Penetrating Aortic Ulcer and Intramural Hematoma

An update on how to differentiate and manage two potentially devastating diagnoses.

BY FOEKE NAUTA, MD; ARNOUD KAMMAN, MD; AND SANTI TRIMARCHI, MD, PHD

Aortic intramural hematoma (IMH) is an acute aortic disease, defined by the presence of hemorrhage within the aortic wall, and no evidence of intimal tear. The penetrating aortic ulcer (PAU) is a chronic aortic condition, defined by an ulcer-like disruption of the intima maturing within the aortic lumen. IMH usually presents with a smooth intima and some degree of atherosclerosis, whereas PAU is associated with systemic atherosclerosis and, often, a thickened intima with craters (Figure 1). Stanson et al accurately described PAU as an ulceration of an atheromatous plaque that disrupts the internal elastic lamina and allows hematoma formation within the media of the aortic wall.[1]

PAU can be the cause of IMH, which may evolve as aortic dissection (AD). IMH is distinguished from AD by the absence of an intimal flap.[2] The Stanford classification defines IMH similarly to AD: IMH type A involves the ascending aorta and arch, whereas IMH type B (IMHB) is localized only in the descending thoracic aorta.[3] The incidence of IMH and PAU is still unclear. IMH has been reported in the literature with an incidence varying between 2% and 45% (approximately 12% among all acute dissections) based on the International Registry of Acute Aortic Dissection (IRAD).[4,5] There is little evidence about the incidence of PAU, although rates of 2.3% to 7.6% in symptomatic patients have been described.[6] In patients admitted with acute AD, an ulcer was identified in 7.6%, which could implicate that PAU causes dissection more often than previously thought.[6]

ETIOLOGY

The etiology of IMH and PAU remains a matter of debate. Both entities show similar mechanisms of inflammation and expression of matrix metalloproteinases and medial proliferative changes with transformation of smooth muscle cells from contractile to mutant phenotypes. Moreover, both commonly show apoptosis and medial degeneration.[7] A suggested concept of IMH formation is that it arises from a ruptured vasa vasorum in the medial layer of the aortic wall, triggering a secondary tear toward the aortic lumen.[2] Hypertension and aortic wall infarction are both associated with this pathophysiology. Another hypothesis is that IMH originates from small entry tears in the intima followed by thrombosis of these tears, making these tears difficult to detect on imaging studies.[2,8] Although there is no definitive verdict, several potential risk factors have been identified for IMH, such as higher age, large aortic diameter, and increased aortic wall thickness.[4,5,9]

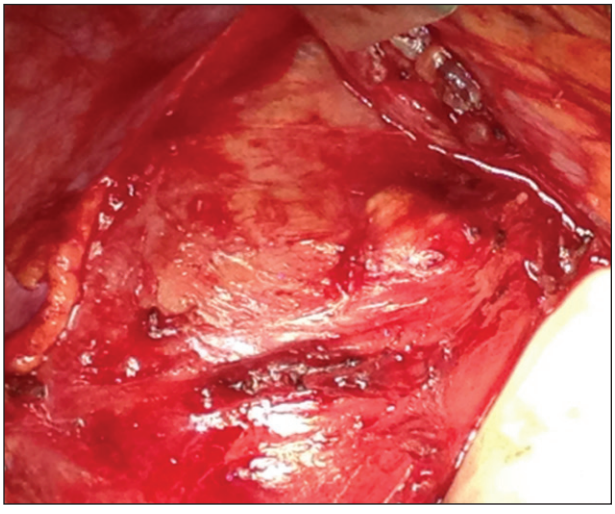

Figure 1. PAU in the descending aorta.

PAU may develop from progressive erosion of atheromatous mural plaques, penetrating the elastic lamina. Arterial

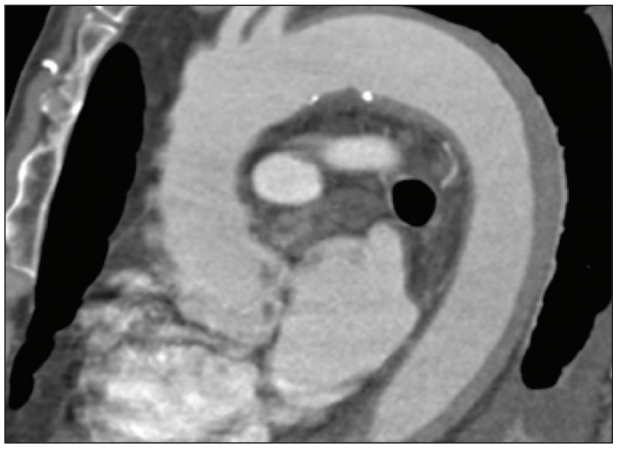

Figure 2. Sagittal view of IMH in the descending aorta with typical aortic wall thickening and linear intraluminal filling defect.

hypertension, hyperlipoproteinemia, and aortic sclerosis have shown to be predisposing features of PAU. Because all of these factors are often more present in older patients, PAU is more frequently seen in the eldery.[10] Nevertheless, PAU may also occur in younger patients as a result of intimal tears that remain stable without AD or IMH progression. Complicated PAU is defined by the development of aneurysms, pseudoaneurysms, dissections, or aortic ruptures. Close evaluation of PAU, by measuring both diameter and depth of the ulcer, is mandatory to prevent aortic complications.[11]

DIAGNOSIS

Clinical

Based on clinical evaluation, IMH cannot be reliably distinguished from classic AD.[8] Tolenaar et al compared clinical presentation between IMHB and acute type B AD (ABAD), showing that IMHB presented predominantly in men (62% vs 33%; $P < .001$) at older age (69 ± 12 vs 63 ± 14; $P < .001$), more often with chest pain (80% vs 69%; $P = .020$) and periaortic hematoma (22% vs 13%; $P = .020$).[5] In addition, IMHB patients presented less frequently with pulse deficits and mesenteric/limb ischemia,[5] similarly to previous observations.[9] The prevalence of overall IMH among patients presenting with nontraumatic acute aortic syndromes ranges widely from 6% to 50%.[9,12-17] Such discrepancy may be explained by differences in imaging definition and patient selection: potentially, referral centers might more frequently observe IMH patients who already developed classic AD.

The clinical presentation of PAU is very diverse. Basically, PAUs are asymptomatic aortic lesions, identified during imaging indicated for other reasons.[10] When comparing PAU alone with PAU plus IMH, the two groups showed similarities in age, prevalence of comorbidities, frequency of presentation with rupture, or extent of repair.[18] PAU with IMH was associated with a higher risk of treatment failure of thoracic endovascular aneurysm repair (TEVAR), defined as need for open or endovascular reintervention, aortic rupture, or aortic-related death ($P = .03$). In this cohort, patients with PAU associated with IMH had more emergent interventions with no difference in all-cause survival at 24 months.[18]

Imaging

It once was thought that IMH was relatively rare compared to AD. However, due to modern imaging, several studies observed an IMH prevalence of 10% to 30% in patients suspected for AD.[11-14,16] CT and MRI imaging techniques have further supported the hypothesis that IMH, PAU, and AD may be variants of the same process. AD presenting with a thrombosed false lumen could resemble IMH on imaging because entry tears are no longer visible. In order to differentiate between these conditions, cross-sectional imaging is considered the gold standard. In IMHB, periaortic hematoma is more frequently observed than in ABAD patients. The presence of pleural effusion can make the distinction between intact and disrupted adventitia challenging. However, the close relationship between the IMH and the adventitia may trigger the development of periaortic hematoma and rupture.[5] Comprehensive imaging analysis can expose specific anatomical clues, as well as intimal lesions in the inner curvature of the aortic arch, which can often be found in patients with IMH. These signs may be helpful in indicating and planning TEVAR.[19]

For IMH, axial imaging reveals thickening of the aortic wall greater than 0.5 cm in an eccentric or concentric pat-

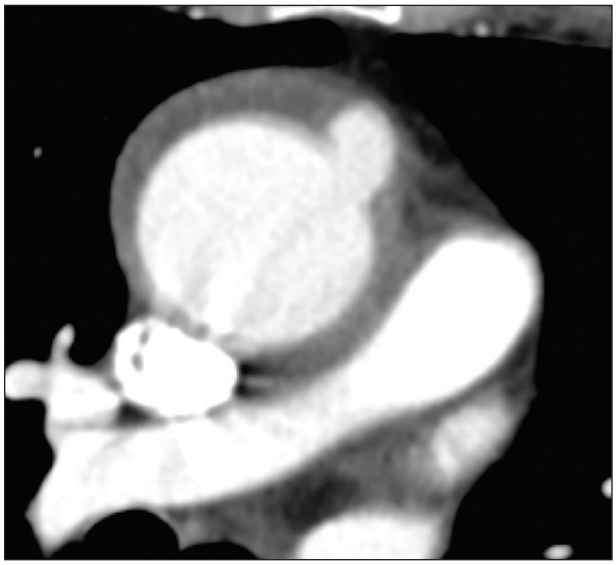

Figure 3. PAU with typical localized collection of contrast extending from the lumen.

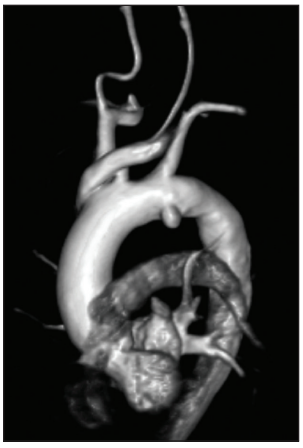

Figure 4. PAU in the arch of the aorta on a 3D-reconstructed MRI scan.

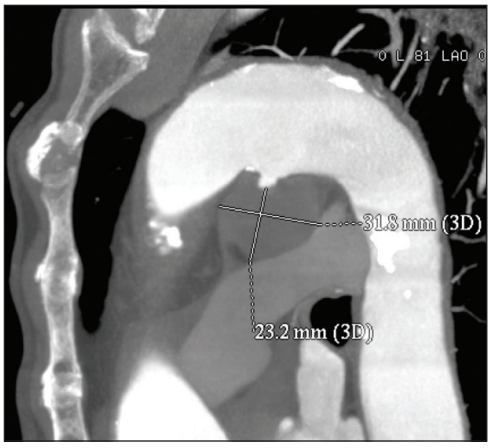

Figure 5. Arch PAU not associated with IMH.

Figure 6. Descending PAU associated with IMH.

tern, with a linear tangential intraluminal filling defect as a distinguishing feature (Figure 2). On the contrary, acute AD with a thrombosed false lumen shows curvilinear intramural clots often missing a well-defined outer wall because of mediastinal hematoma and pleural effusions.[11] In general, IMH affects more frequently the descending aorta, with rates of 50% to 85%.[4,5] Evaluation of aortic diameter measurements between IMHB and ABAD patients showed that the aortic root and sinotubular junction were significantly larger in ABAD patients (3.6 cm vs 3.4 cm; $P = .047$, and 3.4 cm vs 3 cm; $P = .002$, respectively), whereas the maximum descending aortic diameter was equal (both 4 cm).[5]

For PAU, an imaging criteria is a localized collection of contrast extending from the lumen (Figure 3). Some investigators have shown that PAU is mainly located in the descending aorta (61.2%), followed by abdominal (29.7%) and arch (6.8%) (Figures 4 and 5) localizations.[7,20] PAU may present with multiple ulcers and several ranges of diameter and depth; however, indication for treatment has been suggested when it extends more than 20 mm in depth.[3,21] In these patients, mural thrombus has an irregular luminal surface that may locally narrow the lumen. Differently, IMH thrombus has a smooth surface, represented by the aortic lamella, and may extend longitudinally.

PROGNOSIS

IMH and PAU can progress fatally, especially when both diseases are present (Figure 6). IMH concomitant with PAU is associated with an increased risk of expansion and rupture.[11,22] For IMH alone, even though 34% of patients will show regression, 16% to 47% of patients will progress to the development of AD,[2,9,22,23] and 20% to 45% will develop an aortic rupture.[2] The best predictor of IMH regression without complications is a normal aortic diameter in the acute phase.[17] Evangelista et al reported that among 68 IMH patients, 22% developed a fusiform aneurysm, 8% a saccular aneurysm, and 24% a pseudoaneurysm (over a mean time of 45 months).[23] The IRAD database has recently showed similar IMH 1-year mortality compared to classic AD (5.3% vs 8.7% and 10.3% vs 8.2% for type A and B, respectively), with no significant difference in overall in-hospital mortality rates due to diseased descending aorta (4.4% vs 11.1%; $P = .062$) and ascending aorta (26.6% vs 26.5%; $P = .998$).[4] Similar to type A AD, IMH involving the ascending aorta is a lethal condition and is an indication for expeditious surgery because of the risk of cardiac tamponade, rupture, or compression of the coronary ostia.[2,4,9] In patients with descending aortic dissection, it has been reported that abdominal extension is significantly more common in ABAD compared with IMH (64.9% vs 40.2%; $P < .001$). Occasionally, IMH may cause obstruction of an aortic side branch, resulting in end-organ ischemia and necessitating interventional therapy.[5]

The evidence concerning disease progression of asymptomatic PAU is limited. Pseudoaneurysm formation may occur in 15% to 50%. The association of PAU diameter and rupture risk remains unclear, although patients with an ulcer diameter > 20 mm and/or an ulcer depth > 20 mm are associated with high risk of disease progression and should be evaluated as possible candidates for early endovascular or surgical repair.[11,20]

MANAGEMENT

Medical

Primary management of patients presenting with uncomplicated IMHB consists of medical therapy and

intensive monitoring.[4,5,16] Medical management includes urgent blood pressure normalization and left ventricular ejection fraction reduction, as they are the main determinants of dissection extension and rupture. Beta-blockers have been shown to decrease mortality from 67% to 95%[22] and should be given at highest-tolerated doses. Calcium-channel blockers are considered the alternative medication of choice. To normalize the blood pressure caused by stimulation of adrenergic receptors, adequate analgesic therapy should be initiated, preferably with morphine sulphate.[8,11,16,20,22]

In a study by Tolenaar et al, two patients with an IMHB and periaortic hematoma died as a result of an aortic rupture despite adequate medical treatment,[5] stressing the importance of periaortic hematoma as a risk factor for adverse events in emergent IMH cases. However, the differentiation between periaortic hematoma and pleural effusion is essential because pleural effusion is not a sign of impending aortic rupture but rather a reactive fluid collection in the thoracic region.[5] For IMHB patients, refractory chest pain, evidence of increasing size of the hematoma, aortic rupture, and progressive pleural effusion are indications for endovascular or surgical treatment.[22] Whenever IMH involves the ascending aorta, there is a substantial increase in mortality rates, and emergent secondary interventions are needed. IMH located in the aortic arch or descending aorta is less likely to be associated with adverse outcomes, and conservative medical therapy might be performed.[9]

The current literature provides no compelling guidelines for treating asymptomatic PAU beyond the blood pressure control. However, symptomatic PAU has a devastating natural course with progression and rupture; therefore, urgent repair is recommended.[11,20]

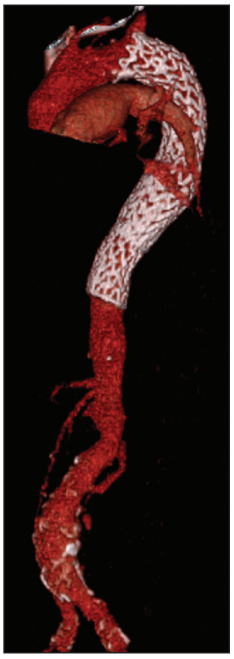

Figure 7. CT-scan after TEVAR in a patient with descending PAU associated with IMH.

Interventional Treatment

Endovascular repair is indicated in symptomatic/complicated IMHB patients due to the risk of rupture[11,20,24] (Figure 7) and is associated with lower perioperative morbidity and mortality than open repair.[19,25-27] The focal character of the aortic lesion makes IMHB patients suitable candidates for endovascular treatment.[5,7] Although the literature provides no convincing guidelines for IMH treatment, it seems reasonable that it is similar to treatment of AD in corresponding segments of the aorta.[3,28] Currently, TEVAR is indicated in patients with progression of IMH toward overt dissection or rupture.[19,28]

Intimal defects without IMH are suitable to treat with TEVAR if they are localized in the descending aorta. If the ascending aorta is involved, surgery is indicated.[29] In patients with intimal defects and IMH, evidence of adjacent atheromatous wall should favor more extensive treatment of the aorta with longer endografts because shallow ulcers are often underestimated on imaging. Treatment with longer endografts provides a safety margin against undertreating the intimal defect.[21] An important risk of TEVAR in extended IMH is that the endograft may tear through the intimal surface into underlying thrombosed false lumen. Thus, the endograft should be anchored in the noninvolved wall above and below the intimal defect.[3] There are no data that support prophylactic TEVAR for patients with uncomplicated IMH with no intimal defect, although in some circumstances, such treatment has been performed. Open surgery should be reserved for patients who cannot be treated with stent graft placement, for instance, IMH cases with ascending/arch involvement (Figure 8).

For PAU patients, TEVAR proved to be a safe option.[18] TEVAR is especially indicated for symptomatic patients with PAU complicated by pseudoaneurysm formation or rupture.[19] PAU patients are often older and debilitated, and therefore, an endovascular technique should be considered as the optimal therapy. However, in patients with PAU complicated by IMH, discussion remains whether to operate in the acute phase or to wait for IMH resolution, as this could be an important issue in improving late efficacy of TEVAR. Patel et al showed that TEVAR treatment with extension into the aortic arch was associated with better long-term results ($P = .011$) and that TEVAR after PAU showed beneficial results over open surgical repair.[30] Endovascular repair was associated with shorter duration of hospital stay and similar late results in the high-risk population of PAU patients compared to open surgical repair.[30] The 5-year freedom from cardiovascular events rate was 67.8%. Given the potential need for reinterventions, TEVAR emerges as the first choice of treatment in patients presenting with PAU. However, due to the extensive atherosclerotic lesions involving the arch, TEVAR resulted in a higher rate of perioperative stroke (8.4% vs 16.2%).

Follow-Up

A 5-year follow-up for both IMH type A and type B is advised.[31] IRAD investigators believe life-long medical

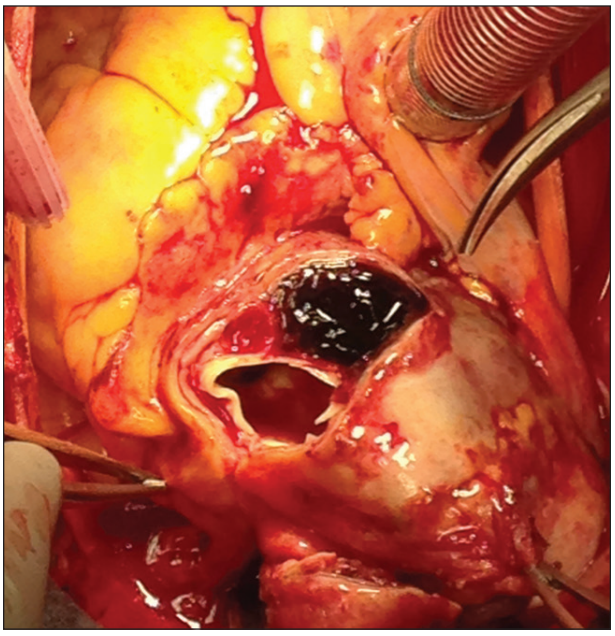

Figure 8. Ascending aortic IMH.

therapy for strict blood pressure regulation is indicated for all patients.[5] In addition, it has been reported that aortic enlargement for IMHB during follow-up was significantly less common compared to ABAD patients (39% vs 61%; *P* = .034).[5]

CONCLUSION

IMH and PAU are diverse aortic diseases with different epidemiology and pathophysiology but strictly associated with each other. Although IMH originates in an acute mode, PAU is a chronic disease that can develop rapidly, both with unpredictable natural courses. Management of IMH is similar to classic AD, with open surgery for treatment of ascending aortic involvement and TEVAR and/or medical therapy for those with only descending localization, based on a complication-specific approach. PAU has various ways of presentation and an unknown incidence that could be underestimated because it often presents with a high occurrence of asymptomatic lesions. Because PAU affects predominantly older patients, when indicated, TEVAR is the treatment of choice. ■

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