**Title:** Intimomedial mucoid arterial degeneration, a rare arterial disorder of forensic significance.

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# Intimomedial mucoid arterial degeneration, a rare arterial disorder of forensic significance

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| **Abstract:** | The corpse of a 43-year-old African woman with a history of aortic aneurysm and hypertension was forensically investigated after her sudden death.<br>The cause of death was related to a cardiac tamponade due to a ruptured aneurysm of the ascending aorta. Post-mortem gross examination showed an abnormal whitish discoloration of the intima with fibrous thickening of the aortic wall. Several arteries (left main and circumflex coronaries, carotid, renal and iliac arteries) showed similar features.<br>Upon histological examination, the aortic aneurysm as well as the other arteries sampled showed mucoid degeneration, excess of mucopolysaccharides and pools of mucin inside the intima and the media associated with collagen and elastic fibers destruction and loss of smooth muscle cells. This pattern strongly suggested the diagnosis of Intimomedial mucoid degeneration (IMMD), a rare arterial disorder consisting in a progressive deposition of mucin into the intima and media, with a strong prevalence in middle-aged black African females with high blood pressure. In addition to the typical features of IMMD, the histological examination of the ascending aorta showed a thickening of the adventita with sparse mixed inflammatory infiltrates and fibrosis, suggesting an additional chronic infectious aortitis. No infectious agent was detected.<br>The body of literature on IMMD is reviewed and the origin of death is discussed in this case report. |

# Intimomedial mucoid arterial degeneration, a rare arterial disorder of forensic significance.

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# Manuscript

**Key points:**

1. Intimomedial mucoid degeneration (IMMD) is a rare arterial disorder predominantly affecting middle aged black African women with high blood pressure.
2. The histological pattern of IMMD is characterized by mucin deposition into the intima and the media as well as collagen and elastic fibers destruction of large- and sometimes medium-sized arteries.
3. IMMD may result in non-atherosclerotic aortic aneurysm. When associated with hypertension, there is an increased risk of arterial rupture.
4. Forensic pathologists should be aware of the possible incurrence of IMMD, a rare illness potentially causing sudden death. In these instances, it is of importance to sample several arteries to establish a proper diagnosis.

**Key words:**

- aortic aneurysm
- non-atherosclerotic aneurysm
- intimomedial mucoid degeneration (IMMD)
- mucoid extracellular matrix accumulation (MEMA).

## Introduction

Intimomedial mucoid degeneration (IMMD) is a rare arterial disorder, characterized by mucinous deposition into the vessels' intima and media and potentially leading to aneurysm formation [1]. It was first described in 1955 in South Africa as predominantly affecting middle aged African women with high blood pressure [1,2].

The etiology of IMMD is unknown. Its pathogenesis consists in a progressive deposition of mucin into the vessels' two inner layers, a decrease in the number of muscle cells and the degradation of the elastic fibers of the affected artery walls [3,4,5]. This process weakens the wall and aneurysm formation may occur, especially when associated with chronic hypertension. IMMD may affect the aorta and extend to other large and medium-sized arteries [1, 3-5].

The essence of the clinical presentation is its acuteness - a ruptured aneurysm or its ischemic complications are potentially lethal [1]. Forensic pathologists may face these vascular diseases and should include IMMD into the differential diagnosis along with arteriosclerosis, connective tissue disorders and vasculitis.

## Case presentation

The body of a 43-year-old black African woman from Congo was transferred to the local University's center of legal medicine after her sudden death. She abruptly collapsed shortly after being informed of the death of a close relative. On site cardiopulmonary resuscitation was unsuccessful. Her medical record revealed a conservatively treated aneurysm of the thoracic aorta - 5.3 cm in diameter, hypertension, obesity and a latent tuberculosis.

Post-mortem CT angiography and the autopsy revealed a cardiac tamponade due to a ruptured aneurysm of the ascending aorta. The size of the aneurysmal sac was 8 cm in height and 4.5 cm in width. The tear was about 2 cm in length and was located on the right side at the outer curve of the vessel. Gross examination of the ascending aorta and aortic arch showed an abnormal whitish discoloration of the intima with fibrous thickening of the aortic wall up to 0.7 cm **Fig.1 Macroscopic abnormal white fibrous thickening of the ascending aorta**. No sign of atherosclerosis was observed. Gross examination of the thoracic and abdominal aorta, renal arteries, iliac arteries, left coronary artery and carotid arteries showed similar features **Fig.2 Macroscopic abnormal white fibrous thickening of the abdominal aorta**. Stepped sampling was performed to further investigate the underlying pathology. Toxicological screening was negative.

Histological examination of the sampled arteries (right carotid artery, circumflex coronary artery, left renal artery, both iliac arteries and infra-renal aorta) demonstrated mucoid degeneration, an excess of mucopolysaccharides and pools of mucin inside the intima and the media (Alcian Blue staining) **Fig.3 Mixoid degeneration with excessive amounts of mucopolysaccharides and mucin pools in the circumflex coronary artery (Alcian Blue, 100x)** and elastin destruction (Miller staining) **Fig.4 Elastin destruction in the circumflex coronary artery (Miller, 100x)**. Smooth muscle actin staining showed a loss of smooth muscles cells **Fig.5 Decrease of smooth muscle cells in the circumflex coronary artery (Smooth muscle actin, 100x)**. This panel of features in this 43-year-old black African woman strongly suggested the diagnosis of IMMD.

In addition to the typical features of IMMD, the histological examination of the ascending aorta showed a thickening of the adventitia with sparse mixed inflammatory infiltrates. Immunostaining (anti-CD3, anti-CD20, anti-CD68, anti-CD138 antibodies) confirmed the presence of macrophages, T lymphocytes, B lymphocytes and plasmocytes in the media and the adventitia, indicating a chronic aortitis **Figs. 6-8 Chronic aortitis (Hematoxylin and Eosin,10x, 100x, 200x)**. These findings strongly suggested an infectious etiology. However no giant cells or granulomas were observed and no indications of a large vessel vasculitis (Takayasu- or giant cell arteritis) were found [6]. Special stains (Gram, Grocott, Periodic Acid Shiff and Ziehl-Neelsen) aimed at identifying an underlying infectious agent and immunostaining against Treponema pallidum were all negative. Masson staining showed a concomitant adventitial fibrosis. This was interpreted as a subsequent chronic inflammatory process. Still, the overall pattern was compatible with the diagnosis of chronic infectious aortitis due to an unknown pathogen. The above findings were observed inside and in the vicinity of the aneurysm.

## Discussion

The prevalence of aortic aneurysms in the general population is 1 - 2%. It increases with age, reaching 10% in older people [7]. In western countries, fatal aortic aneurysms are the 13th highest cause of death and are mostly due to a rupture of the abdominal aorta [7]. Thoracic aortic aneurysm (TAA) more seldom occurs, with a prevalence estimate ranging from 0,16 to 0,34% [8,9]. The majority of TAAs are degenerative and associated with atherosclerosis. Autoimmune processes, infections, connective or vascular tissue disorders can also cause TAA [10].

The pathophysiology of IMMD consists in a progressive deposition of mucin into the intima and the media predominantly in their extracellular compartment. This mucin accumulation leads to the degradation of collagen fibers and is associated with the degeneration and fragmentation of the elastic fibers of the media [3-5]. The deposition of mucin vesicles is also observed inside the smooth muscle cells (cytoplasm first and in the nucleus later) causing muscle cells necrosis [5]. The arterial wall is thus weakened and aneurysm formation may follow. IMMD can affect the aorta and extend to large and medium-sized arteries and its etiology remains unknown [1,3-5]. According to Abdool-Carrim and coauthors, the prevalence of IMMD is ca. 3,5% of all non-traumatic aneurysms in the South African black population [1]. Patients develop aneurysms at younger age than atherosclerotic patients do (52 versus 65 years) [1]. The prognosis of IMMD depends on the spread of the disease and the degree of acuteness of the clinical situation (rupture of the aneurysm or, more seldom, acute ischemia of the lower limbs). Previous cardiovascular surgical reviews reported that one of the distinctive features of IMMD, which may be of use for clinical diagnosis, was the near absence of a luminal thrombus in the aneurysm sac during vascular surgery. One hypothesis includes a potential fibrinolytic process originating from the aneurysm in IMMD [3-5]. This would also explain why affected patients often suffer from hemorrhage during the surgical repair of IMMD aortic aneurysms [3-5]. Due to the lack of distinctive clinical signs, the diagnosis of IMMD rests essentially on histological features [3].

Although IMMD is a rare vascular tissue disorder, a few others pathologies are histologically closely related. The abnormal mucin deposition in the arterial wall observed in IMMD is histologically similar and could therefore be confused with the more prevalent vascular pathology “Mucoid Extracellular Matrix Accumulation” (MEMA, which was formerly known as cystic medial necrosis) in the newest classification from the *Society for Cardiovascular Pathology* and the *Association for European Cardiovascular Pathology* [3,11]. MEMA is associated with a number of genetic syndromes. However, in contrast to IMMD, MEMA is confined to the media layer and only affects the aorta. Histology usually shows an increase of the mucoid extracellular matrix with trans-lamellar or intra-lamellar expansions of the media in MEMA [11].

Another source of confusion relates to the proximity of IMMD with another rare entity of mural abnormality “Cystic Adventitial Disease“ (CAD). CAD is a pathology with a predilection for males that is characterized by unilateral lesions of the adventitia of peripheral vessels (external iliac, femoral, popliteal, radial and ulnar arteries) [12]. About 350 cases of arterial CAD have been reported in the literature, with 85% involving the popliteal artery [13]. The etiology of CAD is unknown, although several hypotheses exist,

including trauma, degenerative and systemic disorders. Typically, histology reveals multi-locular mucinous or gelatinous cysts in the adventitia [13]. Rare cases of venous impairments have also been reported [5].

In the present situation, death was related to the acute rupture of an aneurysm following an episode of intense emotional stress. The consecutive adrenergic discharge causing tachycardia and hypertensive peak most likely led to the rupture of the ascending aorta. Histologically, in addition to IMMD, chronic infectious aortitis was also diagnosed. As described before, no germ was found. We therefore hypothesized that the IMMD process weakened the aortic wall and thus facilitated the spreading of infection in the vessel's wall. To the best of our knowledge, the association between IMMD and aortitis was not previously described in the literature.

## Conclusion

IMMD is a rare arterial disorder that must be kept in mind with young to middle-aged patients affected by non-atherosclerotic aneurysms, particularly in female black African populations. It is characterized by mucinous deposits in the arteries' intima and media along with the destruction of collagen and elastic fibers. In the case described herein, IMMD was associated with chronic aortitis of the ascending aorta.

Death was induced by the sudden rupture of the aneurysm following intense psychological stress and acute hypertension, which most likely was the cause of the subsequent aortic failure.

To the best of our knowledge, this rare pathology has not been reported in the medicolegal literature. Forensic pathologists should be aware of this rare illness as a potential cause of sudden death. In such instances, it is important to sample several arteries to establish a proper diagnosis.

## Compliance with Ethical Standards

**Funding** : none.

**Conflict of interest** : the authors declare that they have no conflict of interest.

**Ethical approval:** this article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent**: formal authorization for anonymous publication was delivered by the local prosecutor.

## References


1. Abdool-Carrim AT, Robbs JV, Kadwa AM, Kenoyer G, Cooper K. Aneurysm due to intimomedial mucoid degeneration. Eur J Endovasc Surg. 1996;11:324-329

2. Pepler WJ. A study of some of the structural changes of the Bantu aorta. S Afr J Lab Clin Med. 1955;1:203-53

3. Viljoen C, Szymanski P, Osman N, Henning KL, Scholz P, Rayner B et al. Intimomedial mucoid degeneration causing aortic and renal artery aneurysm in a young adult. Cardiovasc J Afr. 2016;27:49-52

4. Raber MH, Meerwaldt R, Van Det RJ. A young man with intimomedial mucoid degeneration of the brachial artery. J Vasc Surg. 2011;53:822-824

5. Katz JR, West DL, Bui JT, Knuttinen G, Chejfec G, Owens CA. Endovascular treatment of intimomedial mucoid degeneration. J Vasc Interv Radiol. 2008;19:1765-1768

6. Jennette JC. Overview of the 2012 revised International Chapel Hill Consensus Conference nomenclature of vasculitides. Clin Exp Nephrol. 2013;17:603-606

7. Ladich E, Yahagi K, Romero ME, Virmani R. Vascular diseases : aortitis, aortic aneurysms and vascular calcification. Cardiovasc Pathol. 2016;25:432-441.

8. Itani Y, Watanabe S, Masuda Y, Hanamura K, Asakura K, Sone S, Sunami Y, Miyamoto T. Measurement of aortic diameters and detection of asymptomatic aortic aneurysms in a mass screening program using a mobile helical computed tomography unit. Heart Vessels. 2002;16(2):42-45

9. Kälsch H, Lehmann N, Möhlenkamp S, Becker A, Moebus S, Schmermund A et al. Body surface adjusted aortic reference diameters for improved identification of patients with thoracic aortic aneurysms: results from the population based Heinz Nixdorf Recall Study. Int J Cardiol. 2013;163(1):72-8.

10. Booher AM, Eagle KA. Diagnosis and management issues in thoracic aortic aneurysm, Am Heart J. 2011;162(1):38-46e1

11. Halushka MK, Angelini A, Bartolini G, Basso C, Batoroeva L, Bruneval P et al. Consensus statement on surgical pathology of the aorta from the Society for Cardiovascular Pathology and the association for European Cardiovascular Pathology: II. Noninflammatory degenerative diseases – nomenclature and diagnostic criteria. Cardiovasc Pathol. 2016;25:247-257

12. Maeda H, Umeda T, Kawachi H, Iida A, Ishii Y, Kono M et al. Cystic adventitial disease of the common femoral artery. Case report and review of the literature. Ann Thorac Cardiovasc Surg. 2017;22(5):315-317.

13. Sharma AM, Norton PT, Zhu D. Conditions Presenting with Symptoms of Peripheral Arterial Disease. Semin Intervent Radiol. 2014;31:281-291

## Abstract

The corpse of a 43-year-old African woman with a history of aortic aneurysm and hypertension was forensically investigated after her sudden death.

The cause of death was related to a cardiac tamponade due to a ruptured aneurysm of the ascending aorta. Post-mortem gross examination showed an abnormal whitish discoloration of the intima with fibrous thickening of the aortic wall. Several arteries (left main and circumflex coronaries, carotid, renal and iliac arteries) showed similar features.

Upon histological examination, the aortic aneurysm as well as the other arteries sampled showed mucoid degeneration, excess of mucopolysaccharides and pools of mucin inside the intima and the media associated with collagen and elastic fibers destruction and loss of smooth muscle cells. This pattern strongly suggested the diagnosis of *Intimomedial mucoid degeneration* (IMMD), a rare arterial disorder consisting in a progressive deposition of mucin into the intima and media, with a strong prevalence in middle-aged black African females with high blood pressure. In addition to the typical features of IMMD, the histological examination of the ascending aorta showed a thickening of the adventita with sparse mixed inflammatory infiltrates and fibrosis, suggesting an additional chronic infectious aortitis. No infectious agent was detected.

The body of literature on IMMD is reviewed and the origin of death is discussed in this case report.

# FIGURE FILE

**Fig.1**

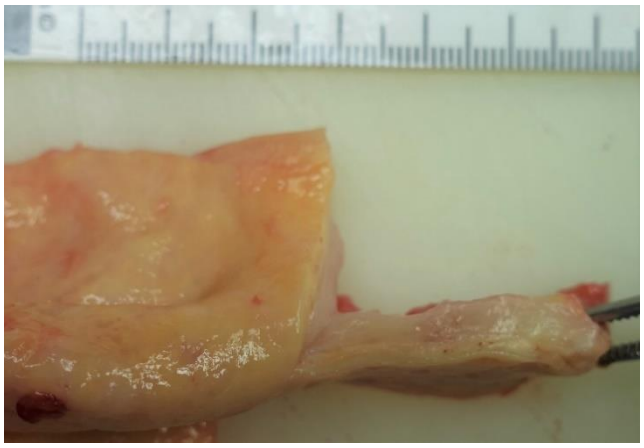

**Fig.2**

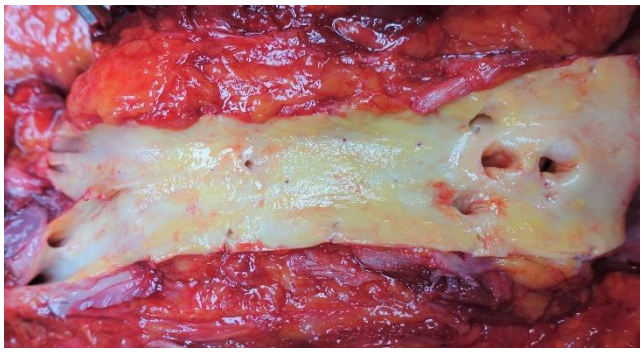

**Fig.3**

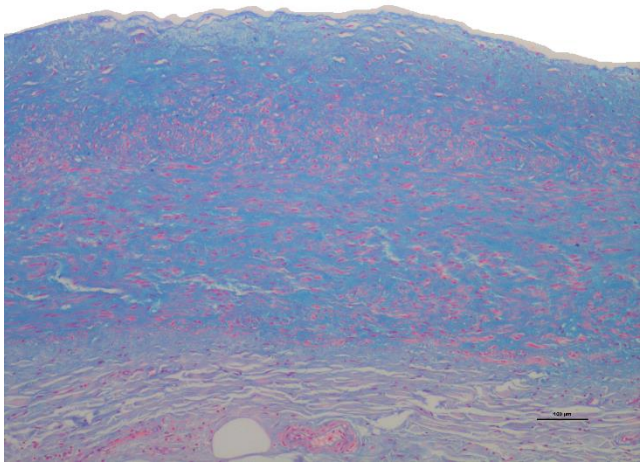

**Fig.4**

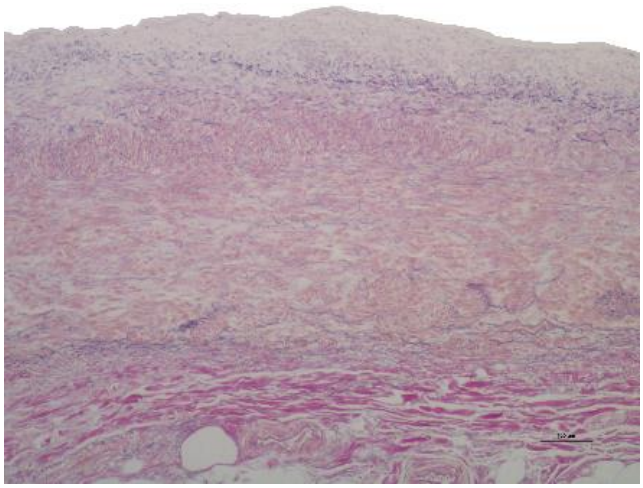

**Fig.5**

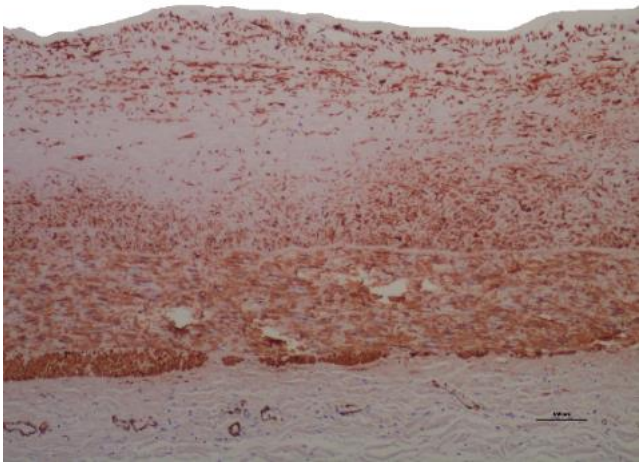

**Fig.6**

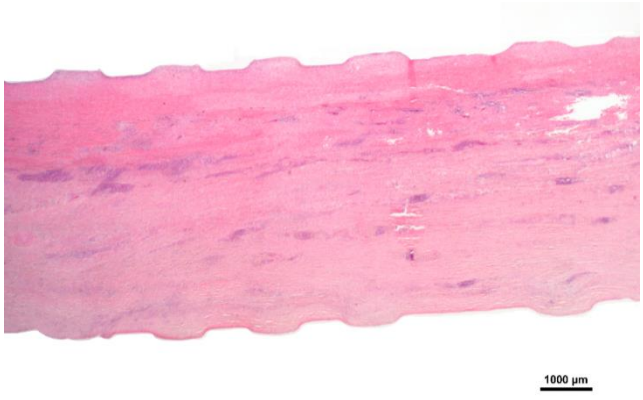

**Fig.7**

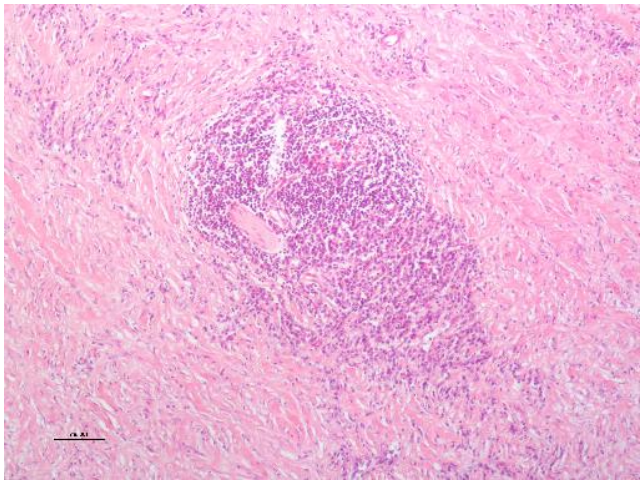

**Fig.8**