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Medical Affairs

ATTR-CM NEWS-BEAT

Key steps to achieving a confirmed diagnosis of ATTR-CM

1. Building a suspicion of ATTR-CM[1-3]

65+ year old Patient with HF and LV wall thickness ≥ 12mm

Clinical signs:
(AL symptoms are excluded)

Cardiac:
- HF symptoms
- Hypotension or normotensive if previous hypertensive

Extracardiac:
- Dysautonomia
- Polyneuropathy
- Bilateral carpal tunnel syndrome
- Ruptured biceps tendon
- Lumbar spinal stenosis
- Vitreous deposits
- Family history

ECG:
- Discordance between QRS voltage on ECG and LV wall thickness
- Pseudo-infarct ECG pattern
- Conduction abnormalities, and arrhythmias

Laboratory:
- Disproportionally elevated NT-proBNP to degree of HF
- Persisting elevated troponin levels

Echocardiography:
- Increased LV and RV wall thickness
- increased atrial septum thickness
- Biatrial enlargement
- Thickened valves
- Diastolic dysfunction
- Granular sparkling of myocardium
- Pericardial effusion
- Reduced longitudinal strain with apical sparing pattern

Cardiac MRI:
- Subendocardial Late Gadolinium Enhancement
- Elevated native T1 values
- Increased extracellular volume
- Abnormal gadolinium kinetics

Early recognition of these signs should trigger diagnostic work-up for ATTR-CM

2. Achieving a definitive diagnosis of Cardiac Amyloidosis (CA)

Once CA is suspected, a timely, **definitive diagnosis** should be obtained. A diagnostic approach for patients with suspected cardiac amyloidosis should include **testing for monoclonal protein** and **scintigraphy or biopsy**[2].

Invasive diagnostic criteria apply to all forms of CA, whereas non-invasive criteria are for ATTR-CM only[2].

NONINVASIVE

Nuclear Scintigraphy

Nuclear scintigraphy in combination with testing to rule out AL Amyloidosis can diagnose ATTR-CM with high sensitivity and specificity.[1,2]

When signs and symptoms are suggestive of CA, **diagnosis may be made noninvasively with nuclear scintigraphy and testing to rule out AL amyloidosis***.[4,5]

INVASIVE

Endomyocardial Biopsy (EMB)

The gold standard for the diagnosis of ATTR-CM with high sensitivity and specificity if specimens are collected from multiple sites and tested for amyloid deposits by **Congo red** staining. Identification of amyloid should be followed by **classification of the amyloid** protein by mass spectrometry, immunohistochemistry, or Immunoelectron Microscopy. **However, EMB is not needed with a grade 2-3 positivity of scintigraphy with SPECT and normal hematologic tests.**[1,2]

* Ruling Out AL Amyloidosis should be made by three tests screening for presence of monoclonal gammopathy: Serum Free Light-Chain (FLC) Assay, Serum and Urine Electrophoresis with immunofixation (SPIE, UPIE)[2]

Genetic Testing

Genetic testing should be performed to differentiate ATTRm (hereditary ATTR due to a mutation in the TTR gene) from ATTRwt (wild-type)[1-3,6]

ATTR-CM Diagnostic Algorithm proposed by the 2021 ESC Guidelines for the diagnosis and treatment of chronic heart failure

Cardiac amyloidosis suspected
HF and LV wall thickness ≥12 mm
AND age ≥65 or at least 1 red flaga

Hematologic tests
- Serum free light-chain assay
- Serum and urine protein electrophoresis with immunofixation

99mTc-PYP, DPD or HMDP scintigraphy with SPECT

- Both abnormal → Histological confirmation to subtype (usually cardiac)[b]
- Abnormal haematology No myocardial uptake → Amyloidosis unlikely
- Normal haematology Grade 1 uptake → Histological confirmation of diagnosis (cardiac/extracardiac)[c]
- Normal haematology Grade 2–3 uptake → ATTR
  - Negative → Genetic counselling
  - Positive or inconclusive → Amyloidosis unlikely
- All normal → Amyloidosis unlikely

Cardiac amyloidosis on CMR imaging

ATTR-CM: from suspicion to diagnosis

In this video, Dr García-Pavía takes us on a deep dive into the diagnostic pathway for ATTR-CM, highlighting four key scenarios in achieving a confirmed diagnosis.

Stay tuned for our upcoming "Cardiac imaging for ATTR-CM: the key to raising suspicion and diagnosing the disease" Newsletter!

Thank you for taking time to review this information.
Please reach out if you have any questions or would like to discuss further.

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