Intramural hematoma and dissection involving ascending aorta: the clinical features and prognosis

Naotaka Motoyoshi, Yoshimasa Moizumi, Tsunehiro Komatsu, Koichi Tabayashi

Abstract

Objective: The clinical features and remedies of acute aortic intramural hemorrhage (IMH) are well discussed. This study prospectively analyzes the features compared with those of Type A aortic dissection, and evaluate the treatment modalities and the prognosis with Type A IMH managed by our original program.

Methods: Eighty-six consecutive patients consisted of acute type A IMH (n = 36) and dissection (n = 50) were diagnosed between January 1994 and March 2002. Patients with IMH were older (mean 67 and 60, P = 0.0017), more hypertensive (P = 0.0015), not hyperlipidemic (P = 0.0042) than those with dissection. The incidences of preoperative pericardial effusion and aortic regurgitation were significantly lower in patients with intramural hematoma than with dissection, respectively (8:28 versus 22:28, P = 0.0366, 4:32 versus 22:28, P = 0.0011).

Results: Ten urgent surgical repairs were performed with type A IMH patients and one patient died postoperatively. The rest 26 patients were treated medically. The mean follow up period was 39 ± 28 months. Among the 26 patients, seven were converted surgical intervention. Cardiovascular event free curve on the 26 patients (Kaplan–Meier, CI: 95%) was 65.6% (45.9–85.3), 59.1% (37.5–80.6) at 2, 4 years. There were six dissection and six IMH patients death during follow up. Two of IMH patients died from cardiovascular event, ruptured aneurysm, or aneurysmal enlargement (>60 mm). Operative mortality, late cardiovascular event, and long-term survival were evaluated statistically.

Conclusions: Type A IMH tends to occur in older, more hypertensive and not hyperlipidemic patients, showed lower incidences of preoperative aortic valve regurgitation and pericardial effusion than dissection. Medical treatment alone was not enough to manage all type A IMH patients, and 47.2% (17/36) of the patients needed surgical intervention. Urgent surgical repair was not necessary for all type A IMH patients to achieve favorable surgical outcome with careful follow-up using imaging modality.

Keywords: Intramural hematoma; Aortic dissection; Clinical feature; Prognosis

1. Introduction

Aortic intramural hemorrhage (IMH) was first described in 1920 as ‘dissection without intimal tear’ by Krukenberg et al. [1]. Currently, IMH is considered to be the same pathological entity as aortic dissection. Svensson et al. proposed a unified standard for variant aortic dissections [2]. They reported that, “IMH was one of the well-recognized forms of aortic dissection in the aortic wall, and the less common intramural hematoma-dissection of the aortic wall in which the dissection was filled with blood clot without a detectable intimal flap”, based on their own cases and on other reports [3]. Therefore, diseases of type A IMH have been dealt with using the same management as for those of type A dissection, based on the pioneering reports of the 1990s [3–5]. These articles emphasized the risk of deterioration after medical treatment alone, for patients with type A IMH.

On the contrary, two clinical differences between IMH and aortic dissection (AD) have recently been revealed. First, spontaneous regression after IMH has been reported...
Second, fewer incidents of severe cardiovascular complications have been reported at onset of IMH than of aortic dissection [8,9]. Fewer vascular events, such as ischemia of the lower limbs and viscera, are typically experienced in IMH cases. Currently, IMH is described as almost resembling an AD entity upon clinical presentation, but with a distinct, unique pathologic character.

We agree that urgent surgical intervention is needed for the patient with type A AD, whereas there may exist a suitable management for the patient with type A IMH. Some challenging reports have been published, sporadically [7,10]. Spontaneous regression after the appearance of IMH still perplexes us as to whether an operation is the better therapy for all patients with type A IMH; urgent surgical intervention might be less essential than in dissection. Some articles have revealed what kind of patient characteristics are related to the arbitrary disappearance (as opposed to a deteriorating prognosis after medical treatment alone) of type A IMH [7,10,11].

This study aims to reveal the clinical features of IMH diseases in comparison to those of type A AD, to prospectively analyze our treatment modalities, and to evaluate the prognosis with type A IMH as managed by our original program, described below. We emphasize that this study does not constitute comparative research between the medical and surgical interventions, but is a prospective study that seeks to identify new areas for debate.

2. Patients and methods

2.1. Patients

Between January 1994 and March 2002, 86 consecutive patients with acute type A IMH (n = 36) or AD (n = 50), were introduced to our institute. All patients underwent computed tomography (CT) and echocardiography within 24 h from onset. The differential diagnostic criteria for type A IMH were as follows: (1) initial imaging modality (CT) showing findings characteristic of Yamada’s description (displaced intimal calcification; increased external aortic diameter; a crescent shaped high-attenuation area along the aortic wall on CT scan; a continuous, spiral course of non-opacified soft tissue in the aortic wall on contrast enhanced CT scan; and, no evidence of aortic intimal ulceration, disruption, or flap) [12]; and (2) the involvement of the ascending aorta.

Table 1 shows the characteristics of all the patients. Patients with IMH were older than those with AD (mean 67 versus 60, \(P = 0.0017\)), and female gender was not predominant in IMH (20:16 versus 29:21, \(P = 0.8210\)). Statistical differences were found in comorbidities such as hypertension (30:6 versus 25:25, \(P = 0.0015\)) and hyperlipidemia (3:3 versus 19:31, \(P = 0.0042\)). The development of pericardial effusion was significantly less frequent in patients with IMH than in patients with AD (8:27 versus 22:28, \(P = 0.0366\)). There were no IMH patients with vascular complications, such as stroke, visceral ischemia, or lower limb ischemia soon after the onset. The incidence of preoperative aortic regurgitation (moderate to severe), as confirmed by echocardiography, was significantly lower in patients with IMH than with AD (4:32 versus 22:28, \(P = 0.0024\)).

2.2. Methods

The management plan for the patients with type A IMH is shown in Fig. 1. On arrival at hospital, acute type A IMH patients were subdivided into two groups, one of which was
comprised of moderate cases that were not complicated by hemodynamic instability, persistent pain, impending rupture, or ruptured aneurysm, while the other included severe cases that did have these complications. Moderate cases were first stabilized with intravenous administration of antihypertensive agents, such as nitrates and calcium receptor antagonists, in order to maintain systolic blood pressure strictly between 100 and 130 mmHg, in the intensive care unit, during the first 3 days after admission. Subsequent in-hospital conservative management was continued using oral antihypertensive drugs, such as beta receptor antagonists, calcium channel blockers, and angiotensin converting enzyme inhibitors. For these medically treated patients, serial CT was performed at 1, 2, and 4 weeks, and 3 months after onset, and thereafter continued once or twice a year. Expeditious surgical operations were advocated for those patients with severe IMH and for all of those with AD. Ascending aortic replacement was performed for the patient with severe IMH, in principal. Of the cases of type A dissection, some needed aortic arch replacement for entry closure. Late surgical conversion was applied to a medically treated IMH case upon presentation of any condition of clinical or radiological deterioration, including persistent pain, progression to overt type A dissection, ruptured aneurysm, and aneurysmal enlargement (≥60 mm). (Some cases with progression to dissection after type A IMH should be treated on an emergency basis – like those with aortic dissection; they should be included in the moderate IMH group, and excluded from the aortic dissection group.)

The definitions of disease regression, progression to overt aortic dissection, and rupture were as follows:

- **Regression** was considered to have occurred if aortic diameter or wall thickness decreased;
- in progression to dissection, a typical flap developed in the aorta, defining two lumens;
- rupture was determined by the presence of extra-aortic blood according to CT scan and/or surgical exploration. Diagnosis of rupture after discharge was based on death certificates or clinical circumstances.

These kinds of definitions were confirmed mainly by CT.

In the follow-up study, the cardiovascular event was defined as:

- aortic rupture or impending rupture;
- progression to overt classic dissection into the previous intramural hematoma;
- aneurysmal enlargement, the diameter of which is more than 60 mm;
- ischemia of other organs within the extent of the aortic disease and directly caused by the disease, represented by clinical symptoms, blood samples, or imaging modalities;
- cardiac tamponade.

Follow-up in this study was obtained entirely from clinic visits, telephone, or letter. Scheduled follow-up occurred at 3–6 months after discharge and included evaluation of imaging modalities (CT).

### 2.3. Statistical analysis

Continuous variables are expressed as the mean ± SD, and categorical variables as numbers and percentages. Continuous variables were evaluated by Student’s t-test or Welch’s test. Univariate analysis of descriptive data was performed using Fisher’s exact test or the χ² test with Yates’ method. Statistical significance was confirmed by a probability value of less than 0.05. The cardiovascular event free curve and long term survivals were estimated by the Kaplan–Meier method and compared using the log-rank test. All computations were performed with the Stat-view 5.0 (SAS Institute, Inc, Cary, NC) statistical software package.

### 3. Results

Fig. 2 showed the results. Among the 36 IMH patients, 26 (72%) were preferred for medical treatment on admission. The other ten severe IMH patients (28%) underwent urgent surgical repair due to cardiac tamponade (eight patients) or rupture (2). One patient died postoperatively. During the subsequent hospital course of the 26 medically treated patients, four (15%) were converted to surgical intervention due either to progression to classic dissection (three patients) or to persistent pain (one patient); none of these died postoperatively. Out of all 36 IMH patients, only

<table>
<thead>
<tr>
<th>Assignment for IMH Patients (n=36)</th>
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<tbody>
<tr>
<td>Acute Severe Moderate</td>
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<tr>
<td>Operation, 9 alive Medication</td>
</tr>
<tr>
<td>Subacute or chronic Conversion to operation (n=7), 7 alive</td>
</tr>
<tr>
<td>Subsequent medication (n=19), 13 alive, 2 cardiovascular deaths, 4 unrelated deaths</td>
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Fig. 2. The figure reveals a pedigree, which is the distribution of the patients with type A IMH under our original management program. Six patients of subsequent medical treated group died during follow-up period. Among them, four patients died from non-cardiovascular event. The causes of death are described in the manuscript.
one (3%) died postoperatively in the subsequent hospital course. The mean follow-up was 39 ± 28 months. During follow-up, three cases were converted to surgical intervention following progression to type A dissection, detected on an outpatient basis. All of them survived. Six medically treated IMH patients died during follow-up; the causes of death were aneurysm rupture (1), lung cancer (1), brain hemorrhage (1), sepsis (1), renal failure (1), and sudden death (1).

The ratios of urgently performed ascending aortic replacements with respect to total operations were statistically similar (7:3 versus 36:14, \( P = 0.7978 \)). Three patients with type A IMH had ascending and arch aortic replacement performed due to arch rupture (2) or aortic arch intimal erosion (1). Aortic cross-clamp time was longer in the operations for AD (116 ± 31 versus 156 ± 64 min, \( P = 0.0068 \)), while the difference in cardiopulmonary bypass time was not statistically significant (211 ± 117 versus 257 ± 98 min, \( P = 0.1957 \)). Postoperative hospital mortality was not significantly different (1.9 versus 6.44, \( P = 0.7191 \)). In seven late-converted cases of type A IMH, three ascending, two ascending plus arch, one descending, and one ascending plus descending aortic replacements were performed. Two cases with descending aortic replacement had had onsite progression to dissection. There were no in-hospital or 30-day deaths in these seven cases. Total postoperative hospital mortality was not significantly different (1.6 versus 6.44, \( P = 0.7999 \)). Spontaneous regression of the diseased portion was seen in 17 medically treated cases of IMH; of these, complete resolution of IMH was seen in six cases.

The cardiovascular event free rates (Kaplan–Meier, CI = 95%) for the 26 early medically treated IMH (moderate) patients were 71.1% (52.9–89.3%) at 1 year, 65.6% (45.9–85.3%) at 2 years, and 59.1% (37.5–80.6%) at 4 years (Fig. 3). The respective actuarial survival rates (Kaplan–Meier, CI = 95%) for all IMH patients were 91.2% (81.6–100.7%), 87.5% (76.0–99.1%), and 81.7% (66.2–97.1%) (Fig. 4).

4. Discussion

Clinical treatment modalities for type A IMH have been well discussed. However, there have been few persuasive studies dealing with a medium to large number of cases. Nienaber et al. reported a statistically worse result with medically treated cases of type A IMH than with surgical repair [3]. Maraj et al. reported similar results [5]. These articles claimed that medical management alone was not sufficient to treat type A IMH, although these studies were neither randomized or prospective. At present, a patient with Type A IMH is usually treated with urgent surgical intervention, based on the recommendations of these articles. However, there exist distinct differences between aortic dissection and IMH, one of which is the spontaneous regression of IMH, as described in some articles [6,7]. This arbitrary phenomenon emerges only occasionally, and no remedy is needed beyond antihypertensive drugs. We observed such regression in six patients in the present study, none of whom had an event involving the ascending aorta after discharge. On the contrary, incomplete regression of the disease during follow-up would not be considered safe. Seven patients among the moderate IMH cases, all of whom had been preferred for medical treatment upon admission and who demonstrated disease regression, were converted to surgical operations. Therefore, there should exist a cut-off point for determining whether or not surgical intervention should be performed, but which to be...
Nishigami et al. reported that disappearance of IMH was commonly observed in cases with a maximum aortic diameter of <45 mm [7]. Our related article referred to this critical divergence. Moizumi et al. also proposed that the optimal cut-off was based on the thickness of the aortic mural thrombus at 2 weeks after admission [11].

Our study had six late deaths in the medically treated group, during follow-up, out of which one or two patients could be suffered a cardiovascular event. One patient, who died of hemorrhagic shock due to ruptured aneurysm, had been initially preferred for medical treatment and observed by periodic CT. During follow-up, he had a stroke and suffered hemiparesis. Follow-up CT revealed aneurysmal enlargement on the descending aorta (not the ascending aorta) the diameter of which had increased to nearly 60 mm. We hesitated to perform a surgical intervention because of the neurological finding. The patient later died from sudden shock, 34 months after onset. Another sudden death occurred 19 months after onset. Because autopsy was not performed cardiovascular event could not be denied, while the previous CT had showed incomplete regression of type A IMH.

The total medical treatment failure ratio was 9/26 (35%), including the seven cases converted to surgical intervention and the two cases of late cardiovascular death. The cardiovascular event free curve for the 26 patients who were initially medically treated for IMH (moderate) reveals an unsatisfactory result (Fig. 3). The duration from onset to a further cardiovascular event ranged 24–185 days (median 100 days). However, this curve might seem to decline more gently than that commonly known for type A aortic dissection if treated medically. Consistent medical treatment was not sufficient to achieve improved outcome, whereas early – but not immediate – surgical conversion might be adequate to deal with some cases of type A IMH.

Conversely, postoperative mortality of about 10% has been reported for cases with aortic dissection [13,14], which is similar to our result. If we had considered IMH to be the same entity as aortic dissection and performed surgical intervention in all 26 cases of type A IMH that were initially treated conservatively we might have had two or three postoperative deaths; but, this is only speculation. There may be little difference to be found in the ratios calculated from the clinically well-known postoperative survival of dissection and our result for the 26 patients, because we had two cardiovascular deaths, including a sudden one by unknown origin. Furthermore, our total survival for type A IMH showed no statistically significant difference when compared with that of surgically treated type A aortic dissection (Fig. 4).

Our colleague, Dr Moizumi, reported a critical cut-off value. Thus, we should initially follow the guidelines provided by that article [11]. This involves a hospital stay of less than 2 weeks, including initial, strict antihypertensive therapy, enhanced CT at 2 weeks after admission, and the decision to perform operative therapy based on the thickness of hematoma in the CT image.

There were statistical differences in patient background between dissection and IMH in the context of age, hyperlipidemia, hypertension, and complications early after onset. IMH affected an older population than did dissection, an observation that is consistent with those reported in the Song et al. studies [8]. Dissection was more prone to exist in younger patients than was IMH, as described in the other report [9]. Curiously, however, Song et al. reported opposing results [9]. Our report was the first to show that cases with IMH or dissection have a different natural history with respect to hyperlipidemia and hypertension. Differences in clinical features of these kinds of have not been pointed out in any previous report. Intimal atheromatous plaque, often observed in hyperlipidemic patients, could have some correlation with the progression to dissection. Some pathological interpretation can be expected.

4.1. Limitations of the study

We found no statistical difference in late results between the cases operated due to type A dissection and those with type A IMH managed by the original program. However, the evaluation (by comparison of survivals) was limited by not being randomized. Moreover, the patients had different clinical backgrounds, in terms of age and comorbidity. If one considers these two diseases to be expressions of the same entity, as Svensson et al. proposed, the comparison becomes somewhat more meaningful.

References

[8] Song JK, Kim HS, Kang DH, Lim TH, Song MG, Park SW, Park SJ. Different clinical features of aortic intramural hematoma versus


Appendix A. Conference discussion

Dr A. Haverich (Hannover, Germany): I think this is a very important contribution and excellent results, at least in the surgical groups. In the medical group, you had a high mortality and you said that only one or two patients died from cardiovascular disorders.

Before we further discuss this paper, we’ll need to know what these medically treated patients died of. Because the discussion reminds me to a situation, like 20 years ago, where people said we also see patients with acute type A dissection, not in the acute phase, but in the chronic phase. So there are certainly survivors of acute dissection. Nevertheless, we have come to an agreement that all patients with acute type A dissection have to be operated on. And as long as we don’t have better long-term data with larger numbers of patients in the intramural hematoma group, I think these patients from the European registry and the worldwide registries should undergo operation at this point. So we do need to know what your patients in the medically treated group died from?

Dr Motoyoshi: That’s a very important question. And first, we should know what kind of patient would be regressive one or progressive one. And I do like to know what kind of patient tends to be suffered by severe IMH. And also IMH patients tend to be older than dissection, and operative risks are getting higher and higher.

Dr T. Carrel (Bern, Switzerland): The question was, do you know the cause of death of these patients who died in the medically treated group?

Dr Motoyoshi: We found late deaths were observed in five medical-treated patients. The origins were lung cancer (one patient), brain hemorrhage (1), car accident (1), and unknown (2). One unknown death occurred suddenly, therefore cardiovascular event was not denied.

Dr J. Bachet (Paris, France): Although we all know that intramural hematoma in some cases may result into real acute dissections, I’m not sure that we should compare these two entities. They are totally different.

In particular, intramural hematoma is never complicated by malperfusion, which is probably one of the most killing features in acute dissections. So I’m quite convinced that you should not mix those two kinds of patients and compare them in the same study.

Dr Motoyoshi: For us this is still very controversial. We are going to present the patents of IMH are less severe than those with aortic dissection, whereas the opposite opinion exists over around European countries. Pathological differences between two diseases have already been well-discussed, and we have confirmed it.

Dr T. Carrel (Bern, Switzerland): You state in your paper that in your decision between medical and surgical treatment, in presence of cardiac tamponade, indication for operation is given. Do we have really to wait to have a cardiac tamponade to operate on these patients, or is the presence of pericardial effusion enough to go to surgery?

Dr Motoyoshi: There is a difference between the pericardial effusion and the cardiac tamponade. In cardiac tamponade, the patient falls into cardiogenic shock. And we define cardiac tamponade as an emergency state in the necessity of pericardiocentesis and pericardial effusion as a risk factor to fall into the surgical conversion.

Dr Carrel: Anyway we would not wait for cardiac tamponade, but if the patient has a relevant pericardial effusion we would operate on.