IRACON 2024 - Bangalore

24.11.2024 / Hall A- Dr Debasish Danda Hall

Session -1: Mini debates:

Talk 1:

Debate on Re-evaluating muscle biopsies in myositis - Invasive Insight:

For

Quoted various criteria for the diagnosis and pointed out that the EULAR/ACR 2017 criteria is the first criteria to introduce classification of IIM without biopsy

Available evidence shows significant pre and post biopsy changes in diagnosis and management strategies – JCM

About 30 to 40% of myositis only has MSA /MAA

False positive rates are higher for these antibodies especially when tested via LIA

MRI though sensitive cannot different IIM from other causes of muscle edema

Muscle biopsy is advocated when

There is clinico serological discordance

More research to identify novel pathogenic mechanism

Identify newer therapeutic targets

Against routine Biopsy

Muscle biopsies are

Invasive procedures

Various types of procedures – needle / conchotome / open or surgical – not standardized

Difficulties in processing the sample and lack of experienced pathologists

Yields non diagnostic pathology in 40% cases

AI models can now augment MRI and improve diagnostic accuracy in IIM

In MRI, when there is more edema, the chances of IIM >MD(Muscular Dystrophy) and when there is more atrophy then the chances of MD>IIM

Role of USG in Myositis: Echogenicity correlates with MRI edema. Has good sensitivity ,but poor specificity and follow up is easy

MSA/MAA- Seen in 40 to 60% of Myositis patients. Immunoprecipitation is better than Line blot in terms of specificity and accuracy

In the presence of Anti SRP or Anti HMG CoA antibodies - muscle biopsy is not needed for diagnosis

Talk 2:

Vitamin D Dilemma – Essential Evaluation or Extravagant Expense in Rheumatological setting:

Essential Evaluatio

~ 15.7% individuals are vitamin D deficient when the cut-off is 30 ng/dl

Testing indicated in osteoporosis, osteomalacia, while on glucocorticoids, antifungal medications, granuloma forming disorders like sarcoidosis, TB

Chances of toxicity is high if Vitamin D is supplemented without testing

Extravagant Expense

What is the estimated average requirement – 16ng/ml as per American guidelines

Meta analysis shows that supplementing vitamin D reduces hip and vertebral fractures

RCTs failed to show any benefit in supplementing Vitamin D in general population

Vitamin D testing is not advisable because

- The optimal level is still under debate
- Lack of assay standardization

- Seasonal variations in vitamin D levels
- Immunoassays are not specific

Don't treat with mega doses of vitamin D

$ Saves cost especially when the test itself is dubious

Talk 3:

Anticoagulation dilemma in APS - To continue or to cease:

To Continue

+ Unprovoked DVT needs long term anticoagulation

+ 40% chances of recurrent thrombosis if anticoagulation is discontinued in LA positive pts

+ High titre ACL antibodies predict recurrent thrombosis in pts with APS

+ Recurrent VTE after stopping anticoagulation is high when the APS antibodies are positive. Relative Risk 8.0

negativization can occur in 1/3rd of APS pts over time. The decision to stop anti coagulation is purely clinical and it's desirable to continue anticoagulation long term

+ Male gender, Triple positivity, antiB2Gp predicts thrombotic relapse

To cease anticoagulation

+ Risk of bleeding is high up to 16% in some series

+ Anti coagulation can be stopped after APL negativization- studies support the same.

+ Can consider stopping when the thrombotic event is provoked, when the aPL profile is not high risk.

Session 2: CARving new pathways. Looking forward to next decade

Talk -1:

The biology of CART therapy -Engineering Immunity:

Fundamental Understanding of Genetic Engineering of CART Cells including development, designing and molecular modifications

***CAR(Chimeric Antigen Receptor) T Cell Therapy* :**

Called the Living Drug- uses its own immune system to kill cancer cells and Personalised therapy – genetically engineered

Costly -usually half a million dollars

Make in India CAR T cell - *NexCAR19* - affordable (10x reduced cost)- 300 pts treated so far mainly for the ALL/AML

Fewer side effects: Negligible neurotoxicity, less- grade 3 Cytokine release syndrome

Received Market authorisation in Oct 2023

Talk-2:

Transforming Cancer Treatment: The Rise of CAR T-Cell Therapy

1. CAR-T cells are peripheral blood cells that express Chimeric Antigenic Receptor to recognise Tumour associated Antigen

2. A dose more that 3 million cells /kg has demonstrated better results for attaining remission in leukemias

3. A second primary malignancy in a small fraction of patients receiving CAR-T remains a concern

4. The risk of flare of autoimmune diseases were minimal on withdrawal of immunosuppression post CAR-T in various studies

5. Viral and vaccine titres are maintained post CAR-T

Talk 3:

Exploring CAR T-Cell Applications in Rheumatology: A Vision for the Next Decade

1. Currently most reports of CAR-T in Rheumatology are anecdotal with mostly case reports and case series

2. CAR-T therapy has been remarkably effective causing both clinical and serological remission

3. Unlike oncology, long term B cell depletion is not necessary when using CAR-T in Rheumatology

4. Need for lymphodepleting agents needs to be studied further in light of side effects

5. Some AIRDs like SLE with or without nephritis have shown better results including complete disappearance of dsDNA and other antibodies

6. Whereas, SSc with ILD have not shown such dramatic outcomes

7. Disappearance of some antibodies like dsDNA and persistence of some antibodies like SRP, Ro may warrant further stratification in future

Session 3- Neurology Networks:

Autoimmune Neuropathies: Emerging Perspectives and Breakthroughs- Updated understanding of autoimmune neuropathies

1. Various antibodies found associated with different phenotypes in GBS- example- GQ1b, GM1, GD1a, GM2, GT1b

2. Various antibodies against myelin derived proteins found in CIDP

3. CIDP with anti MAG antibodies respond best to RTX

4. Anti Neurofuscin associated neuropathy may have combined central and peripheral demyelination

5. Newer antibodies detected in various autoimmune nodopathies like Anti NF 155, NF 186, CNTN 1, CASPR 1

Talk 2:

Cracking NMOSD: Unmasking the Immune Culprits

1. NMOSD is found in multiple autoimmune diseases – SLE, pSS, sarcoid, APS, RA, AS, SSc

2. 3% of patient with NPSLE have AQP4 antibody

3. 27% of NPSLE with demyelinating lesions have AQP4 antibody

4. NEMOS 2023 guidelines recommend steroid pulse followed by oral steroid along with Rituximab or azathioprine or MMF; Tocilizumab may be used in refractory cases

5. USFDA has approved complement inhibitors eculizumab, inebilizumab, satralizumab for antibody positive NMOSD

Session 4: Looking beyond the prescription pad

Targeted Diets in Autoimmunity: Are we missing the Microbiota Magic?

1. 1-3 % body weight composed of microbiome

2. Gut dysbioses increases risk of autoimmune diseases, cognitive dysfunction, etc.

3. Patients of SLE who were on steroids have a lower diversity gut Microbiota; patients on HCQS had a lower diversity too but were low on pathogenic enterobactericeae

4. 3 Possible mechanisms by which lower Microbiota contributes to RA pathogenesis are- inflammatory responses, molecular mimicry, and loss of integrity if intestinal barrier

5. HLA B27 positivity may predispose to AS by altering gut microbiome

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