at the level of the free lateral wall or at the concavity of the aortic arch [24].

The pathophysiological substrate of the acute aortic syndrome is similar to the one of an acute coronary syndrome or an acute ischemic cerebrovascular syndrome, therefore analogies between these entities have been suggested by different authors. In this view, new imaging techniques, such as FDG-PET/CT, provided the possibility to analyse the IMH-related culprit lesions and the vulnerable atherosclerotic plaque components and to define their relevance for disease outcomes. Angio CT could be used for identification of the culprit plaque volume and for quantification of plaque components, based on the measurement of plaque density in Hounsfield units. Different reports indicated a good correlation between the markers obtained using the intravascular ultrasound (IVUS), considered as the gold standard for evaluation of coronary plaques vulnerability. However, it could be technically challenging to measure the size of the lipid core with Angio CT because of blooming artifacts induced by calcifications [25].

Analyzing the vulnerable plaque components in acute coronary syndrome cases, Benedek et al. showed that

a cut of point below than 30HU highly correlates with the vulnerability degree of the coronary plaques [26]. In further studies, using the intravascular ultrasounds and Angio CT, they identified the presence of a low-density core within the culprit lesion as a powerful vulnerability marker. Similar assessment of carotid atherosclerotic plaque volume and characteristics, evaluated with Angio CT, showed that high plaque volumes and large lipid-rich necrotic cores predispose to plaque ulceration, which subsequently leads to acute ischemic attack. In contrast, the calcification proportion was inversely associated with plaque ulceration [27,28].

Cardiovascular calcification score, as assessed by Angio CT, represents a powerful marker of risk for future cardiovascular events. A high calcium score represents an advanced stage of the atherosclerotic process, characterized by large the calcium deposits within the vessel wall [29]. Yorgun et al. proved that the thickness of the epicardial adipose tissue and the critical coronary stenosis are the most significant predictors of aortic atherosclerotic processes, thus indicating that Angio CT is an extremely useful technique for assessing the atherosclerotic progression not only at the level of the coronary arteries but also within the aortic wall [30].

Conclusion

IMH represents a form of an acute aortic syndrome which requires a careful assessment in order to prevent the progression to serious complications. Angio CT assessment plays a key role in assessing patients with intramural hematoma, being superior to any other available non-invasive methods for identification of the vulnerable plaques within the aortic wall, plaques that present a high predisposition to rupture. The method could help to identify the stable patients with intramural hematoma who are at high risk for future rupture into the vessel wall, in order to optimize their treatment strategy and avoid the potential complications.

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