Diagnostic and Therapeutic Approaches of Mixed Cryoglobulinemia in PITER cohort

**BACKGROUND**

Cryoglobulinemic vasculitis (CV) is a both autoimmune and lymphoproliferative disease, clinically benign, sometimes with a severe presentation, but possibly evolving into lymphoma. Mixed cryoglobulins (MGs) are immune complexes that reversibly precipitate when the temperature is lower than 37°C and that consist of IgM with rheumatoid factor (RF) activity. Most CV patients are HCV positive (70-90%) and conversely 40-60% of HCV infected patients produce CGs of whom 5-30% with symptomatic CV. For these peculiarities in the clinical manifestation and in the diagnostic criteria MC remain an elusive disease.

**AIM**

The aim of this study was to evaluate:

1. the diagnostic approach of MC in a wide real-life cohort of Italian patients with HCV chronic infection
2. clinical profile
3. results of DAA treatment of MC in consecutive patients enrolled in PITER framework

**METHODS**

Total patients of the cohort: 8005

- Total evaluated HCV+ patients: 1678 (21%)
- 771 (46%) tested positive for MC

266 (34%) MC had typical symptoms and were considered as confirmed MCS

496 (66%) patients have asymptomatic cryoglobulinemia (MC+), 907 (54%) patients tested negative for MC (MC-)

A specific questionnaire regarding clinical and laboratory diagnostic approach of MC and related symptoms was applied. Results of DAA treatment of HCV chronic infection in patients with MC were also reported.

**RESULTS**

- Centers that considered MC
  - 36% evaluated MC presence routinely
  - 64% following a clinical suspicion

**The MC laboratory diagnosis**

- Cryocrit+Complement+RF in 58% of centers
- Cryocrit testing only in RF positivity in 42% of centers
- Cryo test were non conducted adequately in 39% of centers

**CONCLUSIONS**

The present, ongoing study, is a first Italian prospective, multicentric, real-practice analysis conducted on a wide population of HCV-chronically infected patients.

Despite the importance and the clinical relevance, in the Italian real practice, the presence of MC was evaluated only in about 20% of patients.

Among those, the rate of patients carrying CGs is about 46% of whom 34% have typical symptoms.

The variability of MC diagnostic approach, suggesting that the CM presence is underestimated, and in the centers where it is not routinely assessed, the percentage of MC patients showing clinical manifestations is probably overestimated.

In a subgroup of patients treated with DAA that reached the SVR12, the preliminary results showed that: the great majority experienced a disappearance or an improvement of all the baseline symptoms (complete clinical response) or of at least 50% of initial symptoms (partial clinical response). The good clinical and virological results of DAA-based therapy, in this very large, real-life population, further stress the importance of a better appraisal of this condition and consequent wider treatment.

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