

Current Controversies & Update of Sarcoidosis

SARCOIDOSIS

- Multisystem granulomatous disorder of unknown origin characterized by activation of T-Lymphocytes and mononuclear phagocytes at sites of disease.
- Most commonly affects Lungs & Intra-thoracic lymph nodes.
- Diagnosis is securely established from compatible history, histology → Non- caseating granulomas in more than one organ & absence of competing Dx like TB\Fungal Disease\ Malignancy.

PATHOGENESIS :

Antigen Triggered :

Evidence :

1. T-cell Ag receptors (TCR) monoclonal.
2. ↑ in mRNA for TCR.

Genetic Susceptibility :

- Data from monozygotic twins who do not live in same environment, ↑ prevalence of disease in siblings of affected individual suggest genetic involvement.
- Not a single gene disease.
- Multiple genes interact with one or more environmental triggers to provoke first phases of disease.

EVIDENCE

Racial Difference :

- Scandinavians with African – American have highest prevalence.
- Latin Americans higher prevalence than white people.

Familial Sarcoidosis :

- RR for Sarcoidosis in siblings of affected individual was 36-73 (McGrath DS et al Thorax 2000 ; 55 : 751-4)
- Odd's Ratio of familial disease from ACCESS study was 5.8.

Inference :

- Familial sarcoidosis present in majority of population.
- Family members of sarcoidosis cases have several fold increased risk of disease compared with general population.

Key Candidate Genes :

MHC → HLA class I bind endogenous antigen
↓ peptides and present them to CD8 + cells.

HLA Class II bind peptides from exogenous antigens & present them to CD4 + cells.

MHC Class I :

HLA B7 ass. with high prevalence of sarcoidosis in African-Americans, HLA B8 ass. With ac. Onset and short duration.

MHC class II :

Japanese pts. : HLA DR5, -DR8, -DR9 alleles

Germans : HLA-DR5 ass. With chr. Disease
DR3 ass. With acute disease.

Scandinavian study : HLA-DR3 → ac. onset and short duration.
HLA-DR 14, DR 15 chr. Disease.

CAUSE OF SARCOIDOSIS

- Sarcoid granulomas are formed in response to a persistent, poorly degradable antigenic stimulus.
- Non-infective agents : Pine Pollen, Clay soil, talc, beryllium, zirconium. None of these theories have endured.

Infective :

Evidence Supporting :

1. Seasonal Variation :

Ac. Onset with erythema nodosum and arthralgia peak in spring months seen in Sweden / Greece/Spain/ New Zealand

2. Clustering :

- Hill SE (Thorax 1987 ; 42 : 427-30) noted time space clustering.
- Cases whose place of residence during an infective period of 5 yrs. Before and 2 yrs. After the DX were separated by distance of <100 m.
- Communicable agent was likely the major causative factor in the disease.
- Edmondstone WM (Thorax 1988 ; 43 : 342-3) 7.5 times greater number of nurses with the condition than expected.
- Individuals in close proximity to sarcoidosis cases may be at a higher risk of disease, possibly due to a transmissible agent.

MICROBIAL CANDIDATE ORGANISM :

i) Mycobacteria :

Passage Experiments in mice by Mitchell et al proved that there was a transmissible agent for Sarcoidosis and this was mycobacteria (confirmed by demonstration of AFB in tissues, growth in LJ medium).

Almenoff et al. used ab. Against M.TB whole cell Ag. (HR37RV) identified cell wall deficient forms (L forms).

- Possible therefore in Sarcoidosis, mycobacterial lysis might result in modified form of organisms persisting and driving a granulomatous response.
- These cell form deficient forms remain attractive potential triggers for sarcoidosis → Difficult to detect by routine culture methods. These organisms can pass through fine filters.

b) Anti-Mycobacterial Ab. Study :

Chapman et al → ppt. Ab. To atypical mycobacteria in 78% of sarcoid pts.

c) Molecular Studies :

PCR based studies : MTB found in <10%.

Reasons :

- Techniques : Too much DNA, -ve reaction if target DNA is of low copy number.
- Sensitivity : AFB -ve, culture -ve samples PCR + ve is 10-30%. By analogy, if sarcoidosis is mycobacterial triggered then positivity rates no greater than this can be expected.
- However, mycobacterial DNA fingerprint are seen in some pts. with sarcoidosis but not seen in all.

- Over the years, there has been a ↓ in incidence of TB, this is not paralleled by new cases of sarcoidosis.
- Involvement of heart and salivary glands is peculiar to sarcoidosis and is not commonly described with mycobacterial infection.

In Summary :

Pointers of mycobacterial inf.

- i) Histopathological appearance of granuloma.
- ii) Presence of mycobacterial disease existing co-incidentally, succeeding or antedating sarcoidosis.
- iii) Finding of organisms in occ. granuloma together with occ. caseation.

- iv) Transmissibility in animal expts.
- v) Nucleic acid detection studies.
- vi) Comparison with leprosy in which tuberculoid (paucibacillary) and lepromatous (multi-bacillary) are found, inference can be drawn that sarcoidosis might represent tuberculoid form of pathological response to mycobacteria.

Against :

- 1) Absence of Caseation
- 2) Organisms are demonstrated rarely.
- 3) Absence of response to ATT.
- 4) Tuberculin anergy.

ii) Propionibacteria P. acnes : Normal skin and intestinal commensal.

- 1999, Ishige et al demonstrated P. acnes in 12 of 15 pts. with sarcoidosis but in only 3 of 15 pts. In control group, using PCR technique.
- Eishi Y et al → PCR demonstrated P.acnes / P. granulosum in all but 2 LN from pts. with sarcoidosis.

iii) Other organisms :

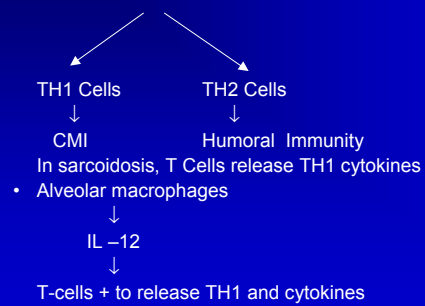
Rickettsia helvetica, Chlamydia pneumoniae, Borrelia burgdorferi, viruses (Human herpes virus 8).

SUMMARY

1. Evidence for a microbial trigger for sarcoidosis is not unequivocal.
2. Propionobacteria ass. is the most attractive but putative mycobacterial ass. is persistent.
3. No single agent stands out with certainty.
4. Microbial involvement has been shown in disease as diverse as peptic ulcer disease, CAD, there is a possibility that microbes are an important triggers to sarcoidosis that falls well short of infection.

T cells :

- ↑ in No. esp. CD4 + cells.
- CD4 + - 2 functional subsets.



↓
IL-2, IFN- γ , IL-16

- ↑ IL-2 levels in lymphocytic alveolitis ass. with poor prognosis.
- Activated T-cells ass. with ↑ sIL-2 receptor (sIL-2R)

ALVEOLAR MACROPHAGES :

- ↑ in no. of activated alveolar macrophages.
- Release cytokines : IL-1, TNF- α , MIP-1 α , MCP-1, IL-8, IL-12, IL-18.
- Poor prognosis and disease activity :
- i) IL-8 (potent neutrophil chemotactic factor)

↓
↑ no. of neutrophils.

Neutrophilic alveolitis reflects ongoing inflammation ass with disease progression.

- ii) MIP - 1 α , MCP-1 ass. with ongoing inflammation.
- iii) IL-12 indicates poor prognosis.
- iv) IL-18 induces release of IFN- γ from T-Cells results in further stimulation of macrophages and cytotoxic T-cells.
- v) TGF- β ass. with spontaneous resolution.

ROLE OF TNF- α IN SARCOIDOSIS

- TNF α : Higher in active disease.
- TNF α binds to 2 kinds of receptors : TNF RI and TNF R II.
- Soluble forms of these receptors \uparrow in RA/ Crohn's disease and Malignancies .
- sTNF R II – Imp. Parameters of disease activity in serum and BAL fluid.

- \uparrow TNF α \rightarrow in asymptomatic disease : higher
(In BAL fluid) risk of disease progression.



Symptomatic disease : Higher rate of relapse.

Chr. Sarcoid pts. with \uparrow TNF- α do not respond to steroids.

Reasons :

TNF- α \downarrow sensitivity of monocytes to dexamethasone.



Corticosteroid resistance

BASIC SCIENCE 'FACTS' OF SARCOIDOSIS

- Sarcoidosis : Granuloma with fibrinoid necrosis, rarely caseation.
- Sites of inflammation have activated T-cells and mononuclear phagocytes.
- These cells express pro-inflammatory cytokines & chemokines which are critical in granuloma formation and CMI.
- Ass. with dominant, polarized Th-1 immune response.
- Granulomatous inflammation is ass. with oligoclonal T-cell population.

Sarcoidosis as TH-1 disorder :

- Dominant TH-1 disorder.
- IF- γ , IL-12, IL-18 (γ -IFN enhancing factor) levels increased.

EVIDENCE :

- Pathogenesis of sarcoidosis may involve TH-1 promoting infectious agents (mycobacterial/ propionobacterial organisms).
- Sarcoidosis is induced/relapses with use of TH-1 promoting biological response modifiers such as IFN- α , IL-2 therapy.

TREATMENT OF SARCOIDOSIS

A) General Principles From Clinical Observations :

1. Granuloma formation dictates clinical course and therapeutic response.

↓

Therefore suppression of granuloma formation results in preservation of organ function and minimize long term fibrotic outcomes.

2. Corticosteroids : Effective in suppressing granuloma formation over both short term and long term. Non corticosteroid therapy variably effective.

3. Threshold level of drug effect for most pts.

→ Below which : Progression of granuloma

→ Above which : Suppression of granuloma

4. Kinetic of granuloma formation variable :

Some progress slowly

Some rapid progression

↓

Organ dysfunction

5. Different tissues respond differently to drugs.

Antimalarials – effective in skin & mucosal disease (Nasal sinus, URT) than pulmonary disease.

STRATEGIES FOR TREATMENT OF SARCOIDOSIS BASED ON STAGES OF INFLAMMATION IN DISEASE

Step 1 : Inhibit Ag Presentation
(Anti-Malarial Drugs)

Step 2 : Suppress Granuloma Formation
(Corticosteroids, Immunosuppressives, Anti TNF agents)

Step 3 : Enhance Ag Clearance
? Peptide based therapy (future)

Step 4 : Inhibit Fibrosis
(Corticosteroids, Immunosuppressives, Anti TNF agents)

1. Treatment to suppress initiation of granuloma formation :

Strategies :

1. Reduce Ag deposition
2. Enhance Ag clearance
3. (-) Ag processing and presentation

1. Reduce Ag deposition : Antibiotic therapy

- Doxycycline, Minocycline → Effective against propionibacteria.
- Dapsone, Clofazimine → Anti mycobacterial effects.
- Beneficial in subset of sarcoidosis pts.

- However, these agents have anti-inflammatory effects.
- Effective in only few anecdotal cases

2. Anti-Malarial Drugs Choroquin/Hydroxy Chloroquin :

MoA : (-) Degradation of proteins by acid hydrolases within lysosomes.

(-) MHC – peptide complexes.

Net effect :(-) Ag presentation to T-cells.

II. Treatment of Progressive granulomatous inflammation :

1. **Corticosteroids** : Broad spectrum anti-inflammatory effects on multiple cells – T-cells/macrophages/granulocytes.

(-) Expression of pro-inflammatory cytokines such as IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-8, IL-11, IL-12, IL-19, IFN- α & TNF.

(-) Arachadonic acid metabolism :

overall - \downarrow cell activation

- Enhanced apoptosis of activated T-cells.

2) Azathioprine :

MoA : (a) Azathioprine

\downarrow Thiopurine –S-methyltransferase

6-Mercaptopurine.

Accumulation of 6 –thioguanine nucleotides in target organs \rightarrow Imp. Mediator of immuno suppression.

- b) (-) T-cell and B-cell proliferation and cytotoxic T-cell function.

Toxicities : BM suppression

: GI S/E

: Hepatitis

: Oncogenic effects

Use : Reserved for progressive organ threatening disease not responding to safer alternatives.

3) Methotrexate :

MoA : Folic acid analogue that (-) dihydrofolate reductase and transmethylation reactions.

Net effect : Interfere with purine metabolism and polyamine synthesis.

High doses : Anti-Proliferative.

Low doses : Anti-Inflammatory (due to \uparrow release of adenosine)

\downarrow

(-) TNF, IL-6, IL-8

(-) Release of ROI

(-) Lymphocyte proliferation

Toxicity : Hepatic, BM, Pulmonary.

Use : Maintenance treatment of serious organ threatening disease.

4. Cyclosporin : T-cell (-)

T-cell activation → 2 signals → TCR complex



Costimulatory molecules CD 28, CD40 on T cell surface.

These drugs block signal 1.



IL-2 (-)

- However, cyclosporin not very effective.
- Toxicity : Renal, malignancy.
- Use : Serious cases failing more standard therapies.
- Efficacy : 0-80%

5. **TNF Inhibition** : TNF plays critical role in granuloma formation.

a) Pentoxifylline : Methylxanthine derivative :

- Non-selective phosphodiesterase (-)
- (-) TNF production by mononuclear cells including alveolar macrophages.
- May have a limited role because it is difficult to achieve therapeutic doses due to frequent GI S/E.
- Dose : 400 mg TDS
- Efficacy : 50-70%

b) **Thalidomide** :

(-) TNF production by mononuclear cells.

- Use : Skin/Mucosal sarcoidosis.
- Toxicity : Teratogenic
 - Peripheral Neuropathy
 - Sedation

c) **Etanercept** : Biologic dimeric fusion protein which binds to TNF and related protein lymphotoxin α .

- Toxicities : 1. Infections risk \uparrow
2. Lupus syndr.
3. Demyelinating disease.

d) **Infliximab** :

- Humanized monoclonal ab. formed of human IgG1 Ab + protein segments from mouse monoclonal Ab against human TNF.
- MoA : Block TNF.
- Limitation : Development of Anti-murine Ab. Which \downarrow its actions.
- Requires concomitant therapy with methotrexate to suppress this humoral response.
- \uparrow risk of recrudescence TB.
- Allergic reaction to chimeric Ab.
- Use : Steroid resistant disease (Anecdotal reports)

- None of these drugs classified as TNF (-) have been shown to be effective in sarcoidosis by rigorous study.
- All these have high cost.
- Notable toxicities.

DIFFERENT STRATEGIES FOR DIFFERENT STAGES OF SARCOIDOSIS

ROLE OF TH-1 RESPONSE :

Early Stages :

Th-1 driven granulomatous response effective in clearing granuloma inducing Ag.

Chronic Sarcoidosis :

Ongoing Th-1 immune response results in impaired organ function.

Therefore,

1. Minimize immuno suppression early in disease.
2. In chronic stages focus should be on minimizing granulomatous inflammation.

TREATMENT OF PROGRESSIVE PULMONARY FIBROSIS

- Persistent granulomatous inflammation

↓

Fibrosis

- Probably, there is a switch to Th-2 response in late stages resulting in elaboration of pro-fibrotic cytokines like IL-4.
- No data to support Anti-fibrotic agents such as colchicine/perfenidone in fibrocystic sarcoidosis.
- Anti-fibrotic biologic agents : IFN

↓

ass. with relapse of sarcoidosis

- For now, anti-inflammatory drug therapy that (-) granuloma formation → retard/prevent progressive fibrosis.

FUTURE DIRECTIONS :

1. Identify tissue Ag so that effective action can be taken against them.
2. Suppress granuloma : Less toxic more targeted approach.
3. Regulating T-cell response by targeting MHC/Ag/TCR complex and downstream pathways. Drug blocking T-cell costimulatory pathway may induce T-cell anergy or tolerance. (Rapamycin, mycophenolate mofetil).
4. (-) Pro inflammatory cytokines like TNF

↓

Limits immunopathology esp. In chr. Sarcoidosis.

- 5. Enhance anti-inflammatory cytokines like IL-10.

Overall Goal : Suppress granuloma



Limit tissue injury and fibrosis in pts. demonstrating progressive organ dysfunction.

DIFFICULT TREATMENT ISSUES IN SARCOIDOSIS

Management Issues

When to start therapy :

- Specific conditions requiring therapy
 1. Cardiac involvement
 2. Neurologic involvement
 3. Hypercalcemia
 4. Ocular disease not controlled by topical therapy
- Pulmonary involvement per se does not require therapy.
 - For Pulmonary disease
 1. Symptomatic
 2. Worsening lung function

Corticosteroid therapy in pulmonary sarcoidosis. (Paramothayan. S, Jones PW JAMA 2002; 287: 1301-1307).

- Analysis of 8 RCT of the role of steroids oral/inhaled or both in outcome of sarcoidosis.
- Treatment of pulmonary sarcoidosis with oral steroids for a period of 6-24 mths. improved CXR findings.
- Pts. not Treatment with steroids had more chances of deterioration compared with those receiving prednisolone.
- In one study, Israel HL et al (Am Rev Respir. Dis 1973 ; 107 : 609-614) showed improvement in CXR/symptoms/Lung functions in steroid group esp. in stage 2 & 3 but not in 1.

- Results from these RCT confirm that stage I do not require Treatment with OCS but those with ILD (stage II/III) may show radiologic improvement.

- ICS in Sarcoidosis :

2 studies OCS (3 mths.) → ICS or placebo (6-18 mths.)

Study 1

- Improved gen. health perception.
- No improvement in symptoms/PFT.

Study 2

↑ in CXR clear in stage 2 compared with stage 1.

2. RCT : ICS alone

Study 1

- No improvement in PFT after 6 mths.
- Symptomatic improvement
- No RCT data to test for a disease modifying effect of CS.
- After a period of 6 mths. – 2 yrs. OCS should be withdrawn under careful monitoring.
- Trials of ICS were small and results too inconsistent to make firm conclusions concerning efficacy of this mode of corticosteroid delivery.

Study 2

- No improvement in CXR, but some improvement in D_LCO .

APPROACH TO TREAT PULMONARY SARCOIDOSIS WITH CORTICOSTEROIDS

AC. PULMONARY SARCOIDOSIS :

- Present early.
- Symptoms of short duration.

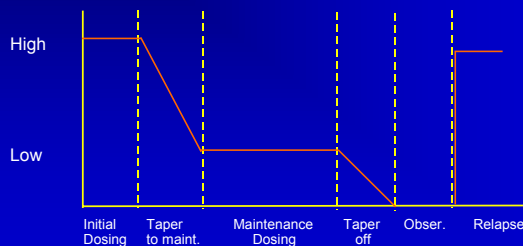
CHRONIC PULMONARY SARCOIDOSIS :

- Symptoms persist > 2 yrs.

DECISION TO TREAT WITH CORTICOSTEROIDS

Patient Subgroup	Decision
1. Asymptomatic Pts.	No treatment
2. Mild Pulmonary Dysfunction	Observation
3. Pts. With excellent prognosis	Observation, Palliative therapy.
4. Mild-Mod. Pul. Dysfunction Mild-Mod. Fun. Limitation	- Observation → Treat if deteriorate. - Treatment if no imprv. after 6 mths.
5. Severe Pul. Dysfunction Severe Functional Limitation	- Treatment

- No long term benefit from corticosteroid therapy in asymptomatic pts., regardless of CXR stage.
- Asymptomatic pts. with (n) PFT should not be treated because of radiographic abnormality alone.



SIX TREATMENT PHASES OF AC. PUL. SARCOIDOSIS

	Phase	Daily Dose, mg	Time Period
1.	Initial Dosing	Prednisone, 30 mg Methyl prednisolone 24-32 mg Prednisone 1 mg/kg.	1 mth. 2 wks. 6 wks.
2.	Taper to Maint.	Prednisone, 30 → 10 Methyl prednisone 24-32 → 12-16 Prednisone 1 mg/kg → 0.25mg/kg.	2 mths. 1 mth. 6 wks.
3.	Maint. Dosing	Prednisone 10 mg Methyl Prednisolone 12-16 mg Prednisone 0.25 mg/kg	9 mths. 5 mths. 10.5 mths.
4.	Taper Off Corticosteroids	Prednisone 10 → 0 Methyl Prednisone 12-16 → 0 Prednisone 0.25 mg/kg → 0	6 mths. 1 mth. 6 wks.
5.	Monitor while not receiving therapy		
6.	Treatment of Relapse	Prednisone, 30 Prednisone 1 mg/kg	1 mth. 6 wks.

- Decision to taper based on stabilization or improvement in symptoms/PFT.
- Sarcoidosis pts. with stable PFT should not have their treatment plan adjusted on the basis of Lab. evidence (S. ACE level, BAL cell count differentials, Ga Scans) of 'active disease'.
- Maintenance period : 6 mths. – 1 yr. → Ass with few relapses.
- Pulmonary symptoms and spirometry are most useful parameters to monitor when deciding if corticosteroid therapy should be re-instituted.

- > 20% relapse occur > 1 yr. after steroid cessation while 10% relapse occur after 2 yrs.
- Observation period post steroid cessation should be atleast 2 yrs.
- Relapse occur 20-50% of pts. in whom steroids are stopped.
- Relapse : Re-institution of high dose steroids for 2-6 wks. followed by tapering scheme.
- Some authors :

↑ Maintenance dose or	}	After Relapse
↑ Maintenance period		

CHRONIC PULMONARY SARCOIDOSIS

- 3/4 of these pts. who require >5yrs. of steroids relapse when steroids are withdrawn.
- Almost all relapses occur within 1-2 mths. of withdrawl.
- Therefore OCS should be weaned very slowly with close monitoring of symptoms, spirometry, CXR.
- Asymptomatic radiographic infiltrates, pul. Dysfunction

↓

Smaller steroid "bursts" may be used rather than higher doses used for initial treatment

- If pt. cannot be completely weaned off



continue lowest maintenance dose.

- Corticosteroid dependence should not be considered corticosteroid failure.
- Low dose steroids may be superior to alternative therapies, or to no therapy.

Alternatives to corticosteroids and when should they be used :

1. Methotrexate :

- Used in chronic sarcoidosis
- Appears to take 6 mths. to become effective.
- Protocol : initial dose – 10 mg/wk



15 mg/wk (max dose)

dose adjusted based on neutropenia or nausea

- CBC, Renal parameters monitored every 8 wks.
- Folic acid 1 mg/day used for GI toxicity.
- Toxicity : GI, stomatitis, Hepatotoxicity, Pulmonary, BM.
- Efficacy : 60-80%.

- Lower and Baughman have used methotrexate extensively.
- Authors summarized their experience of 50 pts. treated with methotrexate for atleast 2 yrs.
- Most Pts. : Significant improvement in 1 or more organs.
- 25-30 pts. on steroids at time of starting methotrexate
 - i) weaned off steroids.
 - or
 - ii) ↓ Effective dose of steroids.

2. Anti-Malarial Agents :

- Steroid sparing in RCT of Chr. Pul. Sarcoidosis (Baltzan M et al AJRCCM 1999; 160 : 192-7)
- Dose : Chloroquin 500mg/day (~300 mg base drug)
Hydroxychloroquin : 200-400 mg/day.
- S/E: - GI
 - Occular toxicity (Eye exam. yearly)
- Efficacy : 30-50%.

3. Azathioprine :

- Efficacy similar to methotrexate
- Usual dose : 50-200 mg/day.

- Monitoring : -CBC, -LFT : every 2 mths.
- Toxicity : Nausea, Abd. Pain, Pancytopenia
- Efficacy : 50-80%
- Hof DG et al (AJRCCM 1996 ; 153 : 281) 21 pts. : improvement of Pul./extra-Pul. Disease.
- 11 pts. relapsed on drug withdrawl

↓

All responded to re-institution therapy.

4. Cyclophosphamide :

- Used for refractory disease esp. neurological disease.
- Dose : 50-150mg/day PO

- S/E : BM depression, Nausea, Haemorrhagic cystitis, Bladder Cancer.
- Efficacy : 80%.

5. Thalidomide :

- Useful
- Dose 100-200mg/day
- S/E : sedation
constipation
Painless peripheral neuropathy
- Precaution : Review mthly adherence to contraceptive programme.

6. Infliximab :

- Anti-TNF Ab.
- Dose : 5mg/kg
- Frequency : Every 4-6 wks.
- Toxicity : ↑ risk of infection.
- Chronic/Refractory sarcoidosis

↓

Use combination therapy (Monitor for ↑ toxicity)

EXTRA PULMONARY SARCOIDOSIS

CNS : 2-7% of sarcoidosis (with/without lung inv.)

- Leptomeninges
Parenchyma
Perivascular involvement
Localised mass lesion (rare)

- Dx : (1) Gadolinium enhanced MRI
(Best Technique)

↓

Enhancement of leptomeninges

F/u : Gd enhanced MRI

1st : 2-3 mths. after starting t/t

2nd : 3-6 mths. Interval.

(2) CSF, S.ACE – Non-specific.

Mx : - Corticosteroids : 1 mg/kg



Gradual reduction of dose

No randomized trails for therapy of neuro sarcoidosis.

- Other Drugs : Methotrexate/Anti-Malarials/ Cyclophosphamide/ Azathioprine

- Lower EE et al (Arch Intern Med 1997 ; 157 : 1864-1868). Retrospective study of 48% pts. :

Favorable response :

Methotrexate	61% pts.
Cyclophosphamide	90%pts.
Compared to OCS alone	
	29% pts.

- IV cyclophosphamide preferred for pts. with severe CNS sarcoidosis refractory to OCS therapy.

Plan : Initial induction with steroids



Slow tapering of steroids



Add 2nd immunomodulatory drug to achieve steroid sparing effect.

Recurrent CNS Sarcoidosis :

Life Long t/t with low dose, alternate day regimens of OCS + immunomodulatory or immunosuppressive agent.

CVS : Symptomatic inv. → 5%

Autopsy studies → 20-47%

Manifestations : Sudden death, CCF, Pericardial effusions, papillary muscle dysfunction, chest pain.

- Dx : 12 lead ECG



Abnormal



Imaging study

- 2D Echo: Macroscopic areas of :

- (i) bright echoes reflecting granulomatous inflammation giving a speckled or "snowstorm pattern"

- (ii) Dyskinesis/akinesis

- (iii) Chamber enlargement

- (iv) Valvular incompetence (papillary muscle dysfunction)

- Tl²⁰¹, Tc^{99m}-pyrophosphate, Ga⁶⁷ scanning.

Tl²⁰¹ Scan : Segmental areas of ↓ uptake at rest



Defects ↓ or disappear on stress imaging (reverse distribution)
(Diff. Myocardial sarcoidosis from IHD)

Endomyocardial Bx : Controversial, Low diagnostic yield.

Treatment :

- Corticosteroids
(Response rates : 29-90%)

- Recurrent ventr. Dysrhythmias and sudden death may occur despite antiarrhythmic agents.

- (May benefit from automatic cardioverter – defibrillator)

- Recurrent disease : Life long low dose steroids + Azathioprine/ Hydroxychloroquin.

CONCLUSION

- Therapy need not be given to all pts.
- Once initiated, atleast 1 yr. of t/t reqd.
- High risk of chr. disease



Monitoring if corticosteroids discontinued.

- Steroid sparing agents useful for chronic pts.