



Gestione clinica delle
epatiti croniche virali

HCV AND RHEUMATIC DISORDERS

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Nuovo Ospedale di Cona
Aula Magna

HCV INFECTION → RHEUMATIC SYNDROMES

Prevalence: ??

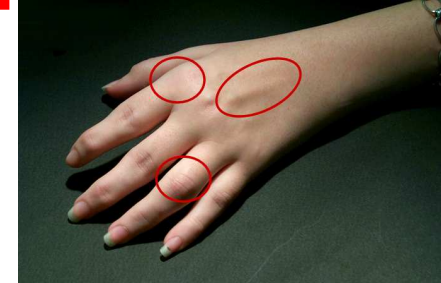
- rheumatology
- gastroenterology
- hepatology
- Infectivology

~5-50%

Vassilopoulos D, Calabrese LH. Rheumatic manifestations of hepatitis C infection. Curr Rheumatol Rep 2003; 5:200–204.

Rheumatic syndromes in HCV infection

- Arthralgias/arthritis
- Mixed cryoglobulinemia syndrome (MCS)
- Sicca syndrome (Sjögren-like)
- Fibromyalgia



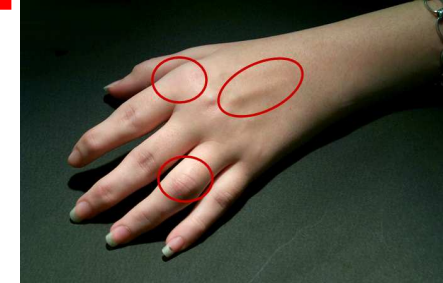
❖ during the course of the HCV
chronic disease

❖ precede the
diagnosis of HCV
infection

Rheumatic syndromes in HCV infection

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❖ during the course of the HCV
chronic disease

❖ precede the
diagnosis of HCV
infection

Arthralgias/Arthritis

Simple arthralgias
20–50%

Inflammatory arthritis
<5%

➤ **virus itself**

- **Directly:**
HCV-associated arthritis
- **Indirectly:**
Cryoglobulinemia syndrome

➤ **co-existent rheumatic disease**

- **Rheumatoid arthritis**
- **Systemic lupus erythematosus**
- **Sjogren's syndrome**

➤ **induced by antiviral therapy (IFN- α)**

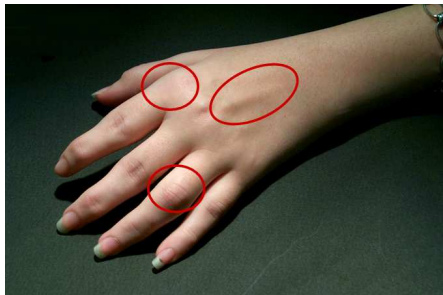
*Cacoub P et al. Arthritis Rheum 1999;
42:2204–2212*

*Buskila D et al. Rheum Dis Clin North Am
2009; 35:111–123*

*Rosner I et al. Semin Arthritis Rheum 2004;
33:375–387*

HCV-associated inflammatory arthritis

-mild polyarthritis of the small joints
(resembling other polyarthritides:RA)



-oligoarthritis affecting
large joints



- ANA ++ (10%)
- RF ++ (>40%)

Diagnostic problems

- SLE
- SJÖGREN

Clinical data

RA

- Anti-CCP
- Erosive arthritis

Rosner I et al. *Semin Arthritis Rheum* 2004; 33:375–387
Bombardieri M ET AL. *Arthritis Res Ther* 2004; 6:R137–R141
Koga T et al. *Clin Exp Rheumatol* 2008; 26:121–124

Treatment

- **HCV–related inflammatory arthritis**
- **HCV– co-existent inflammatory arthritis**

1. HCV-related inflammatory arthritis/arthralgias

NSAIDs

- effective and well tolerated for symptomatic relief
- contraindicated in patients with advanced liver disease

Corticosteroids

- low-dose (<7.5–10 mg/day)
- no significant adverse effects on liver function

Hydroxychloroquine

IFN

- No significant improvement
- ↑Articular symptoms

Resistant cases

Cyclosporine

- antiviral properties (targeting of cyclophilin B)
- no significant adverse sequelae

Methotrexate

Extreme caution!

Vassilopoulos D et al. Arthritis Res Ther 2008;10:215
Arroyo V et al. Am J Med 1986; 81:104–122.
De Ledinghen V et al. Gut 1999; 44:270–273.

2. HCV– co-existent inflammatory arthritis: RA

IFN (+RBV)

- ↑ Articular symptoms

NSAIDs

Corticosteroids

Hydroxychloroquine

Cyclosporine

•Methotrexate

•Leflunomide

- Extreme caution:potentially hepatotoxic
- ACR guidelines (2008): MTX should be avoided in HCV patients

anti-TNF agents

- safety (>nonadvanced HCV-related liver disease)
- antiviral effect?

Ishii N et al. *J Virol* 2006; 80:4510–4520
Saag KG et al. *Arthritis Rheum* 2008; 59:762–784.
Lucidarme D et al. *Hepatology* 2009; 49:1083–1089
Ferri C et L. *J Rheumatol* 2008; 35:1944–1949.

Vassilopoulos D et al. *Current Opinion in Rheumatology* 2010, 22:91–96

Mixed Cryoglobulinemia

the most documented and closely associated
disorder with HCV



Prevalence:
10-50%

vasculitis manifestations:
2-3%

Misiani R et al. Ann Intern Med.
1992;**117**(7):573-7

Ferri C et al. Blood. 1993;**82**(12):3701-4

Clinical manifestations

- purpura
- arthralgias/arthritis
- weakness

- glomerulonephritis
- peripheral neuropathy
- skin ulcers

Diagnosis

- cryoglobulins
- rheumatoid factor
- low complement levels (especially C4)
- positive biopsy findings from target organs (skin, kidney, nerve)

Ferri C et al. Curr Opin Rheumatol. 2006;18(1):54-63

Ammendola A et al. Muscle Nerve. 2005;31(3):382-5

Ferri C et al. Autoimmun Rev. 2007;7(2):114-20

Palpable purpura:the most common clinical finding:
90%

Typical pathological finding :
Leukocytoclastic vasculitis:



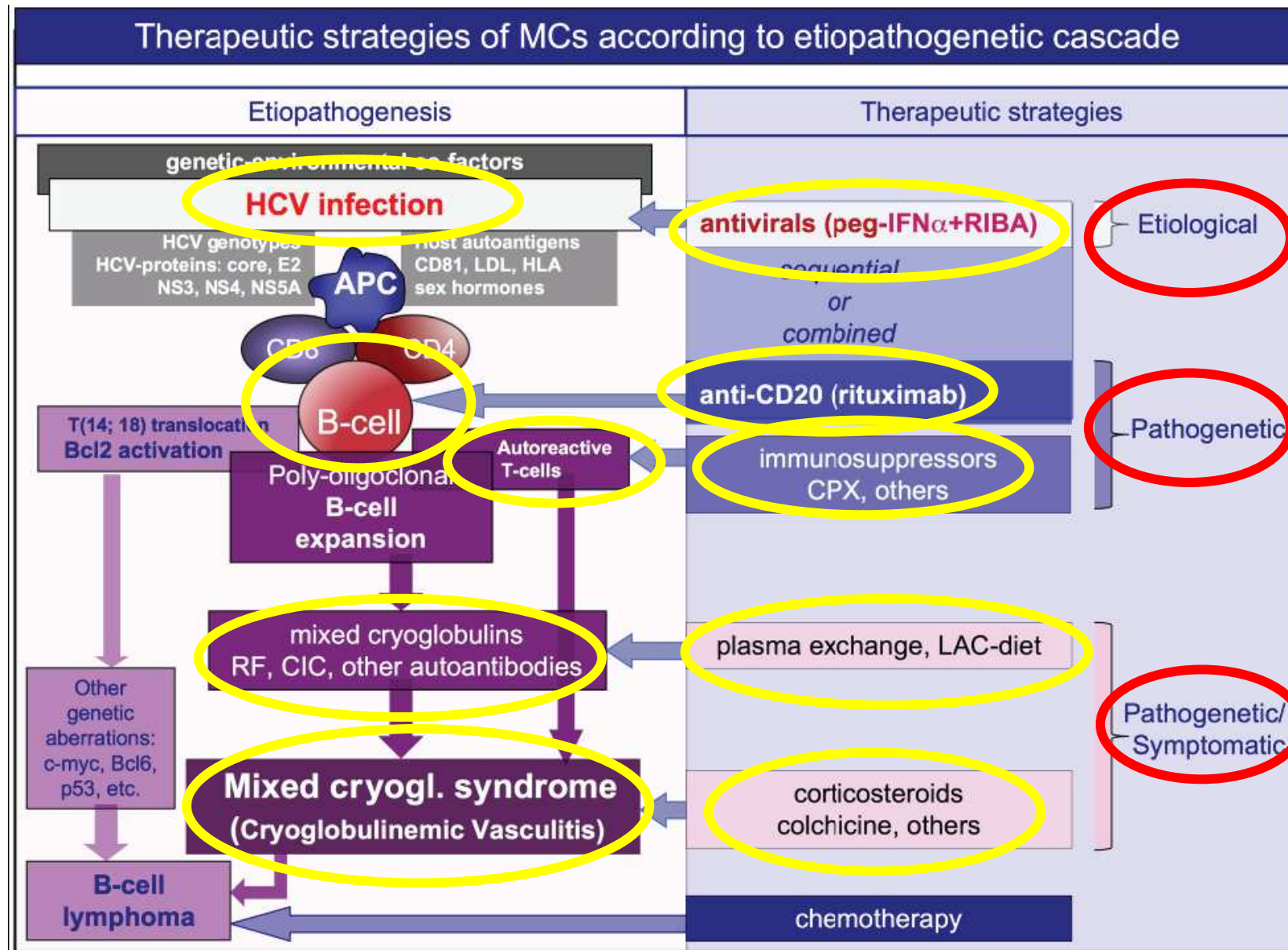
easily detectable by means of **skin biopsy** of recent vasculitis lesions (within the first 24 to 48 hours)

Treatment

➤ **HCV-Mixed Cryoglobulinemia**

1. HCV-Mixed Cryoglobulinemia

Treatment options



Pathogenetic therapy

Corticosteroids

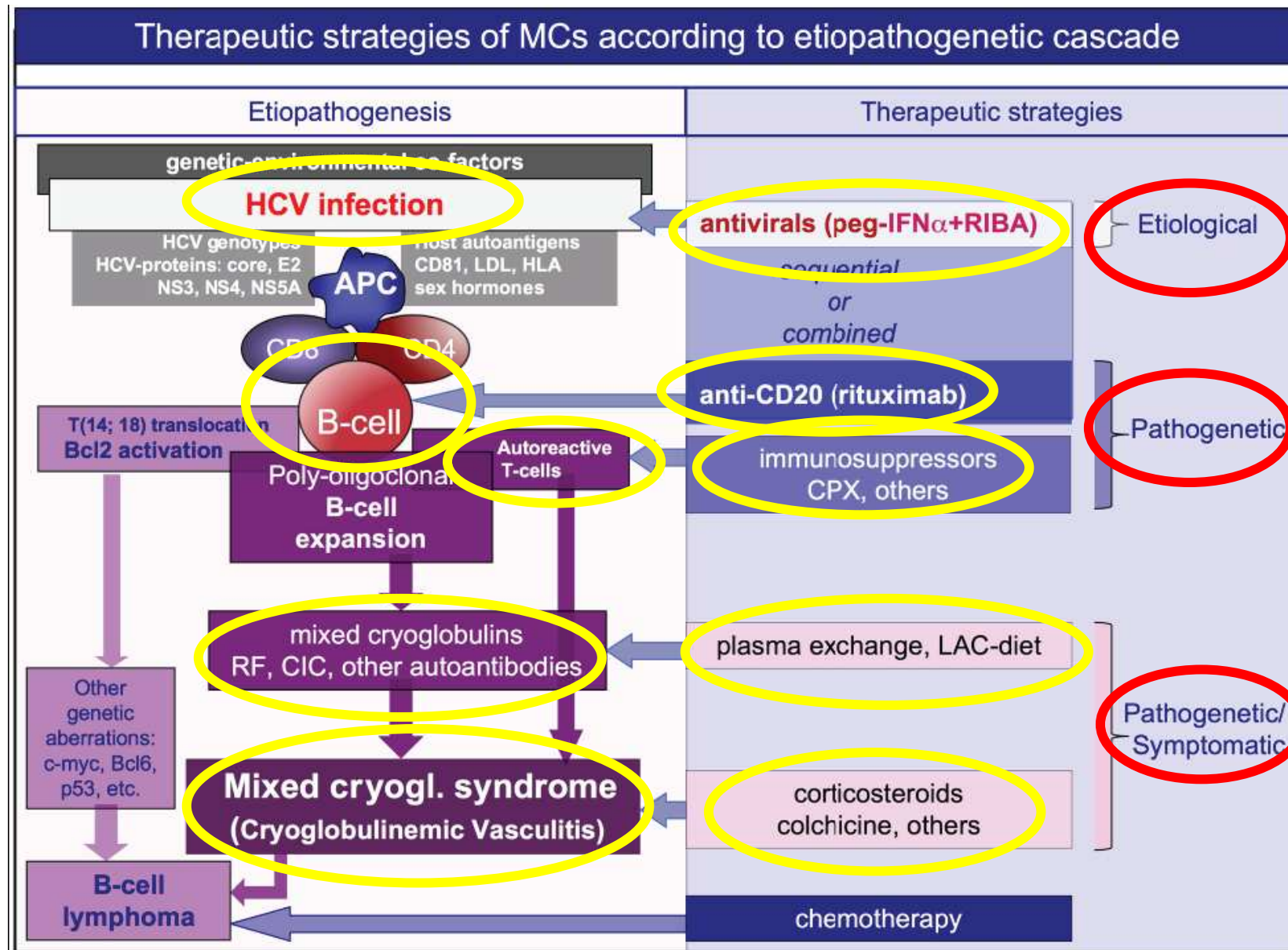
Immunosuppressive
drugs

- Cyclophosphamide
- Chlorambucil
- Azathioprine
- Mycophenolate Mofetil
- Rituximab

Plasmapheresis

1. HCV-Mixed Cryoglobulinemia

Treatment options



Grazie