



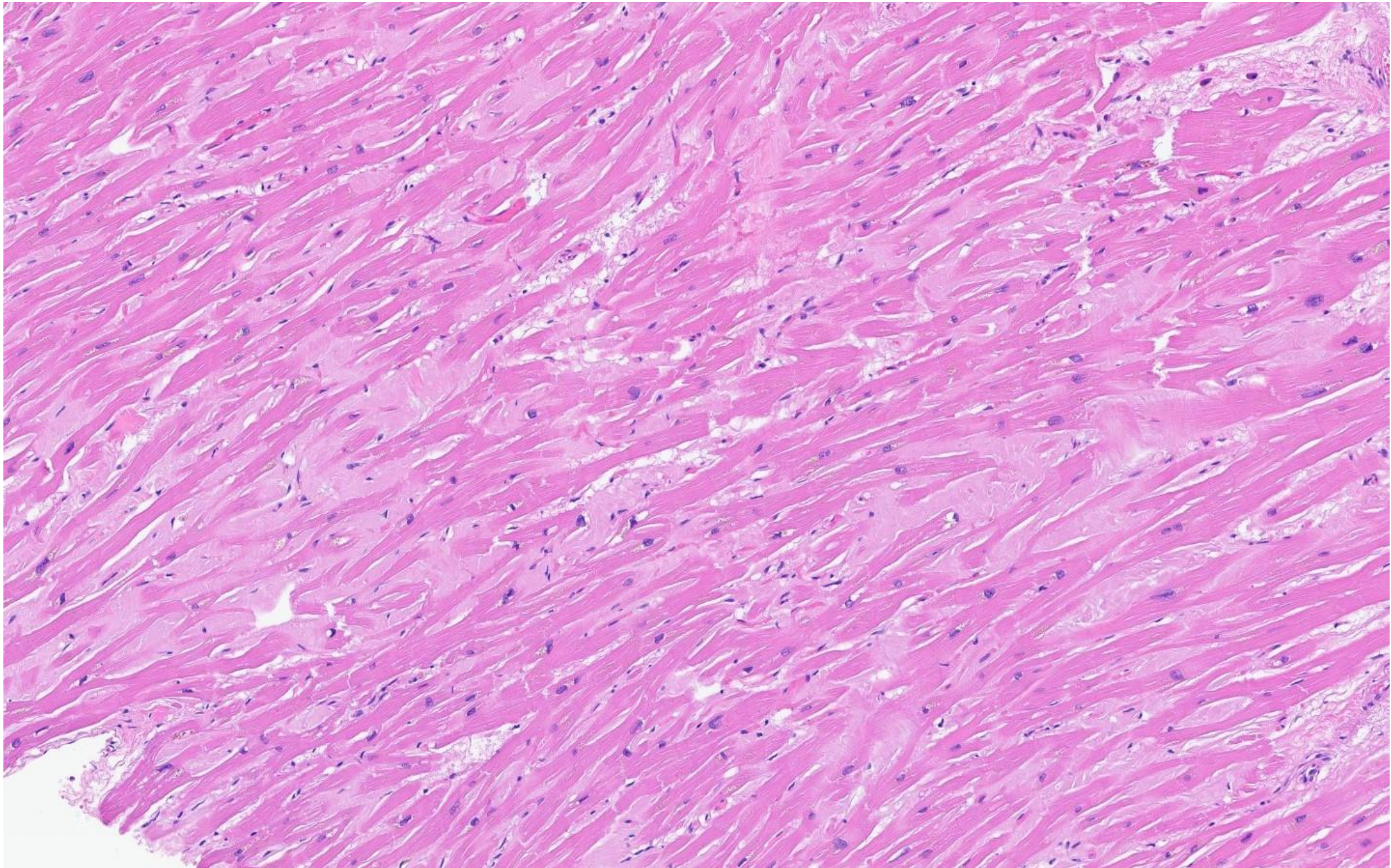
# Case #59

NAME Educational Activities Committee

Case provided by:

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1. The decedent is a 55-year-old man with a past medical history significant for emphysema and hypertension, who was found underwater at a riverbank and pronounced deceased at the scene.

What is the underlying etiology of the lesion identified on the histologic section of the heart?

- Underlying genetic disorder
- Agonal cardiac strain
- Decompositional changes
- Underlying atherosclerotic cardiovascular disease
- Processing artifact

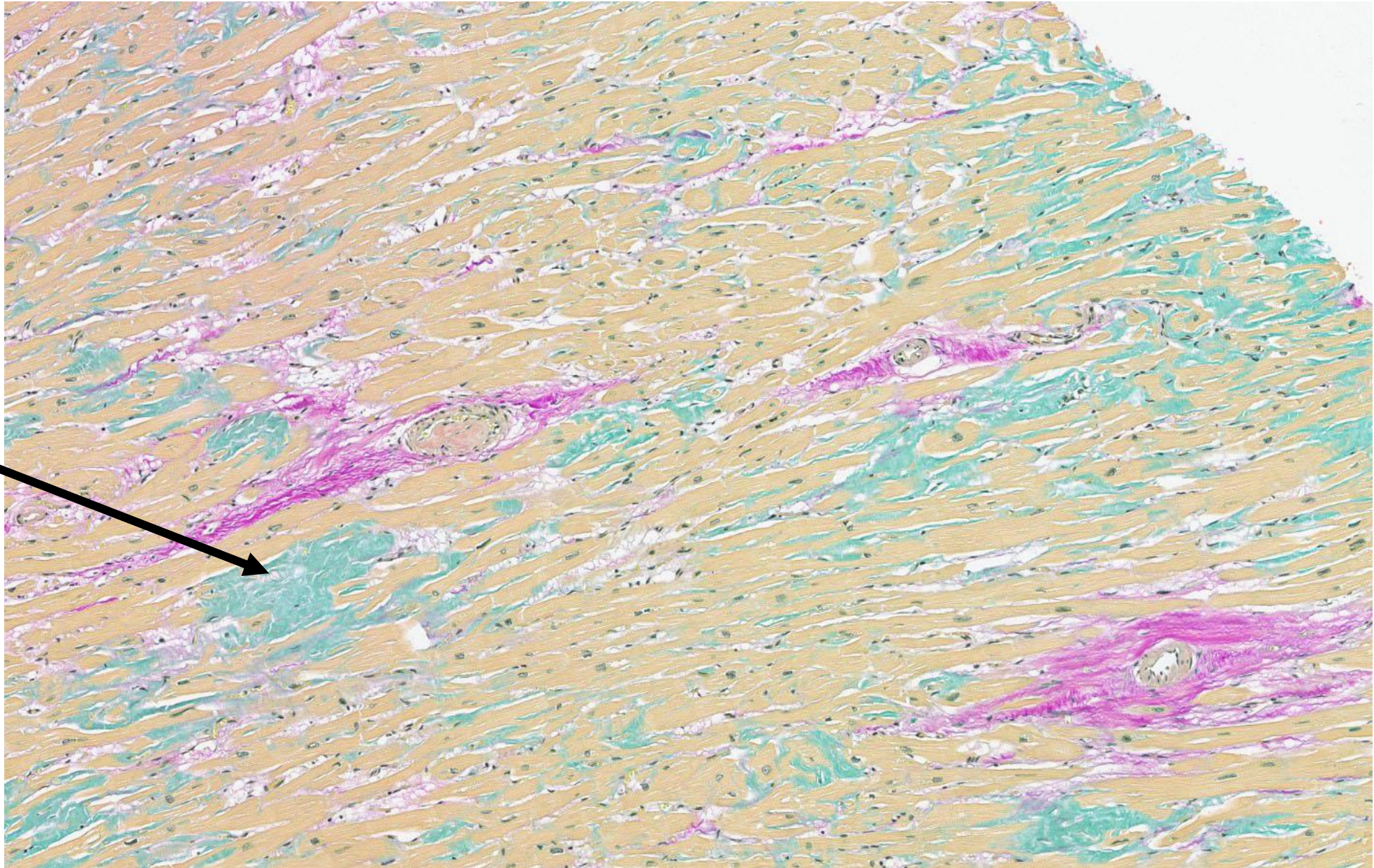
Answer...

## **A. Underlying genetic condition – (CORRECT ANSWER, \_\_ % of responses)**

The picture provided shows a histologic section of the heart with interstitial amyloid deposition. Amyloidoses are a heterogeneous group of disorders characterized by the extracellular deposition of abnormally folded and agglutinated proteins, ultimately leading to end-organ damage. In the heart, amyloid deposition causes an infiltrative/restrictive cardiomyopathy leading to heart failure, which is the leading cause of morbidity and mortality in systemic amyloidosis. Extensive cardiac amyloidosis has also been associated with arrhythmias and sudden cardiac death.

While there are over thirty different types of amyloidogenic proteins, two types of amyloid commonly infiltrate the heart: light chain (AL) amyloid and transthyretin (ATTR) amyloid. These proteins are recognizable by their affinity for Congo red and their yellow-green birefringence under polarized light. Amyloid deposits will also stain bright green with sulfated Alcian blue (SAB) (see picture on next slide). Deposits are commonly seen within the interstitium but may also be seen within the walls of vessels and on the endocardial and epicardial surfaces.





SAB Stain highlighting amyloid (green)



ATTR-type amyloidosis is divided into wild-type and mutated forms. Wild-type amyloid, formerly called “senile amyloid,” has classically been associated with clinical manifestations in older, predominantly male populations. Mutated variants of transthyretin amyloid are caused by mutations in the TTR gene with an autosomal dominant inheritance pattern (although with variable penetrance). Hereditary amyloidoses can present from young adulthood onwards and are named according to the substitution or deletion in the mature protein. Val142Ile is the most common hereditary amyloidosis mutation in the United States and affects primarily Black Americans with increasing frequency in White Northern Italians.



AL-type amyloidosis, is derived from immunoglobulin light chains, which are generally associated with an acquired clonal plasma cell dyscrasia. In addition to cardiac manifestations, other clinical features may include macroglossia, periorbital purpura, submandibular gland enlargement and nail dystrophy. Historically, AL amyloidosis has been thought to be the most commonly form of cardiac amyloidosis; however, the increasing availability of amyloid typing by tandem mass spectrometry and the subsequent emerging research has questioned this mantra.

It has been suggested that ATTR is deposited in the interstitium with a patchy, nodular, and “moth-eaten” distribution, whereas AL is deposited in a more “chicken-wire” pattern with increased vascular deposition. However, these patterns are non-specific and morphologic findings are not sufficient for distinguishing between these two common types. Given the potential genetic impact on surviving family members, proteomic classification of cardiac amyloid should be considered in autopsy specimens.

## **B. Agonal cardiac strain** (\_\_\_ % of responses)

Acute myocardial strain, at its earliest histologically identifiable form, will present with interstitial edema, hypereosinophilia of myocyte cytoplasm and wavy myocyte fibers. The waviness of fibers following infarction results from the forceful pull of the viable fibers on adjacent dead fibers that cannot contract during systole. The margins of infarcts may show an additional ischemic change known as myocyte vacuolization or myocytolysis. The myocytes on our picture look healthy and our interstitial deposits are amorphous and dense and therefore more consistent with amyloid, rather than edema.

## **C. Decompositional changes** (\_\_\_ % of responses)

Changes due to decomposition in histologic sections of the heart can initially appear as minimal interstitial edema and increased separation of myocyte fibers, and eventually will progress to loss of myocyte nuclei and defined cellular borders with increasing postmortem interval. The myocytes on our histologic section appear well preserved and the interstitial deposits are amorphous and dense and therefore more consistent with amyloid.

#### **D. Underlying atherosclerotic cardiovascular disease (\_\_\_ % of responses)**

Underlying atherosclerosis can lead to diffuse deposition of excess fibrous tissue (i.e., collagen types I and III fibers) within the myocardial interstitium. Myocardial interstitial fibrosis (MIF) contributes to left ventricular (LV) dysfunction and predisposes patients to develop heart failure. MIF can be seen as reparative/replacement fibrosis, forming microscars that replace dead myocytes, or reactive fibrosis, where there is accumulation of fibrous tissue in the perivascular space, perimysium and endomysium creating thicker sheaths that surround individual cardiomyocytes. The interstitial deposits in our picture are amorphous and dense and therefore more consistent with amyloid rather than collagen.

#### **E. Processing artifact (\_\_\_ % of responses)**

Tissue artifacts can be introduced into tissue specimen during any one of the many steps of histology processing. The possibilities are extensively varied with common forms of artifact including crush artifact, folding/wrinkles, fragmentation, formalin pigment and/or residual water or air bubbles. Our histologic section does not include any of the above.



# REFERENCES

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