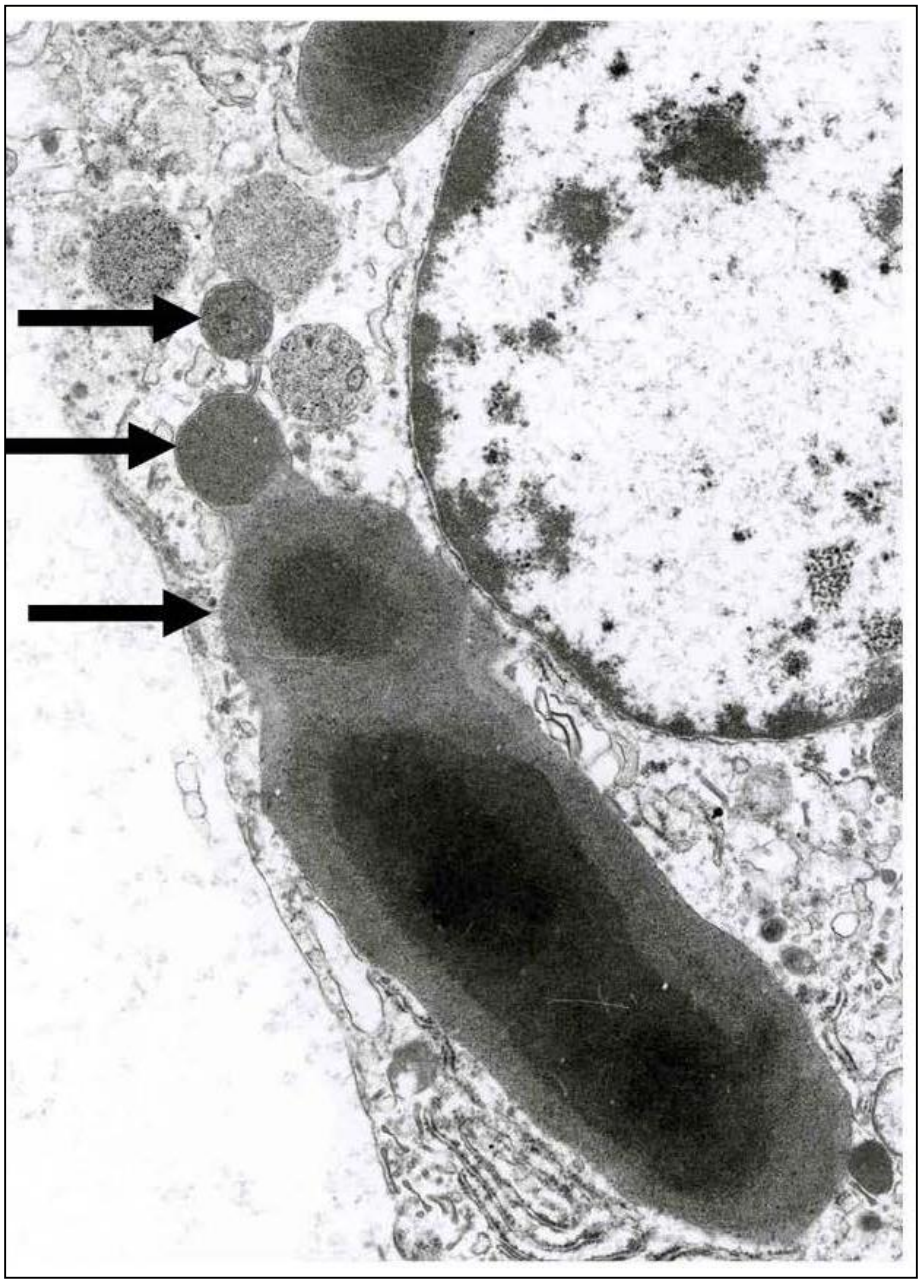


Mysterious Hamazaki-Wesenberg bodies inside a macrophage isolated from sarcoidosis granuloma

AIU Grindelwald 2020

Myocarditis, an epidemy ?

Camillo Ribi

Médecin adjoint, PD-MER

Immunologie & Allergie

CHUV

Myocarditis

Inflammation of cardiac muscle by variety of infectious and noninfectious causes

Acute, subacute, or chronic disorder

Focal or diffuse involvement of the myocardium

Variable clinical presentation, ranging from fatigue/chest pain to sudden death

In the past decade:

- increase of patients referred by cardiologists for ‘inflammatory cardiomyopathy’

- most cases suspected cardiac sarcoidosis

- work-up and treatment challenging

More recently:

Immune-mediated myocarditis during cancer immunotherapy

Distinct in presentation and treatment

Clinical presentation of myocarditis (ESC 2013)

(1) Acute coronary syndrome-like
- (a) Acute chest pain
  - Frequently starting within 1–4 weeks of a respiratory or gastrointestinal infection
  - Frequently associated with severe and recurrent symptoms
  - In the absence of angiographic evidence of CAD
- (b) ST/T wave changes
  - ST-segment elevation or depression
  - T-wave inversions
- (c) With or without normal global or regional LV and/or RV dysfunction on echocardiography or CMR
- (d) With or without increased TnT/TnI that may have a time course similar to acute myocardial infarction or a prolonged and sustained release over several weeks or months

Acute chest pain

(2) New onset or worsening heart failure in the absence of CAD and known causes of heart failure
- (a) New onset or progressive heart failure over 2 weeks to 3 months
  - Dyspnoea
  - Peripheral oedema
  - Chest discomfort
  - Fatigue
- (b) Impaired systolic LV and/or RV function, with or without an increase in wall thickness, with or without dilated LV and/or RV on echocardiography or CMR
- (c) Symptoms possibly started after a respiratory or gastrointestinal infection, or in the peri-partum period
- (d) Non-specific ECG signs, bundle branch block, AV-block, and/or ventricular arrhythmias

Evolving heart failure

(3) Chronic heart failure in the absence of CAD and known causes of heart failure (see point 2 above)
- (a) Heart failure symptoms (with recurrent exacerbations) of >3 months duration
- (b) Fatigue, palpitation, dyspnoea, atypical chest pain, arrhythmia in an ambulant patient
- (c) Impaired systolic LV and/or RV function on echocardiography or CMR suggestive of DCM or non-ischaemic cardiomyopathy
- (d) Non-specific ECG signs, sometimes bundle branch block and/or ventricular arrhythmias and/or AV-block

Chronic heart failure/arrhythmia

(4) 'life-threatening condition', in the absence of CAD and known causes of heart failure comprising
- (a) Life-threatening arrhythmias and aborted sudden death
- (b) Cardiogenic shock
- (c) Severely impaired LV function

Fulminant myocarditis and/or Life-threatening arrhythmias

A. L. Caforio, et al. *Eur Heart J* 2013; 34

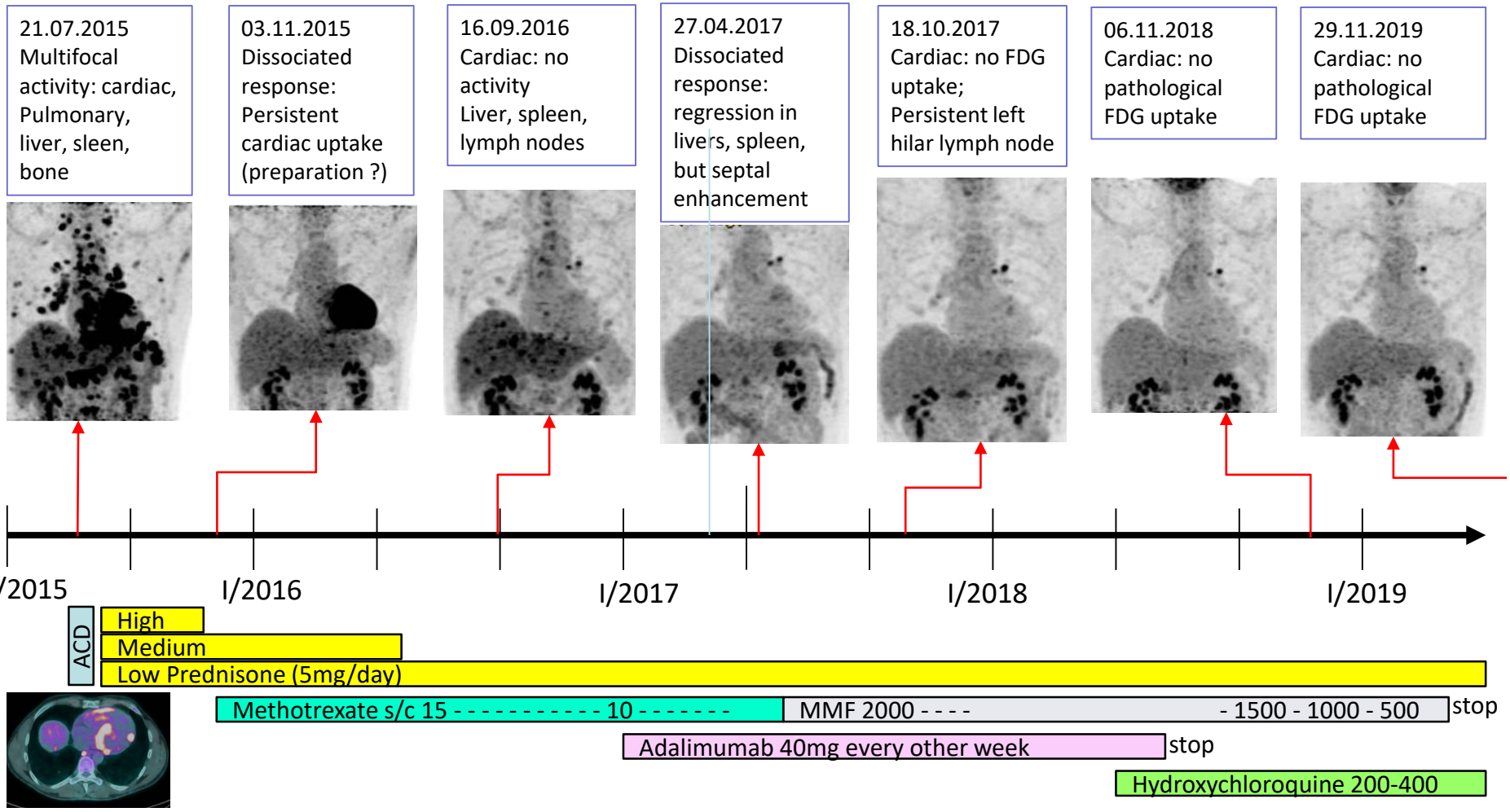
Causes of myocarditis

Infectious	Viral	Coxsackie, influenza, parvovirus B19, herpes group…
	Bacterial	Bartonella, Legionella, mycoplasma…
	Spirochetal	Lyme, Syphilis, Leptospirosis….
	Rickettsiae	Coxiella, typhus…
	Protozoal	Chagas, malaria, toxoplasma..
	Helminthic	Strongyloides, toxocara, schistosoma…
Toxic		Alcohol, cocaïne, anthracyclines, cyclophosphamide…
Hypersensitivity		Drugs (antibiotics, clozapine…), venom
Radiation		
Systemic disease		Celiac, **sarcoidosis**, connective tissue disease, vasculitis…

47-year old patients with new-onset dyspnoea

Dyspnoea and I° AV-Block Better **Palpitations** Skin **Nodule** elbow MTX intolerance **Palpitations** Asymptomatic

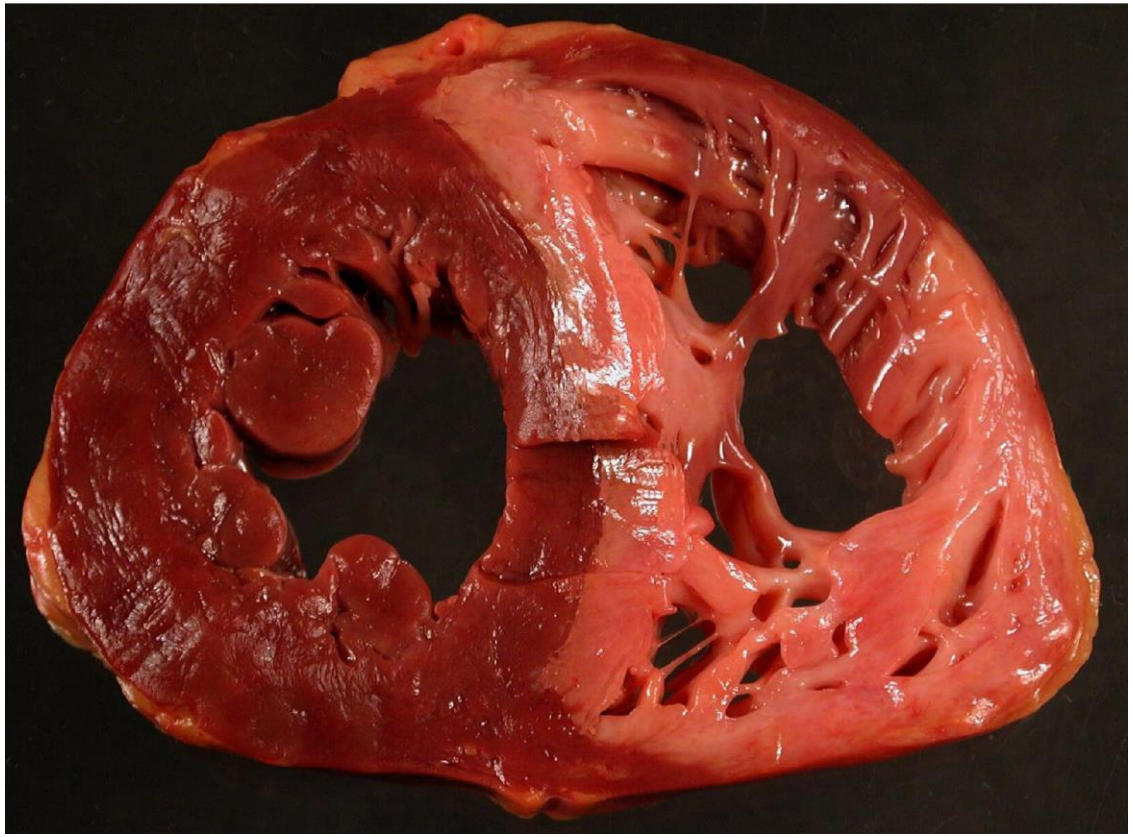
No histological proof / lab evidence of sarcoidosis Skin biopsy: **granuloma**



Cardiac sarcoidosis: macroscopic involvement

Postmortem studies: any part of heart may be affected (atria, ventricle, valves…)

Predilection: basal septum, left ventricular wall, papillary muscle, right ventricle

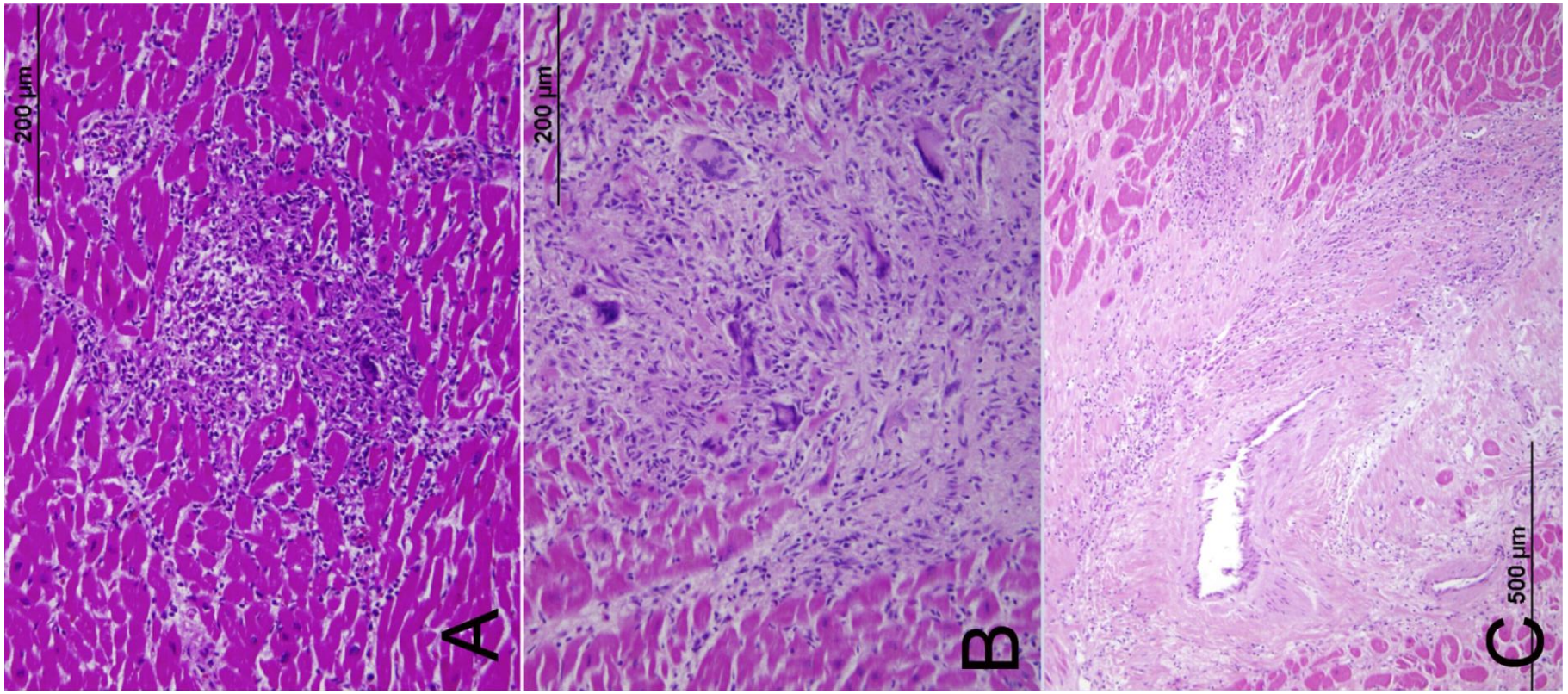


Peculiar right-sided predilection for sarcoid scars, with demarcation at the mid-septum (2 hearts in this series)

F. Tavora, et al. *Am J Cardiol* 2009; 104

Cardiac sarcoidosis - Histology / lesional state

Early (~lymphocytic) (B) Active granulomatous (C) Late (scar tissue)

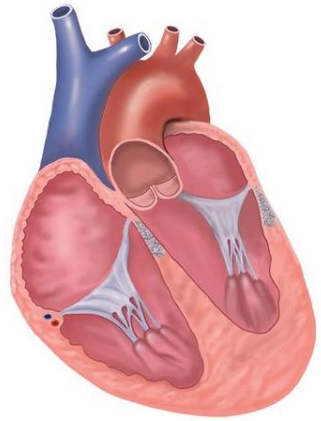


In sudden cardiac death: intermediate (granulomatous) > late >> early changes

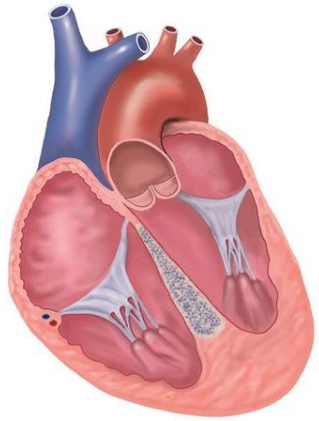
sub-epicardial > mid-myocardial > sub-endocardial

Clinical manifestations of cardiac sarcoidosis

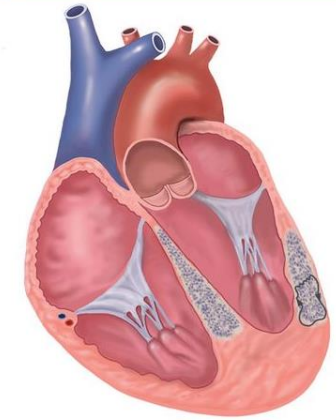
Region involved	Manifestations
Conduction system	Right bundle branch block or complete heart block
Conduction system	Ventricular arrhythmia
Left ventricular myocardium	Systolic and diastolic heart failure
Valves, papillary muscle	Valvular disorders
Pericardium	Pericardial effusion
Coronary arteries	Myocardial ischemia and infarction
Non-vascular distribution	Myocardial fibrosis
Conduction system, myocardium	Sudden cardiac death (**13-25%**)



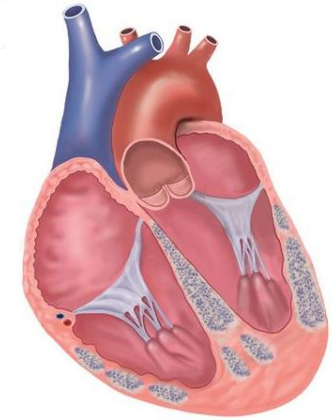
Small patches of basal involvement, usually clinically silent



Large area of septal involvement, often clinically manifest as heart block

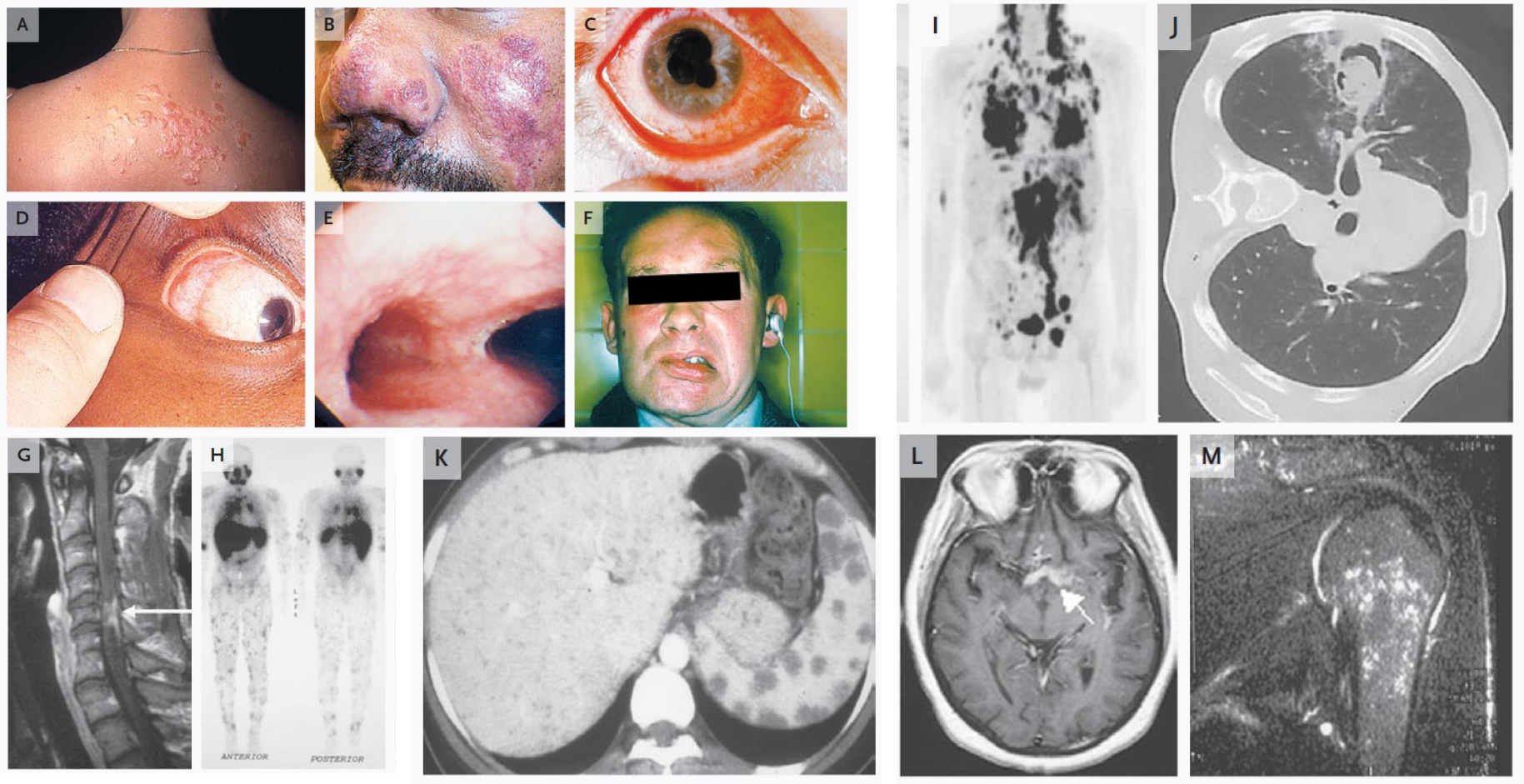


Re-entrant circuit involving area of granuloma/fibrosis leading to VT



Extensive areas of LV and RV involvement, often clinically manifest as heart failure +/- heart block +/- VT

The many clinical features of sarcoidosis



Cardiac involvement: Up to 25% of patients with systemic sarcoidosis

(cardiac involvement more frequent in autopsy series)

Iannuzzi MC, et al. N Engl J Med 2007

Isolated inflammatory cardiomyopathy

Accumulating evidence for the existence of isolated cardiac sarcoidosis (ICS)

Formal diagnosis only in case of histological proof (rare)

Uncertainty regarding epidemiology, optimal treatment and prognosis

Compared to systemic sarcoidosis with cardiac involvement,

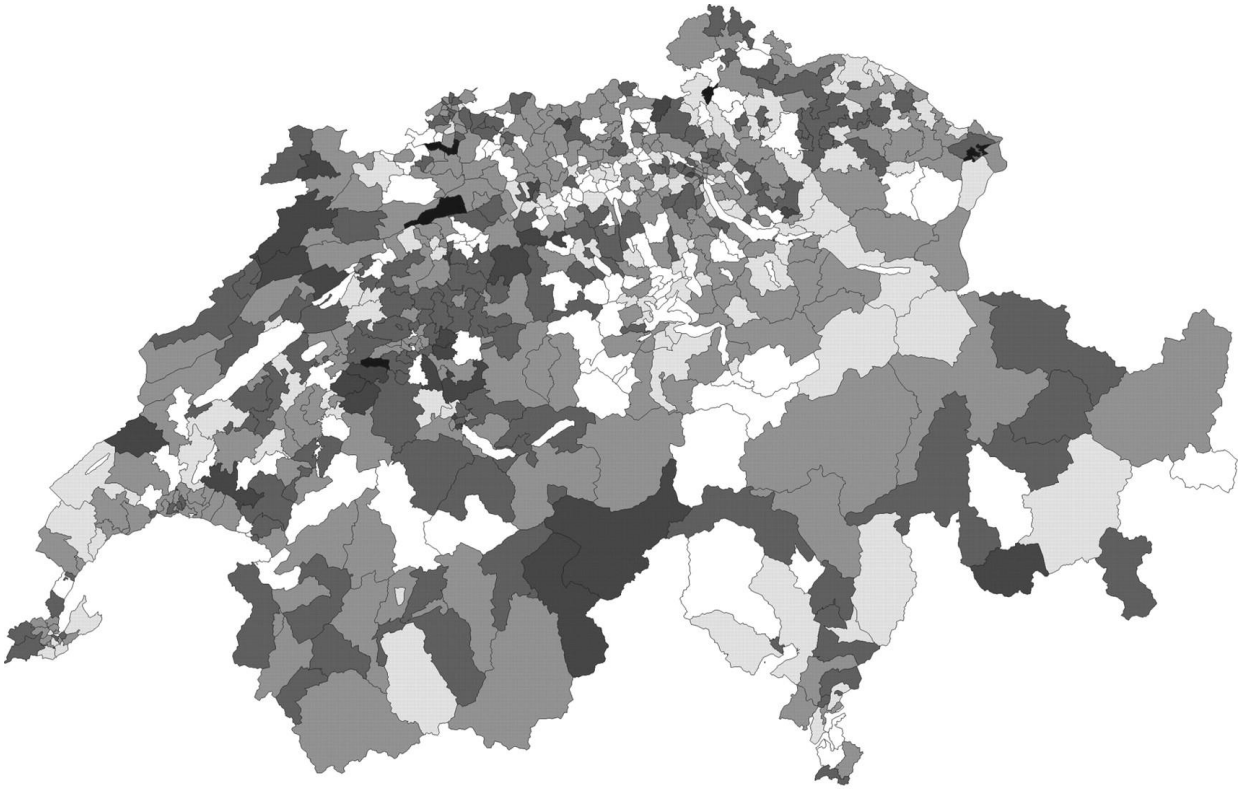
patients with ICS have

- worse LV systolic function at presentation
- more ventricular arrhythmias
- worse event-free survival

Epidemiology of sarcoidosis

Prevalence in Switzerland (active, diagnosed sarcoidosis): ~ 44/100'000

- worldwide: 3 x more frequent in patients of African descent (and more severe)
- 2/3 of cases in young adults (25-45 years)



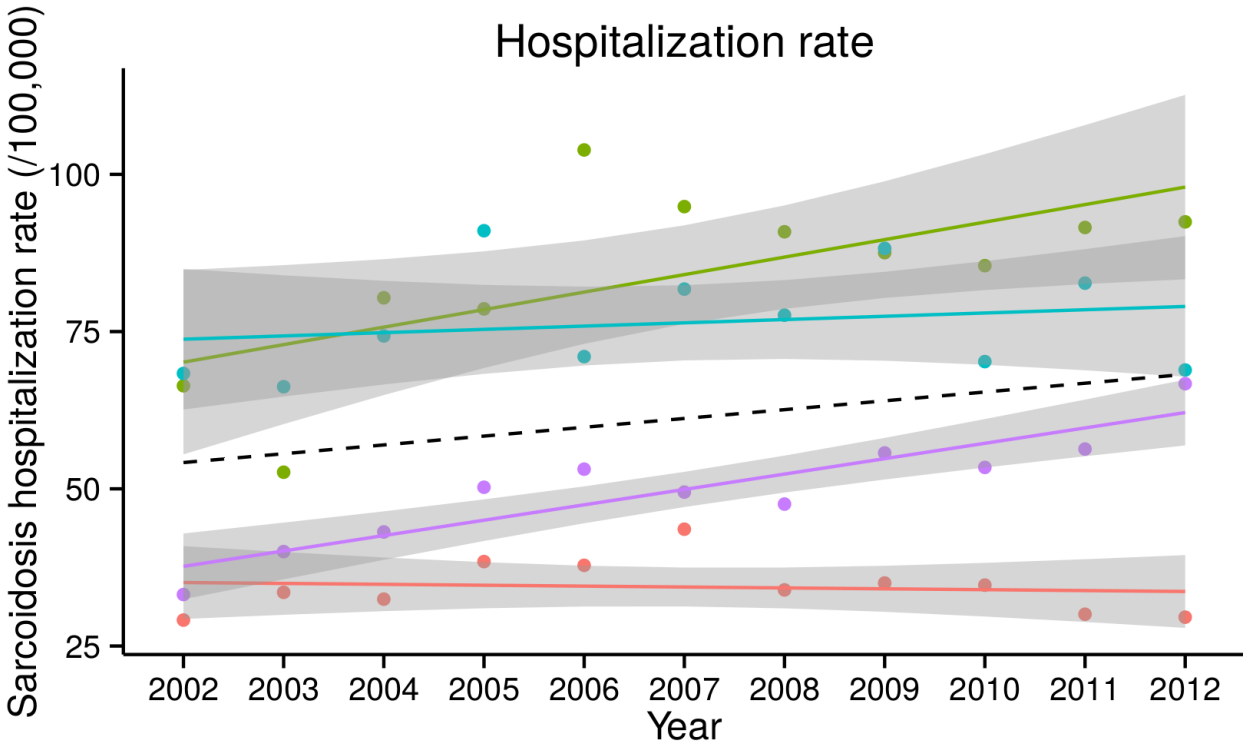
Deubelbeiss U, et al. Eur Respir J 2010

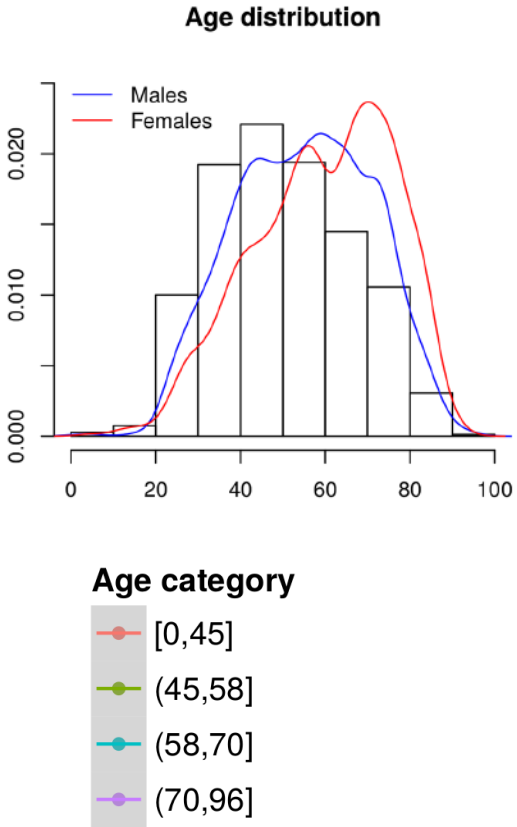
increased in areas with

- metallurgy
- water supply
- potato farming
- grasslands…

Patients with sarcoidosis hospitalized in CH 2002-2012

Sarcoidosis was the main reason of hospitalization in 30%





S. Pohle, et al. *PLoS One* 2016; 11

Causes of sarcoidosis

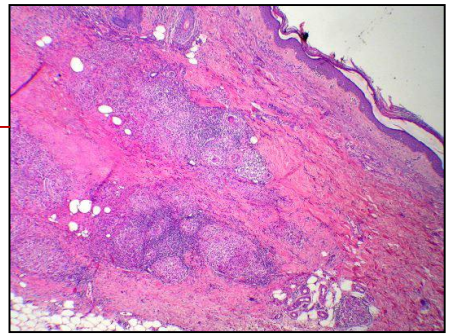
Genetic predisposition (polygenic)

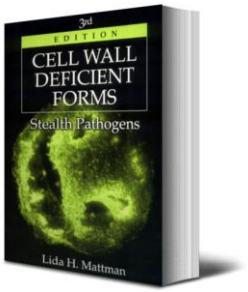
- familial clustering possible : OR 5.8 for 1st degree relative with sarcoidosis
- sarcoid-like manifestations in common variable immunodeficiency
- association with other conditions such as celiac disease

Arguments for environnemental factors:

- Reports of small epidemics confined in space and time
- Kweim-Siltzbach reaction
- Cases of transplanted sarcoidosis
- Dust from WTC bombing (incidence x 8 in NYC after 2001)
- Incomplete forms of mycobacteria (disputed)
- Other infectious agents ?

Injection of sarcoidosis spleen extract into skin (obsolete)



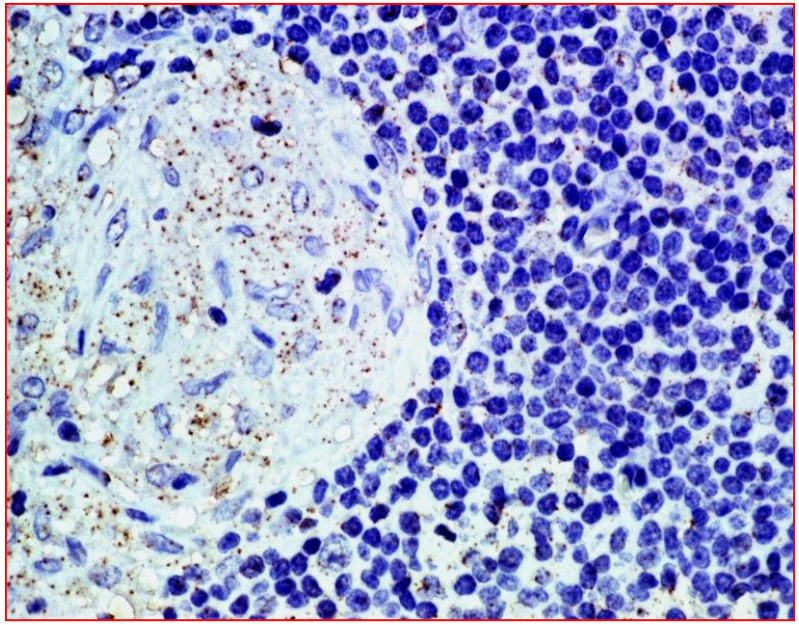


Propionibacterium (Cutibacterium) acnes

Gram-positive rod colonizing skin and mucosa

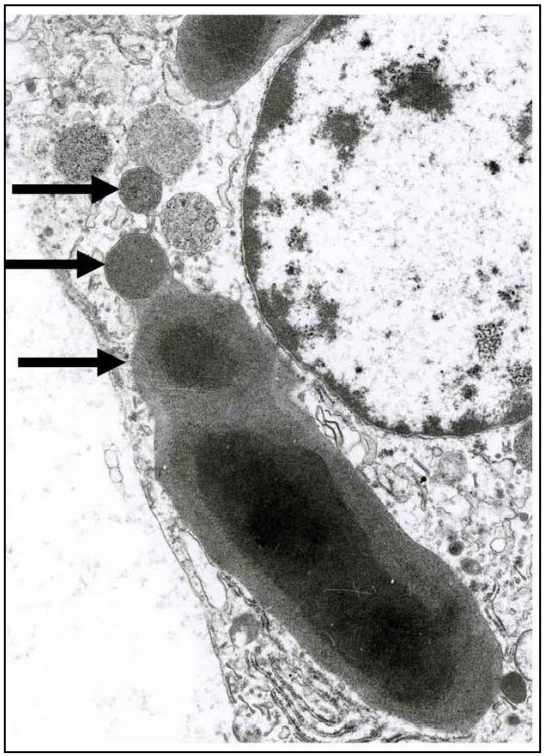
Only microorganism to grow in cultures from sarcoid tissue

Increasingly reported in various tissue biopsy



In situ hybridization using catalyzed reporter deposition for signal amplification with digoxigenin-labeled oligonucleotide probes that complement 16S rRNA of P. acnes

Hamazaki-Wesenberg bodies



Phagolysosomally-degraded P. acnes or intact forms of intracellular bacteria ?

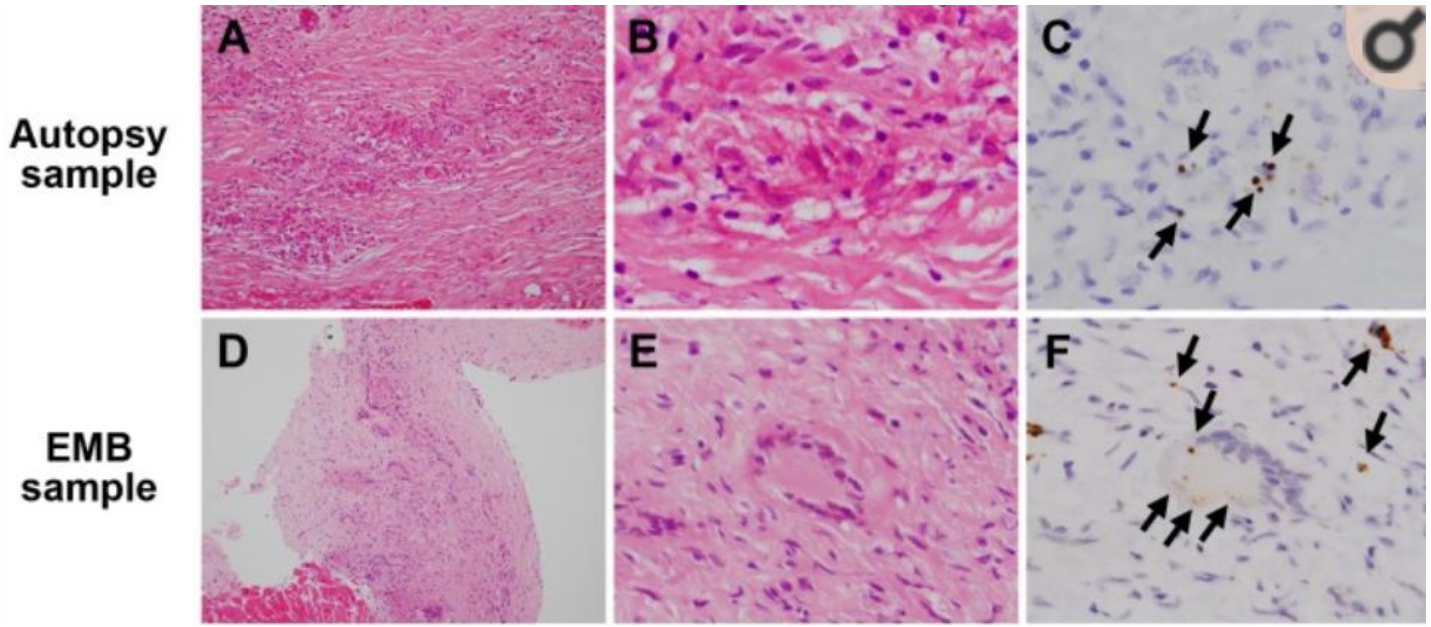
Goto H, et al. Br J Ophthalmol 2017

P. acnes in cardiac sarcoidosis

Cardiac sarcoidosis (N=25); other types of myocarditis / cardiomyopathy (N=54)

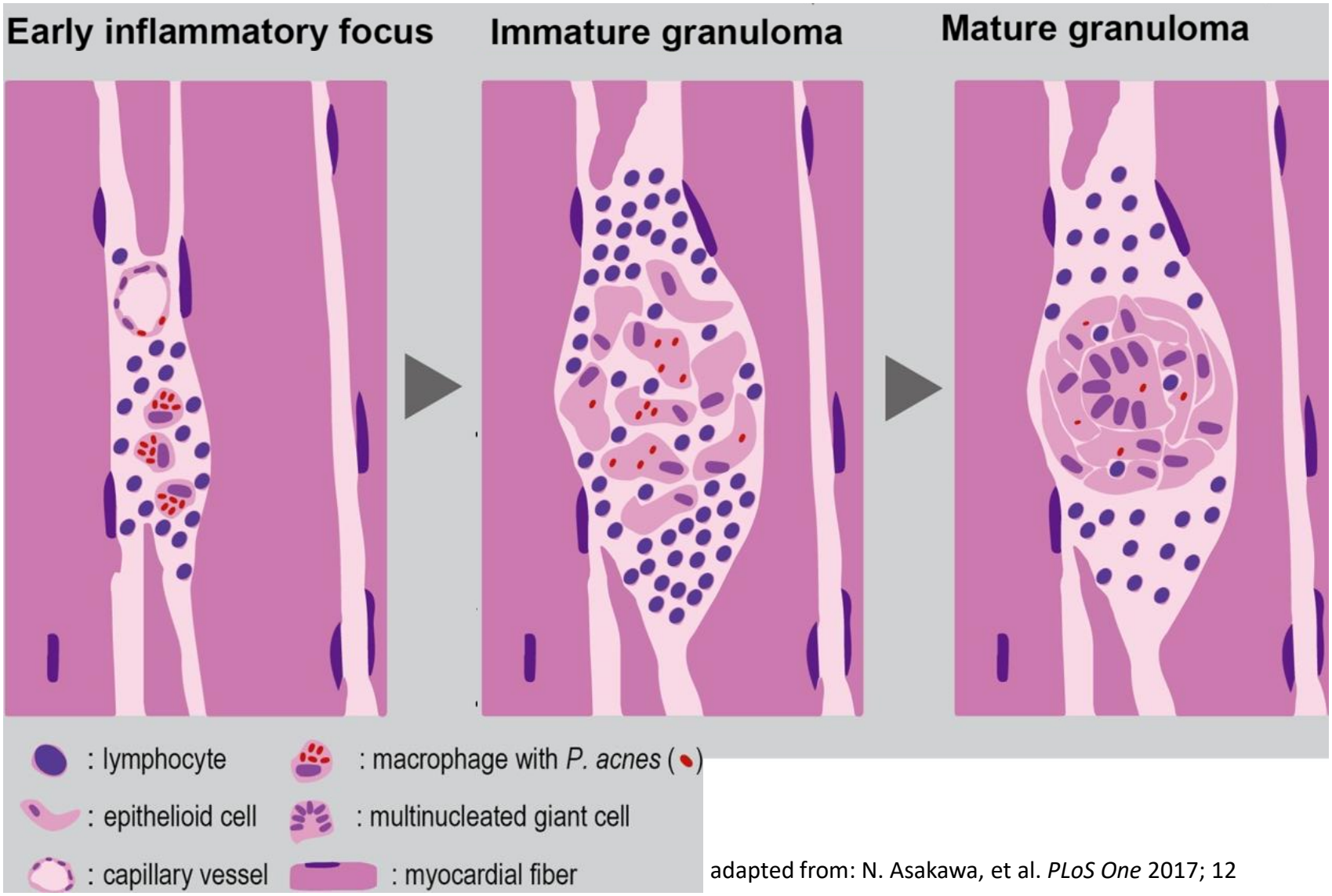
- immunohistochemistry with P. acnes-specific ab: positive **only** in sarcoidosis

- Cardiac sarcoidosis:	62% granuloma	62% major foci	42% minor foci
- P. acnes positivity:	63%	63%	73%



N. Asakawa, et al. *PLoS One* 2017; 12

Pathogenic role of P. acnes in cardiac sarcoidosis ?



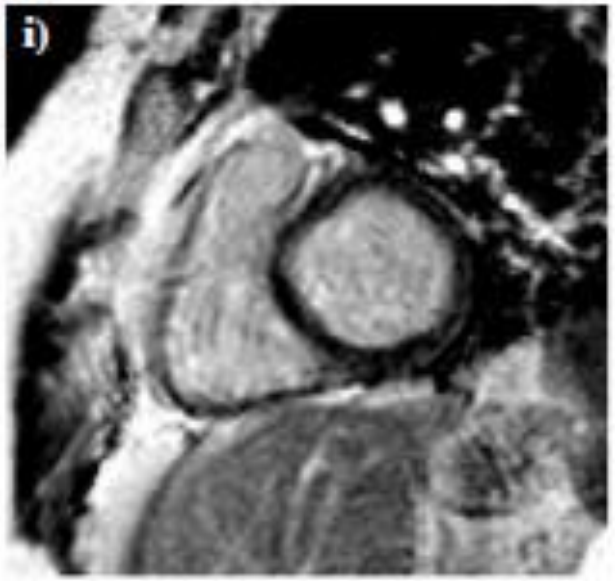
adapted from: N. Asakawa, et al. *PLoS One* 2017; 12

Cardiac Magnetic Resonance

Very sensitive and specific test (>90%) in several studies

Characteristic features for cardiac sarcoidosis:

- late gadolinium enhancement (LGE) in the myocardium
- pattern of patchy and multifocal uptake with sparing of the endocardial border



LGE also prognostic factor in cardiac sarcoidosis:

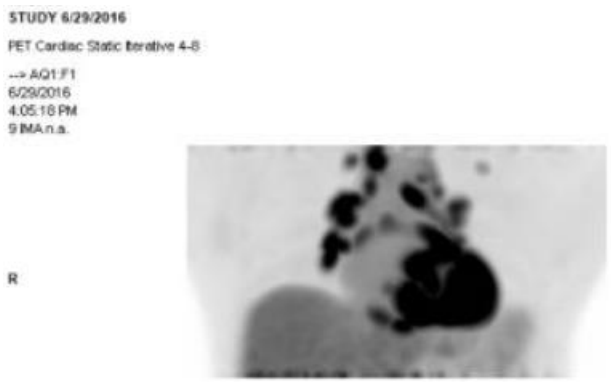
- associated with increased risk of ventricular arrhythmia or death

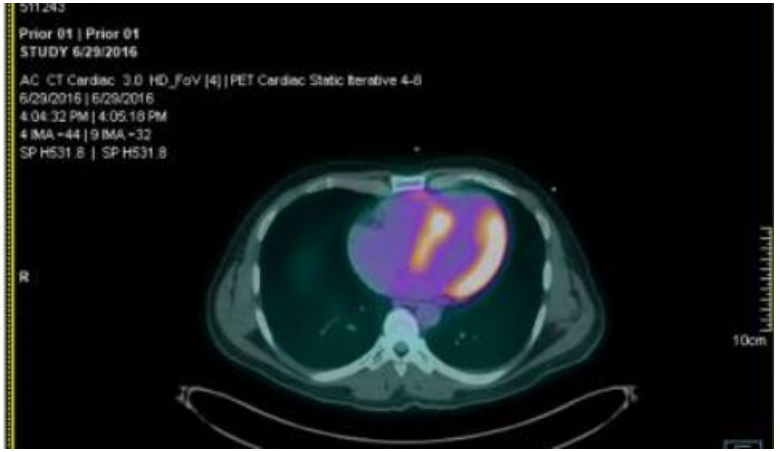
P. Mankad, et al. *Curr Cardiol Rep* 2019; 21

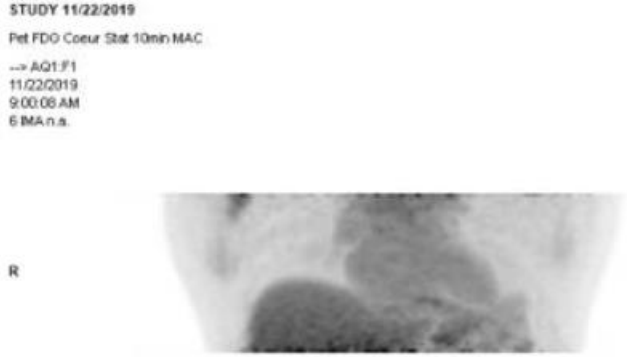
Value of 18-FDG PET-CT

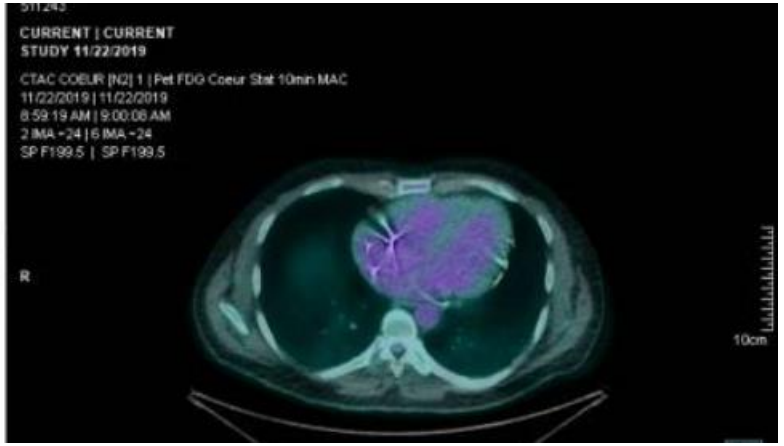
Example of a 49-year old patient with relapsing cardiac sarcoidosis (under MTX)

PET-CT at the time of relapse and after 4 months of low-dose CS/anti-TNF/MTX

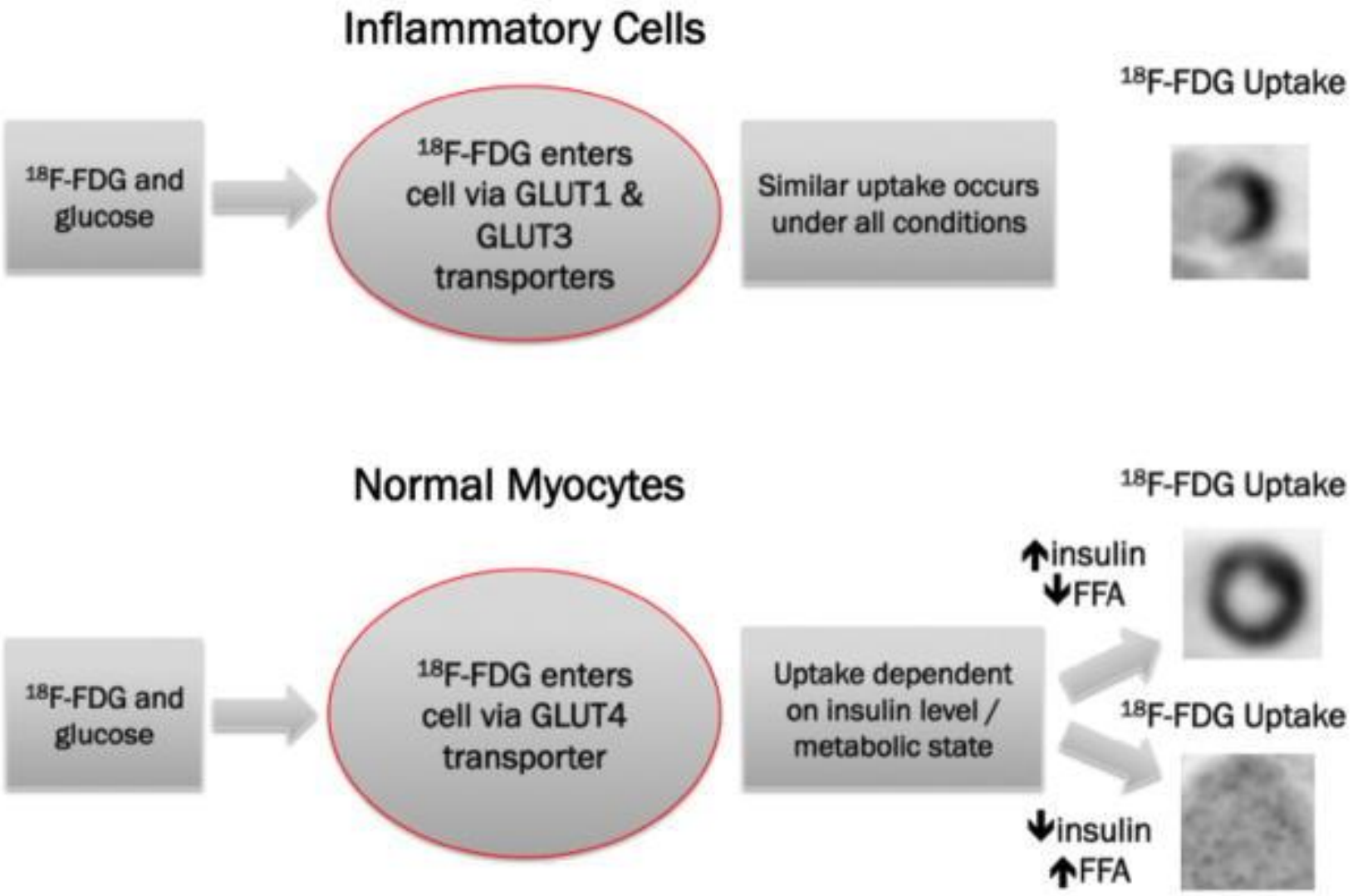








Principles of cardiac FDG-PET imaging



M. T. Osborne, et al. *J Nucl Cardiol* 2017; 24

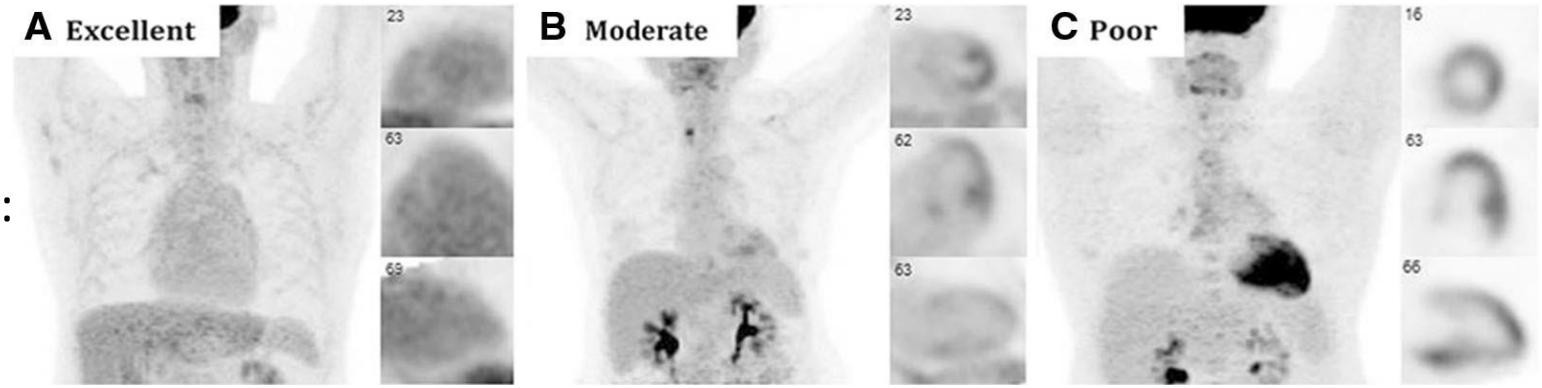
Optimal conditions for cardiac FDG-PET

If done on an out-patient basis: prior approval by insurance company

Suppression of physiological myocardial glucose metabolism:

- low-carb (high-fat, high-protein) diet (CHUV: for 72h)
- avoidance of vigorous exercice 12 to 24 hours prior to the exam
- fasting prior to exam (CHUV: for 12h)
- administration of i/v heparin (increases free fatty acids)

Quality of preparation:



M. T. Osborne, et al. *J Nucl Cardiol* 2017; 24

Somatostatin-receptor targeted imaging as alternative

Cardiac PET with Ga68 coupled to SSR type 2 agonist (DOTATATE, DOTATOC etc…)

ID	Prior immunotherapy and start date	Cardiac FDG uptake (SUV_{max})	Nodal FDG uptake (SUV_{max})	Days to Dotatate	Cardiac Dotatate uptake (SUV_{max})	Nodal Dotatate uptake (SUV_{max})	Cardiac concordance	Nodal concordance
1	Methotrexate 2.5 mg weekly > 1 year	Focal (6.58)	Increased (8.4)	139	Focal (1.33)	Increased (1.86)	Concordant	Concordant
2	None	Multifocal (6.89)	Increased (11.47)	35	Multifocal (1.70)	Increased (2.74)	Concordant	Concordant
3	None	Focal on diffuse (10.97)	Increased (22.6)	70	Focal (2.05)	Increased (2.40)	Concordant	Concordant
4	None	Focal (4.15)	Increased (7.01)	37	Focal (1.09)	Increased (2.46)	Concordant	Concordant
5	None	Focal on diffuse (2.77)	Negative (2.10)	22	Heterogeneous (1.34)	Negative (0.97)	Concordant	Concordant
6	None	Focal on diffuse (5.22)	Negative (4.14)	37	Heterogenous (2.21)	Negative (1.84)	Concordant	Concordant
7	None	Multifocal (11.48)	Negative (2.01)	51	Diffuse intense (1.84)	Negative (1.19)	Concordant	Concordant
8	Prednisone 20 mg daily 5 days before Dotatate	Focal on diffuse (6.50)	Increased (4.47)	61	Negative (0.91)	Increased (1.79)	Discordant	Concordant
9	Methotrexate 15 mg weekly > 1 year	Focal on diffuse (9.18)	Increased (5.95)	13	Negative (0.99)	Increased (2.01)	Discordant	Concordant
10	Prednisone 15mg daily 5 months before FDG	Focal (2.33)	Negative (1.08)	15	Negative (1.28)	Negative (1.03)	Discordant	Concordant
11	Prednisone 15 mg daily 25 days before FDG	Focal on diffuse (7.85)	Negative (1.59)	16	Negative (1.11)	Negative (1.24)	Discordant	Concordant
12	None	Focal (5.91)	Negative (2.85)	27	Negative (1.19)	Negative (1.54)	Discordant	Concordant
13	None	Focal on diffuse (5.47)	Negative (2.0)	55	Negative (0.67)	Negative (1.38)	Discordant	Concordant
Total	38%	6.5 [5.2-7.9]	4.1 [2.0-7.0]	37 [25-55]	1.28 [1.1-1.7]	1.8 [1.2-2.0]	54% concordance	100% concordance

P. E. Bravo, et al. J Nucl Cardiol 2019

Echocardiogram, Brain natriuretic peptide and CRP

Transthoracic echocardiogram

Useful for assessing cardiac involvement in biopsy-proven extracardiac sarcoidosis

Sensitivity 71-84% when combined with symptoms and/or Holter

- Reduced LVEF: one of the strongest prognostic indicators

Brain natriuretic peptide

BNP identified CS with a sensitivity of 85% in 172 patients with sarcoidosis

- predictor of heart failure among CS patient

T. Kiko, et al. *Int Heart J* 2018; 59

C-reactive protein

Statistically slight elevation in sarcoidosis and heart failure/ventricular tachycardia

- clinical utility disputed (mean CRP 5.8 vs 4 g/l)

Mankad P, et al. *Hear Rhythm Soc* 2019

Sensitivity of biological markers in sarcoidosis

Angiotensin converting enzyme (ACE)

Sensitivity depends upon assay and disease activity: 29-59% (60-90% active)

Uninterpretable in cardiac failure treated with ACE-inhibitors

Elevated in other conditions such as primary biliary cirrhosis, Gaucher's disease, tbc, leprosy, histoplasmosis, hyperthyroidism, diabetes mellitus, HIV...

Serum lysozyme

Sensitivity of elevated serum lysozyme for predicting sarcoidosis 69%-79%

Increases with the number of organs involved, decreases under treatment

More sensitive but less specific than ACE

Also elevated in leprosy, tuberculosis, pernicious anemia, osteoarthritis, hematologic malignancy, renal insufficiency…

Value of endomyocardial biopsy (EMB)

Sensitivity of EMB for the diagnosis of CS suboptimal (20–40%)

- in part be due to the patchy nature of the disease
- limited access of biopsy sites using standard techniques
- procedure not without risk !

Could guided EMB increase the yield ?

- 1st EMB during electro-anatomical mapping in a case of ICS: negative
- repeat EMB in low-voltage regions in right ventricular septum: granuloma

But:

- not all patients demonstrate low-voltage regions accessible from the right
- low voltage area my represent active inflammation or non-specific fibrosis

Sensitivity of other biopsies in sarcoidosis

Peripheral adenopathy :	90 %
Yanardag H, et al. Can Respir J 2007	
TBNA + Trans-bronchial lung biopsy :	80 %
Agarwal R, et al. Respir Care 2013;58:683-693	
EBUS-Trans-bronchial needle aspiration :	80 %
Agarwal R, et al. Respir Med. 2012;106:883-892	
Trans-bronchial needle aspiration:	60 %
Agarwal R, et al. Respir Care 2013;58:683-693	
Minor salivary glands:	50 %
G. Stalder, review of the literature 2015	**In our experience: only exceptionally positive**
Skeletal muscle biopsy (gastrocnemius):	**?** 100% (N=22 with hilar adenopathy)
Andonopoulos AP, Clin Exp Rheumatol 2001;19:569-72.	**Was negative in all our patients with suspected CS**
	not any more part of the work-up

Work-up for suspected inflammatory cardiomyopathy

What we do/order in CHUV when called by fellow cardiologists:

usually upon results from cardiac MRI/PET-CT/endomyocardial biopsy

Careful history and clinical examination: lymph nodes, scars, tattoos, joints….

Lab: ESR, CRP, full blood count, Calcium, albumine, creatinine, urine sediment

Muscle enzymes, troponine, liver tests, thyroid function

ANA, ANCA, anti-transglutaminase ab, ACE, ferritine, immunoglobulins

Borrelia, Chagas (if travel to Latin America), Elispot, HIV, hepatitis

Other: Eye exam (fundoscopy), pulmonary function tests +/- HRCT

If lung alterations suggestive of sarcoidosis: BAL and guided biopsies

If nothing suggests extra-cardiac sarcoidosis: consider lip biopsy

Porretta AP, et al. Rev Med Suisse 2016;12:1035-41

Diagnostic criteria for cardiac sarcoidosis

Histological diagnosis group

HRS criteria for CS diagnosis, 2014	Japanese Society of Sarcoidosis and Other Granulomatous Disorders, 2017
Presence of myocardial tissue demonstrating non-caseating granuloma on histological examination with no alternative cause identified.	CS diagnosed when EMB or surgical specimens demonstrate non-caseating epithelioid granulomas.

Diagnostic criteria for CS (clinical diagnostic group)

<table>
<tr><th>HRS (2014); Probable CS if:</th><th>JSSO (2017); Cardiac sarcoidosis if</th></tr>
<tr><td rowspan="3">A. There is a histological diagnosis of extra-cardiac sarcoidosis
AND
B. ≥ 1 of the following:
- Corticosteroid and/or immunosuppressant-responsive cardiomyopathy or heart block
- Unexplained reduced LVEF (< 40%)
- Unexplained sustained (spontaneous or induced) ventricular tachycardia
- Mobitz type II second-degree block or third-degree heart block
- Patchy uptake on dedicated cardiac PET (in a pattern consistent with CS)
- CMR with LGE (in a pattern consistent with CS)
- Positive gallium uptake (in a pattern consistent with CS)
AND
C. Other causes for the cardiac manifestation(s) have been reasonably excluded</td><td>A. Epithelioid granulomas in organs other than heart
AND
B. ≥ 2/5 major criteria for cardiac involvement, OR
1 major + ≥ 2/3 minor criteria</td></tr>
<tr><td>A. Clinical findings strongly suggestive of pulmonary or ophthalmic sarcoidosis
AND
B. ≥ 2 major criteria OR 1 major + ≥ 2 minor criteria for cardiac involvement
AND
C. ≥ 2/5 paraclinical criteria for sarcoidosis:
- Bilateral hilar lymphadenopathy
- Elevated serum ACE activity / elevated lysozyme
- High serum soluble IL-2 receptor levels
- significant uptake in ^{67}Ga citrate or ^{18}F-FDG-PET
- BAL lymphocytosis with CD4/CD8 ratio > 3.5</td></tr>
<tr><td>Major criteria for cardiac involvement
- High-grade AV block or fatal ventricular arrhythmia
- Basal thinning of ventricular septum or abnormal ventricular wall anatomy
- Abnormally high uptake with ^{67}Ga citrate or ^{18}F-FDG-PET
- LVEF < 50%
- CMR with LGE

Minor criteria for cardiac involvement
- ECG: ventricular arrhythmias, BBB, axis deviation, or abnormal Q waves
- Perfusion defects by myocardial perfusion scintigraphy
- EMB: monocyte infiltration and moderate-severe interstitial fibrosis</td></tr>
</table>

Diagnostic criteria for isolated cardiac sarcoidosis

JSSO (2017); Isolated cardiac sarcoidosis if
Prerequisite 1. No clinical findings characteristic of sarcoidosis are observed in any organs other than the heart. (The patient should be examined in detail for respiratory, ophthalmic, and skin involvements of sarcoidosis. When the patient is symptomatic, other etiologies that can affect the corresponding organs must be ruled out.) 1. ^{67}Ga scintigraphy or 18F-FDG PET reveals no abnormal tracer accumulation in any organs other than the heart 2. A chest CT scan reveals no shadow along the lymphatic tracts in the lungs or no hilar and mediastinal lymphadenopathy (minor axis > 10 mm).
Isolated cardiac sarcoidosis is diagnosed histologically when endomyocardial biopsy or surgical specimens demonstrate non-caseating epithelioid granulomas.
Isolated cardiac sarcoidosis is diagnosed clinically if Abnormally high cardiac uptake with ^{67}Ga citrate or ^{18}F-FDG-PET **AND** 3 other major criteria for cardiac involvement:
Major criteria for cardiac involvement - High-grade AV block or fatal ventricular arrhythmia - Basal thinning of ventricular septum or abnormal ventricular wall anatomy - Abnormally high uptake with ^{67}Ga citrate or ^{18}F-FDG-PET - LVEF < 50% - CMR with LGE

Adapted from: Terasaki F, et al. *Annals of Nuclear Cardiology* 2017 and P. Mankad, et al. *Curr Cardiol Rep* 2019; 21

Treatment of sarcoidosis - in general

Pulmonary sarcoidosis: 50% of cases will heal within 3 years

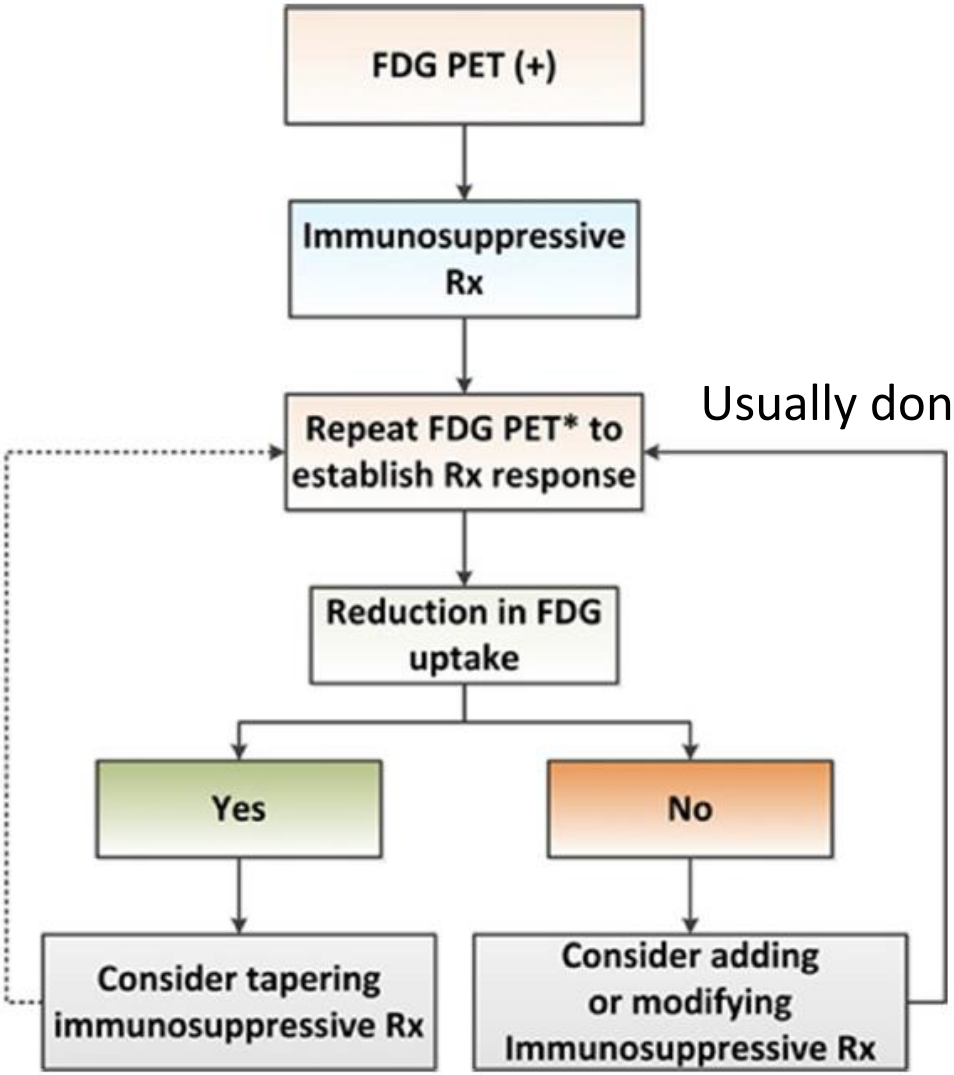
Systemic sarcoidosis is fatal in 0.5-5% of cases, especially if heart involved

Current treatment mainstay = corticosteroids

- **combine with** immunosuppressive drugs if refractory or for steroid sparing:
  - **2nd line: - methotrexate** (standard dose 10–25 mg weekly + folic acid) s/c

    we advocate subcutaneous injections for the following reasons:
    - improved biodisponibility
    - less gastro-intestinal symptoms
    - better compliance and monitoring
  - **Alternatives:** mycophenolate, azathioprine (pregnancy), antimalarials
  - **3rd line: TNF-blocking agents** (infliximab, adalimumab), **JAK inhibitors** (tofa)

Use of FDG-PET imaging to guide therapy



Usually done after 4-6 months

R. Slart, et al. *J Nucl Cardiol* 2018; 25

Treatment of cardiac sarcoidosis (CHUV)

If doubt regarding isolated cardiac sarcoidosis: wait 3 months and do 18-FDG-PET

If ICD freshly implanted: wait 2-3 weeks before starting immunosuppression

Start Prednisone 0.5mg/kg/day + Methotrexate 10-20 (usually 15) mg/week **s/c**

Taper steroids over 3-4 month to Prednisone max. 10mg/day

Do cardiac 18-FDG PET-CT

- If no/partial response: add 3rd line (preferably infliximab, after ok insurance)
- If complete response: taper steroids to 5mg/day, maintain methotrexate

Do cardiac 18-FDG PET-CT after 6-12 months

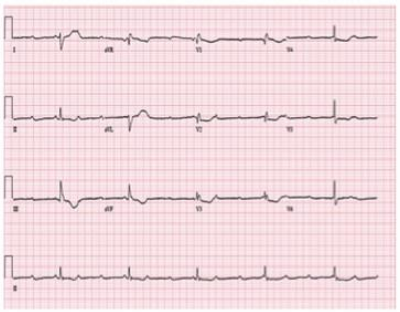
- if recurrence of FDG uptake: add 3rd line
- if complete response: maintain MTX, taper Prednisone completely

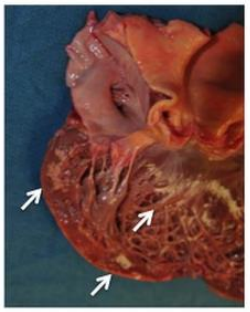
Do cardiac PET-CT after 1 year…. If remission: decrease MTX,

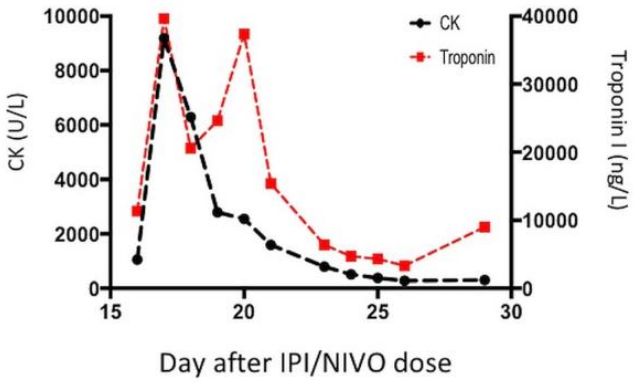
Immune-related myocarditis – part of the epidemic

Signs and symptoms are non specific

Fatigue, weakness
Oedema
Dyspnea
Palpitations
Chest pain
Hypotension
Fever







Diagnosis
=
Therapeutic emergency :

Transfer to cardiology ICU
(risk of rapid progression)

High dose corticosteroids

<u>If suspected :</u>
ECG
Troponin
BNP

echocardiography
+/- CMR

Differential diagnosis (do a CT-scan):
- Pulmonary embolism
- Pneumonitis
- Viral myocarditis

Champiat B. ESMO 2019; S. D. Saibil, et al. Curr Oncol 2019; 26

Immune-related myocarditis

More frequent that initially expected

High mortality:

Review of 88 myocarditis cases reported in the literature – fatal vs non-fatal outcomes (N=50)

Parameter	Patients who died, N = 27	Patients who survived, N = 23
Clinical features		
Mean age in years	63.1, 23–83	63.6, 35–80
Male/female	17/10	11/12
Mean time to development of symptoms, range in weeks	5.5, 0.71–31 (reported in 23/27)	7.7, 1–52 (reported in 18/23)
Immune checkpoint inhibitor (ICI) used	5 anti-CLA-4 (19%), 16 anti-PD-1 (59%), 6 combination (27%)	16 anti-PD-1 (70%), 1 anti-PDL-1 (4%), 6 combination (26%)
Previous autoimmune diseases	1/27	2/23
Preexisting cardiovascular conditions/risk factors	14/27	3/23
Other ICI-induced immune related adverse events	17/27	8/23
Complicated presentation	19/27	17/23
Rhythm or rate abnormalities		
- Complete heart block	- 12 cases	- 4 cases
- Ventricular tachycardia/fibrillation	- 10 cases	- 4 cases
- Atrial flutter/fibrillation	- 2 case	- NR
Echocardiography features	Reported in 21/27	Reported in 21/23
Left ventricular ejection fraction (LVEF) < 50%	- 10 cases	- 16 cases
Immunomodulators used	Steroids in 22/27, other immunosuppressants in 7/27, IVIG in 4/27, plasmapheresis in 2/27, ATG in 2/27	Steroids in 23/23, other immunosuppressants in 5/23, IVIG in 5/23, plasmapheresis in 2/23, ATG in 2/23

No differences in terms of immunosuppressive treatment used…

R. Pradhan, et al. Int J Cardiol 2019;

Conclusions (1)

Increased incidence of inflammatory cardiomyopathies

- probably due to more widely available sensitive techniques (CMR, PET)

Most cases of cardiac sarcoidosis are not confirmed histologically

- endomyocardial biopsy risky and with modest yield
- if extra-cardiac signs of sarcoidosis: try to get histological proof of granuloma
- current biomarkers of limited sensitivity

Increased recognition of **isolated cardiac sarcoidosis** as nosological entity

- latest Japanese criteria adapted to include isolated cardiac sarcoidosis
- diagnostic criteria need to be validated prospectively

Conclusions (2)

Value of 18-FDG **PET in diagnosis and follow-up**:

- proper patient preparation to suppress cardiac glucose uptake is essential
- may give false-positive results if poor preparation or perfusion defects
- best yield when combined with cardiac MRI
- value of PET imaging with somatostatine receptor agonists to be determined…

Treatment:

- implantable defibrillator in high-risk patients
- immunosuppression: combination of Prednisone + Methotrexate
- if insufficient: anti-TNF (infliximab 5mg/kg, off-label)
- goal: resolution of cardiac 18-FDG uptake