ALARMING PULMONARY MANIFESTAION OF UNUSUSL DISEASE

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CASE PRESENTATION

17 years old boy usually healthy except for one episode of epididymitis at the age of 16

Parents are related and Family Hx was positive for FMF

4 month Hx of fever and shivering

Pleuritic chest pain

Weight loss of 4 kg

During that period he visit different hospitals 12 time and was hospitalized 5 times

WORK OUT IN PREVIOUS HOSPITAL

Diagnosed with pneumonia in the R. lung - received Zinnat, Rulid, Rocephin, Moxypen, Doxycilin and Azenil in different occasion but continue to have fever and complain about chest pain

Lab – Hg 9.8-10.7mg% (combined FA & B12 def) WBC- 10-19x10^3 CRP – X2-3 of normal

CT of the chest X2 – 1st month – RUL+RML infiltrate 3rd month residual of old infiltrate and new infiltrate on the left lung

Infection work up –viral serology , HIV, Rose ben gal Q fever – NEG

RF, ANA, ANCA - NEG

Gastroscopy – acute inflammation with few erosion in antrum

BMA – normal

He supposed to have PET CT and colonoscopy and discharged according to parents request

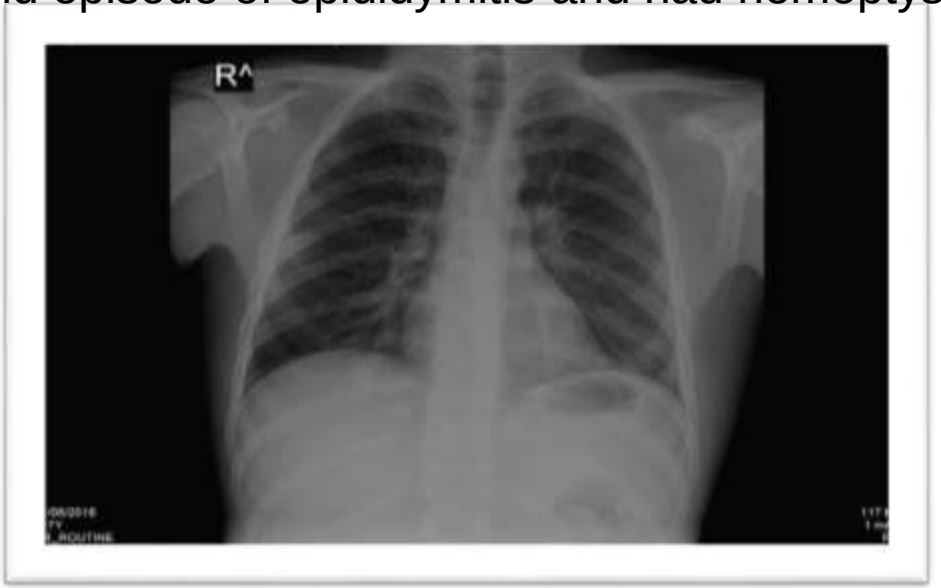
In the last month prior to his admission he was treated with colchicine for suspected FMF

WORK UP AT RAMABM

P/E He look pale , single oral aphtous and decrease air entry to both lung bases

Hg g/dl	PLT x10^3	WBC x10^3	CRP (0-5) mg/dl	TRANSF. SAT	fibrinogen	ALBUMIN g/dl	CALPROTEIN (0-50)
10.2	227	12.9	205	8.6(20-60)	556	2.5	348

During hospitalization : Continue to have fever and high inflammatory markers had another mild episode of epididymitis and had hemoptysis in few occasion



WORK UP AT RAMABM

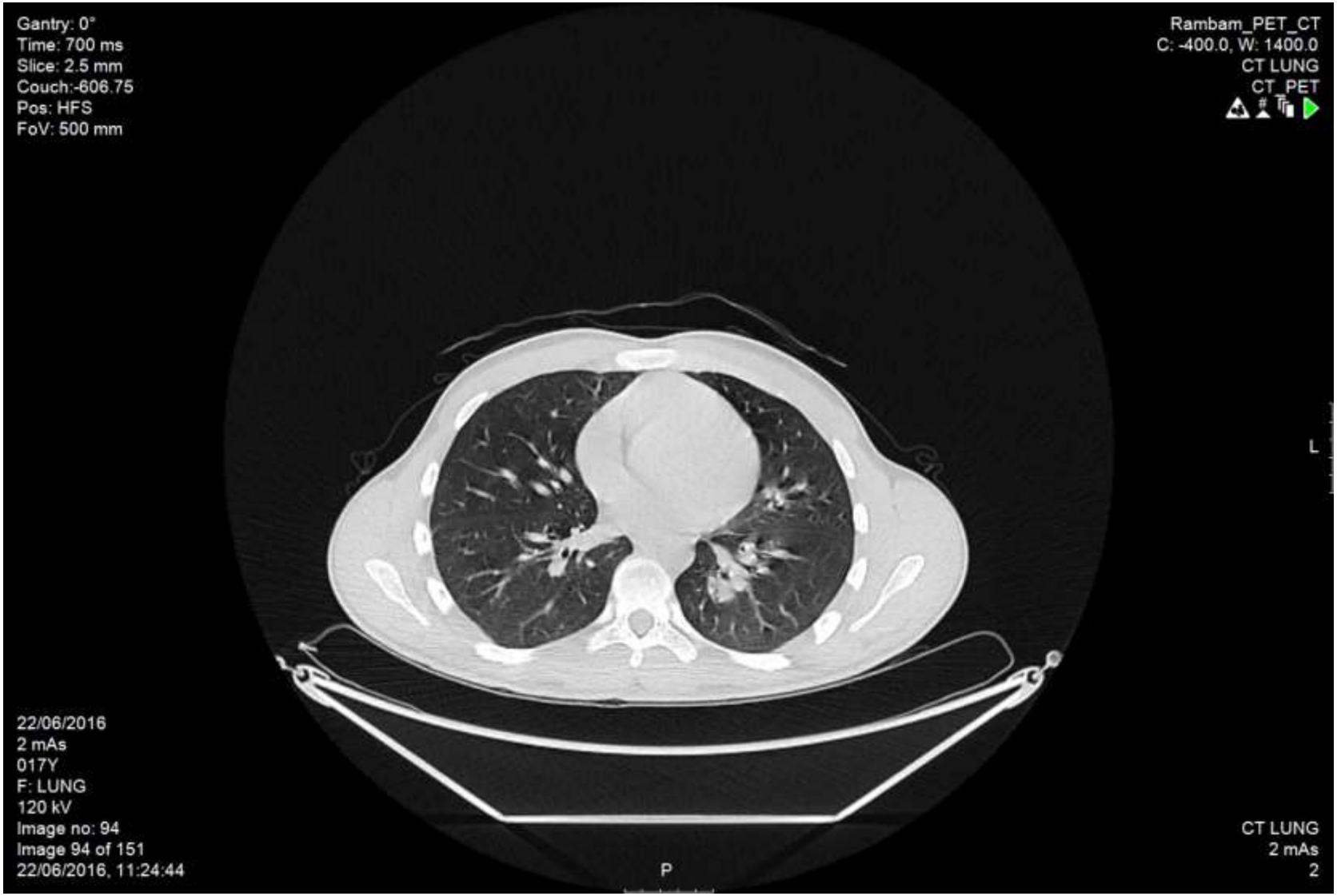
Colonoscopy -Moderate active and eosinophil rich terminal ileitis- Findings may also be associated with but are not diagnostic of IBD

TTE- N

ACE-N

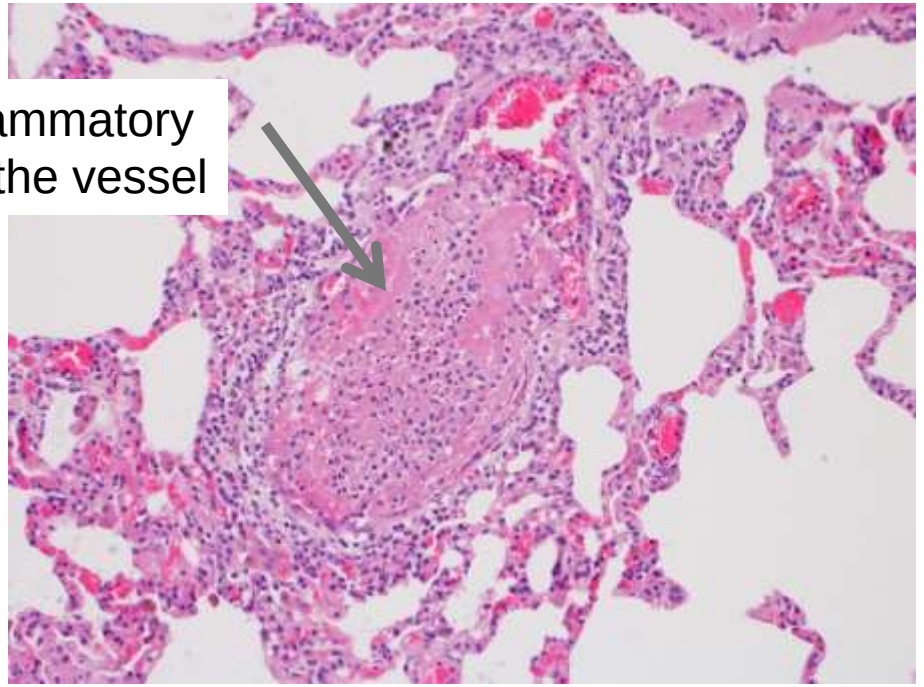
PPD- N

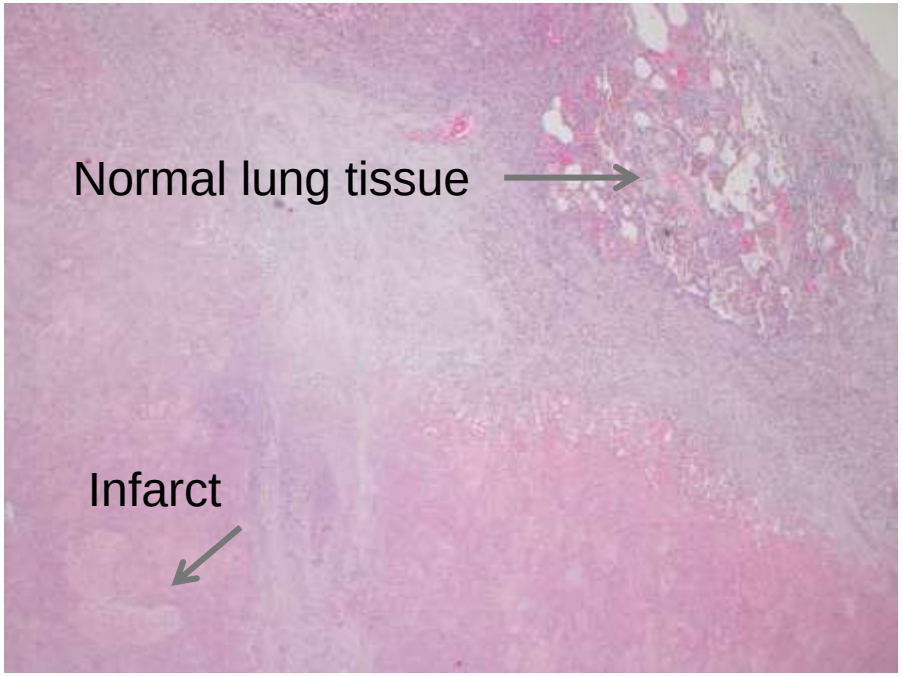
PET CT



PET CT – Bill lung infiltrate and uptake

Open lung biopsy





2 sample necrosis surrounded by fibrosis with hemosiderin in the alveolar space.
No evidence for vasculitis or microorganism.
Emboli? Thrombus ?

WORK UP AT RAMBAM AND FOLLOW UP

He was started with pulse MP with dramatic improvement in lab and clinical symptoms with gradual tapering down

Gradually dropping prednisone dose to 15 mg on that dose started to develop Fx again

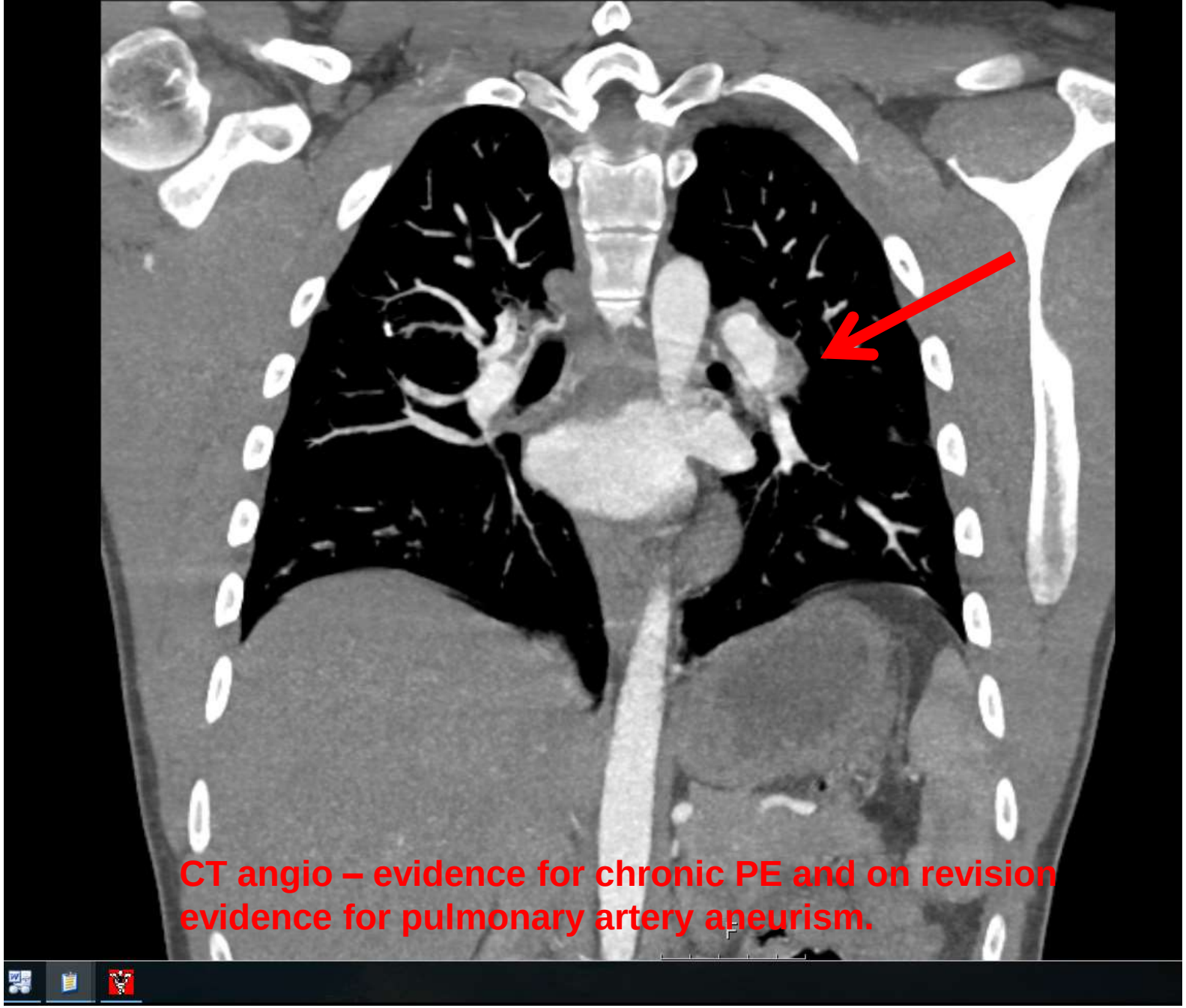
DIFFERENTIAL DIAGNOSIS

Problems list:

- FUO
- high inflammatory markers
- pulmonary infiltrate – evidence for emboli?
- recurrent epididymitis

Differential diagnosis

- PAN
- Behcet
- IBD


CT angio – evidence for chronic PE and on revision evidence for pulmonary artery aneurism.

HLAB51 –pos

Pathergy test – Neg

Eye exam – mild intermediate uveitis

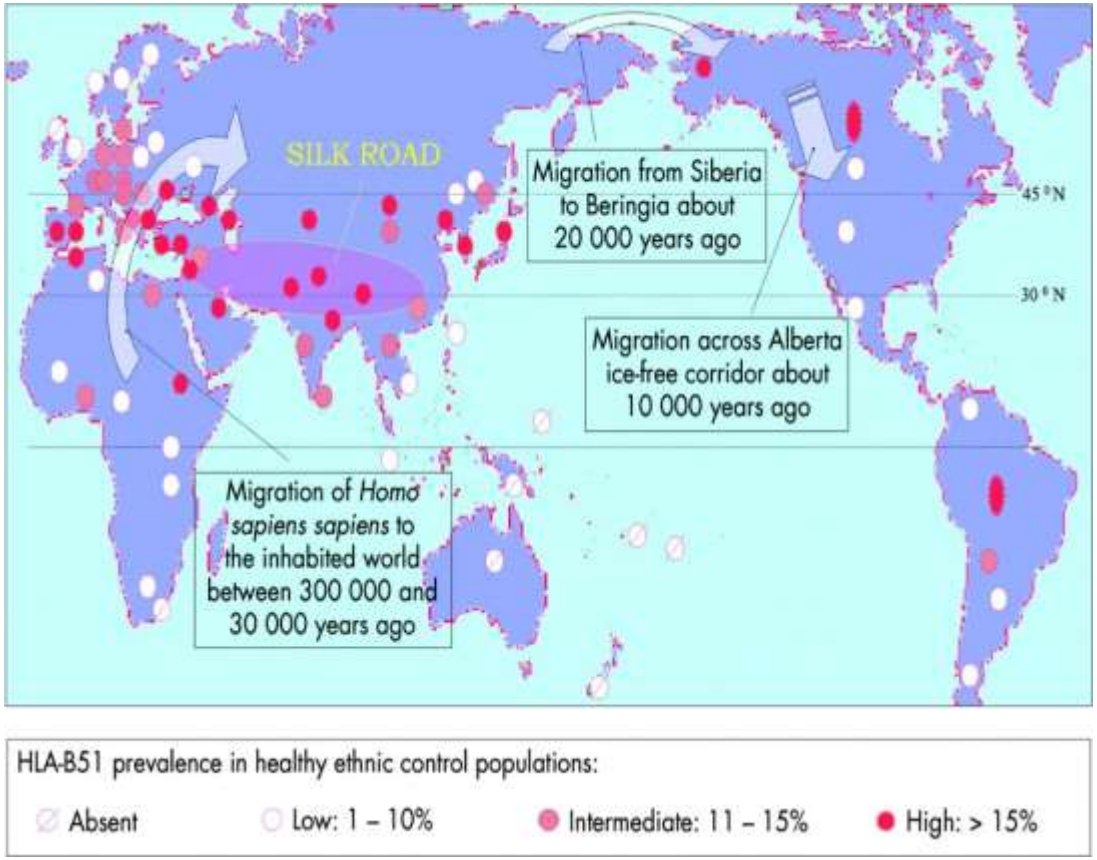
DIAGNOSIS

Behçet's disease

(Hughes–Stovin syndrome)

BEHÇET'S DISEASE

- **Behçet's disease (BD) is a multisystem disorder characterized by skin mucosa lesions**
- **It may also involve the eyes, blood vessels, joints, gastrointestinal system, and central nervous system(clusters)**
- **In those if Mediterranean &middle easter origin Behçet's disease is more common in men in Asia more in women**
- **The symptoms of Bechet's disease tend to be more severe in men**

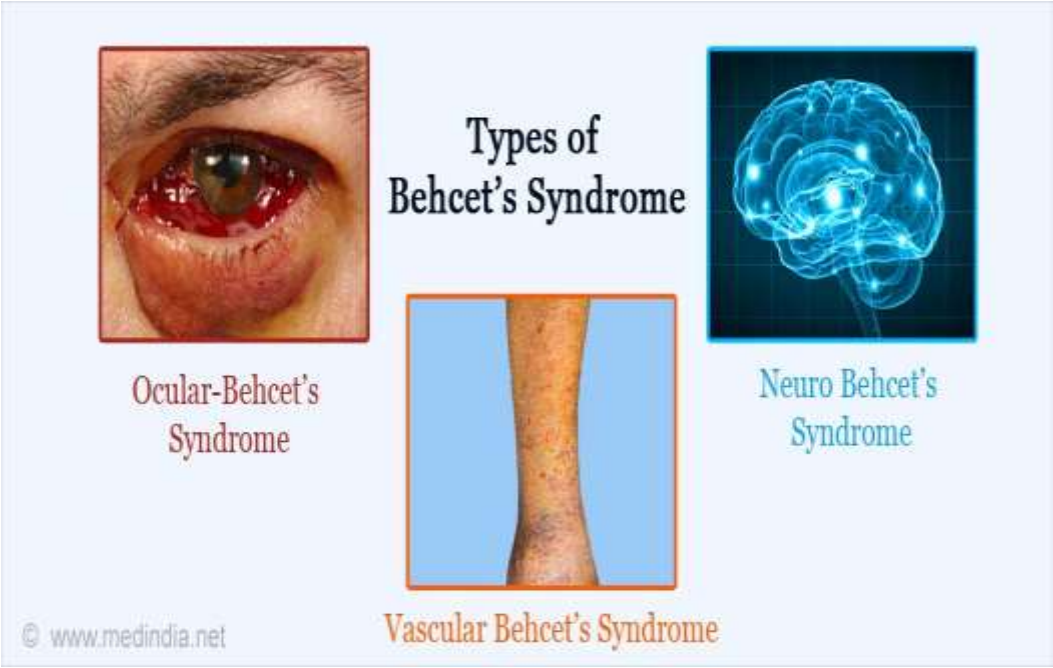


BEHÇET'S SYNDROME INTERNATIONAL STUDY GROUP CRITERIA

Required Criteria

Recurrent oral ulcerations: at least 3 times 12 month period

Minor Criteria



A. Recurrent genital ulcer

B. Eye lesion: anterior uveitis, posterior uveitis, or cells in vitreous ,retinal vasculitis

C. Skin lesions: erythema nodosum seudofolliculitis or papulopustular lesions, or acneform nodules

D. Positive pathergy test

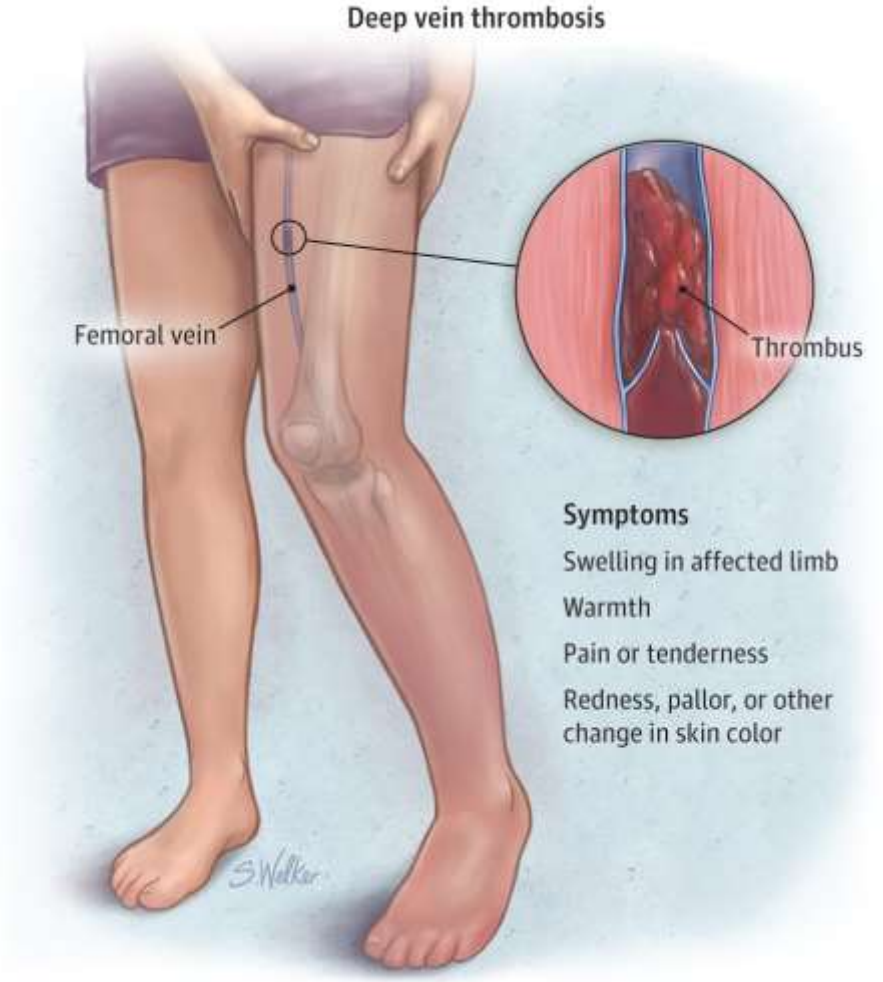
CONSENSUS CLASSIFICATION CRITERIA FOR PEDIATRIC BEHÇET'S DISEASE FROM A PROSPECTIVE OBSERVATIONAL COHORT: PEDBD

Item	Description	Value/item
1	At least 3 attacks/year	Recurrent oral aphtosis
1	Typically with scar	Genital ulceration
1	Necrotic folliculitis, acneiform lesions, erythema nodosum	Skin involvement
1	Anterior or posterior uveitis, retinal vasculitis	Ocular involvement
1	With the exception of isolated headaches	Neurological signs
1	Venous thrombosis, arterial thrombosis, arterial aneurysm	Vascular signs

Three of 6 items are required to classify a patient as having pediatric BD

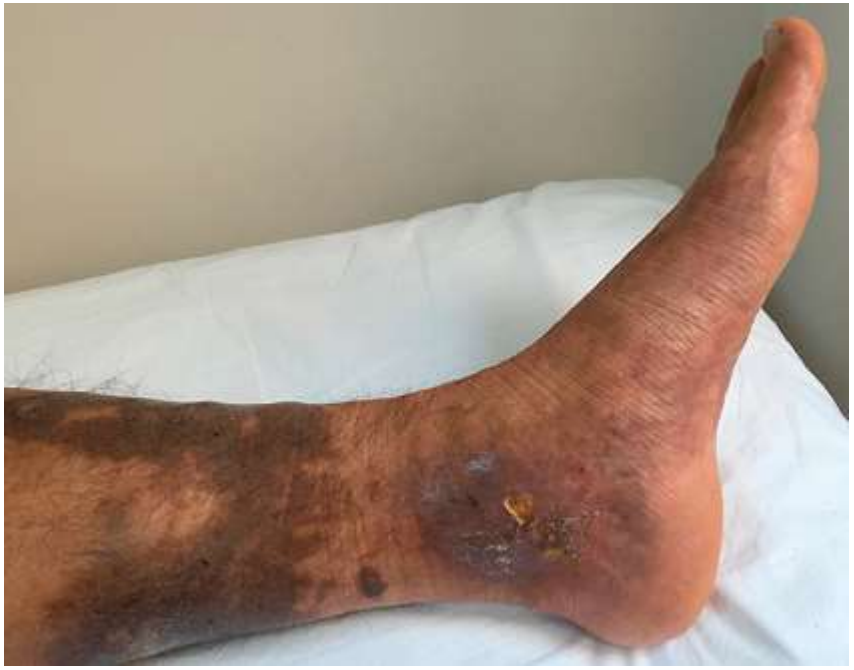
BEHÇET'S VASCULAR INVOLVEMENT

- **BD is unique among the vasculitides and it affect mainly the venous rather than the arterial**
- **The thrombotic tendency is associated with vascular inflammation and not with thrombotic factors**
- **The most common place is the lower extremely but IVC,SVC, hepatic vein, cerebral venous sinus and the r. side of the heart**



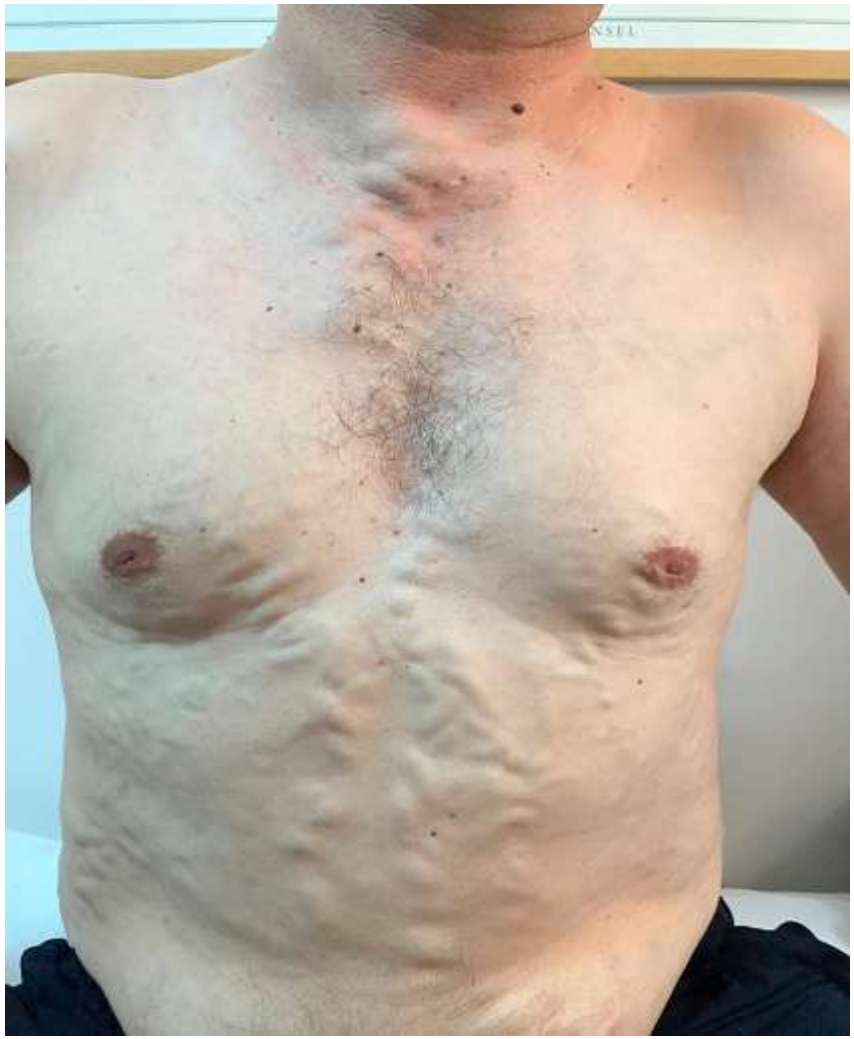
BEHÇET'S VASCULAR INVOLVEMENT

- **Frequency range from 5-40% (our series 15%)**
- **75% within 5 y's of disease onset (20% simultaneously)**
- **Pathology: inflammatory thrombus formation typically adherent to the inflamed vessel wall, tissue like thrombous usually not complicated by thromboembolism**
- **<u>Outcome</u> : relapsing course 20% in 1st years 40% in 2nd year**
- **Damage due to vascular stasis**



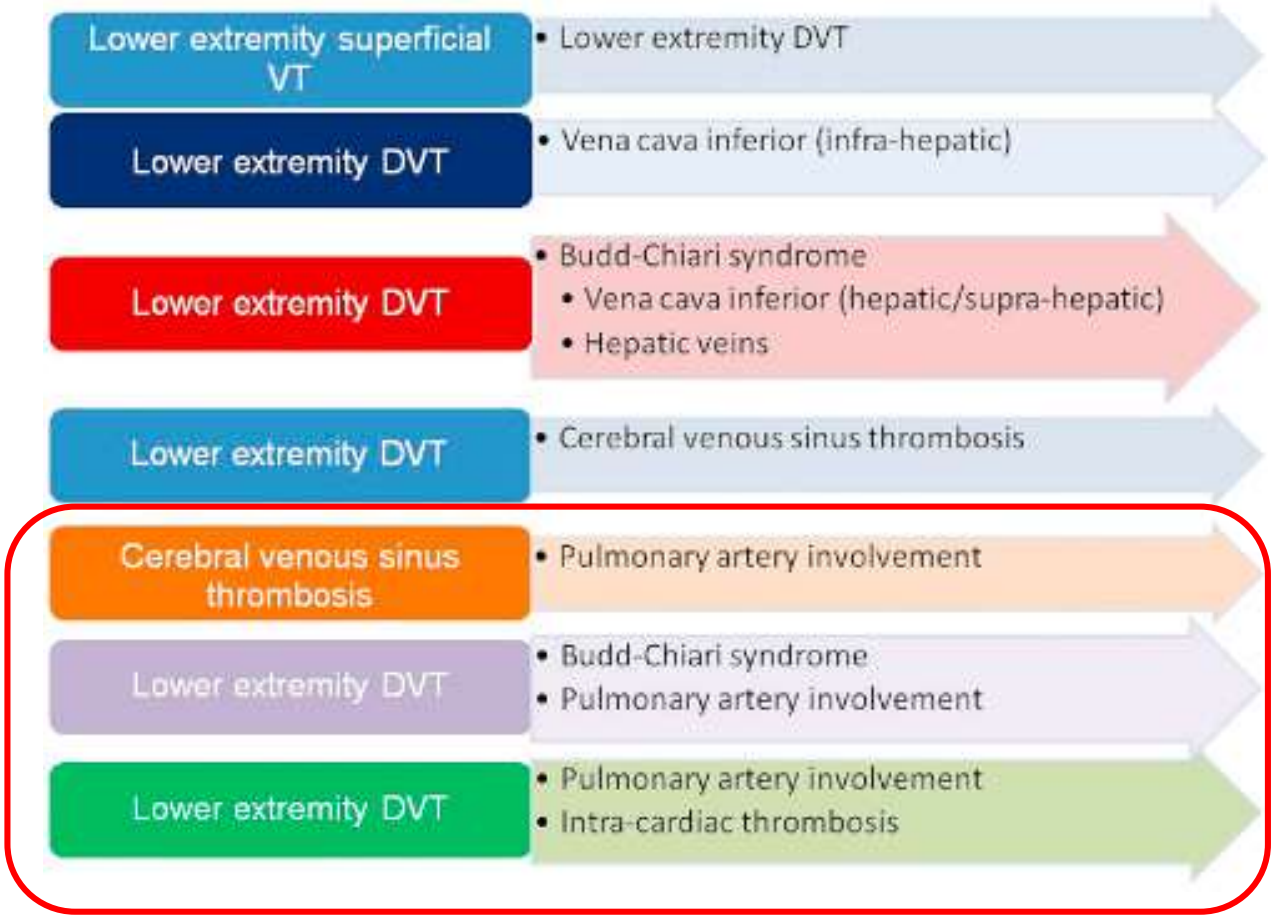
DIFFERENTIATE VASCULAR BD INVOLVEMENT VS NON BD CAUSE

- **BD are more likely to be male and younger**
- **BD more relapses, less complete recanalization, more collateral formation, and more bilateral involvement**
- **Both superficial and deep veins are involved**
- **Post-thrombotic syndrome and venous claudication are considerably more frequent**



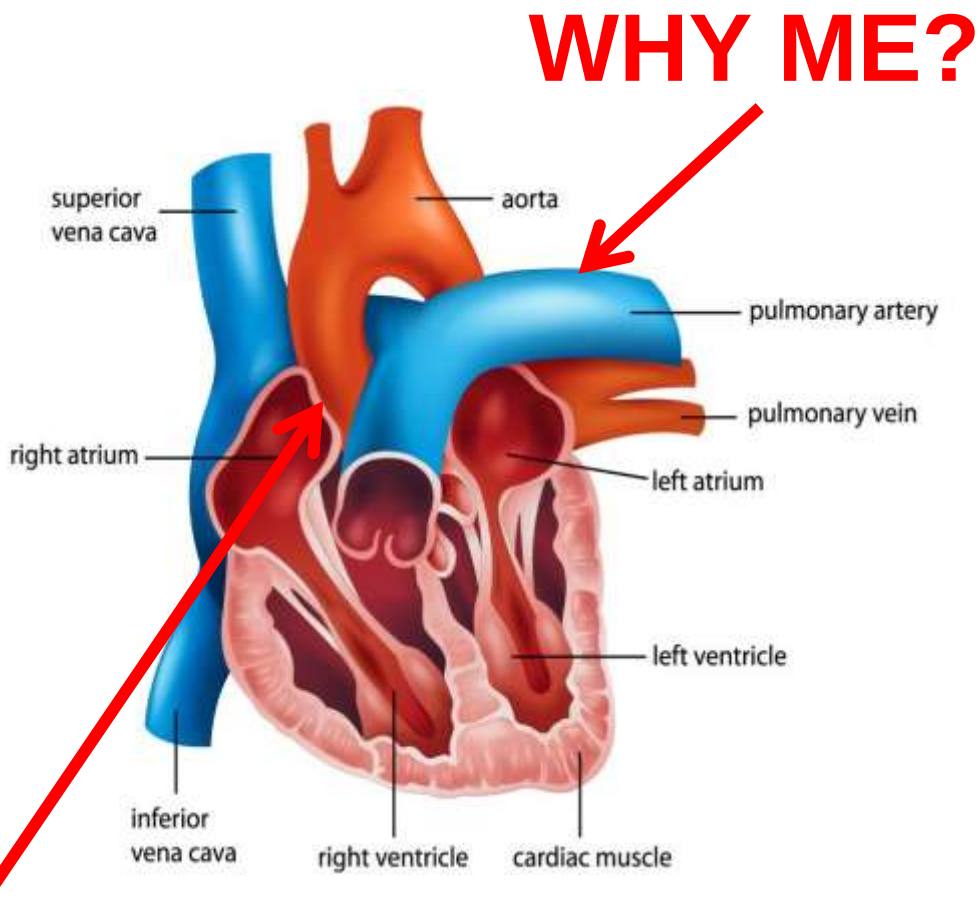
BEHÇET'S VASCULAR INVOLVEMENT

Several types of vascular involvement may accumulate in the same individual



BEHÇET'S ARTERIAL INVOLVEMENT

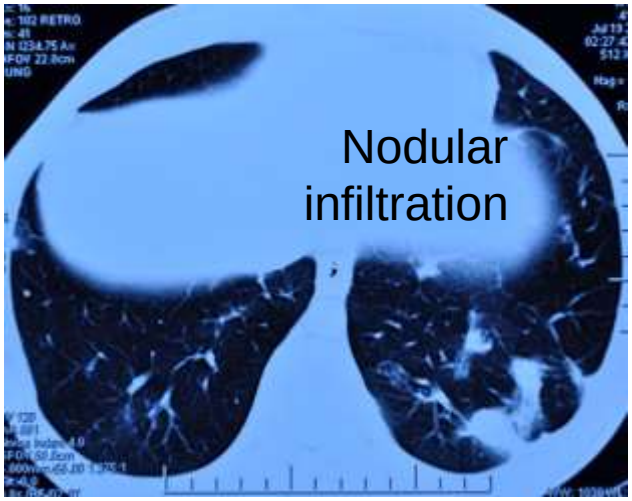
- Pulmonary artery resemble venous structure because of thinner walls less elasticity and lower pressure
- Vascular involvement is seen mainly among men
- Arterial disease is manifest mostly in the form of aneurism and rarely as thrombotic occlusion
- Aorta and peripheral artery can also be involved but rarely

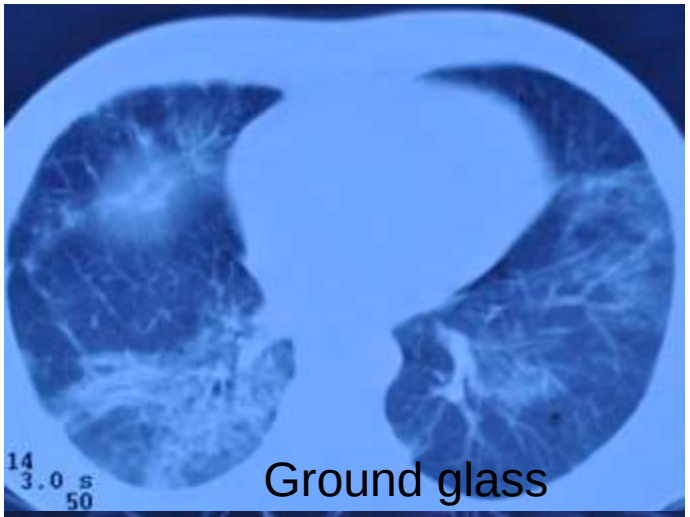


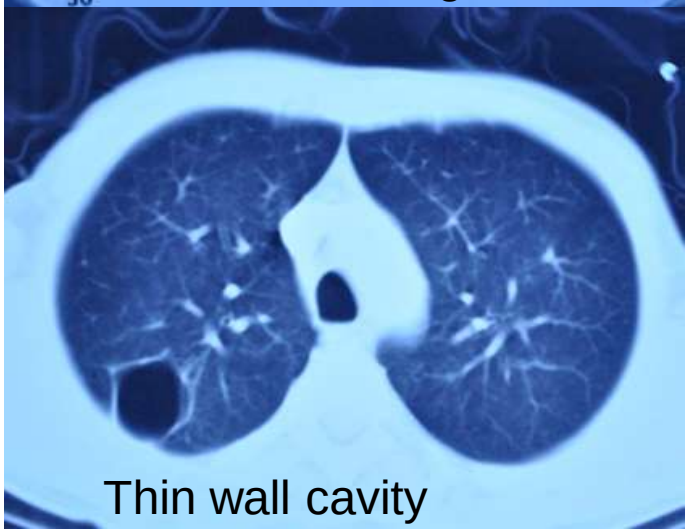
You are not alone

PULMONARY INVOLVEMENT WITH BEHÇET'S

- **The true prevalence of pulmonary involvement is unknown but range from 1-18%**
- **Pulmonary artery aneurism and pulmonary artery thrombus are the most frequent one and occur usually within few years of disease onset**







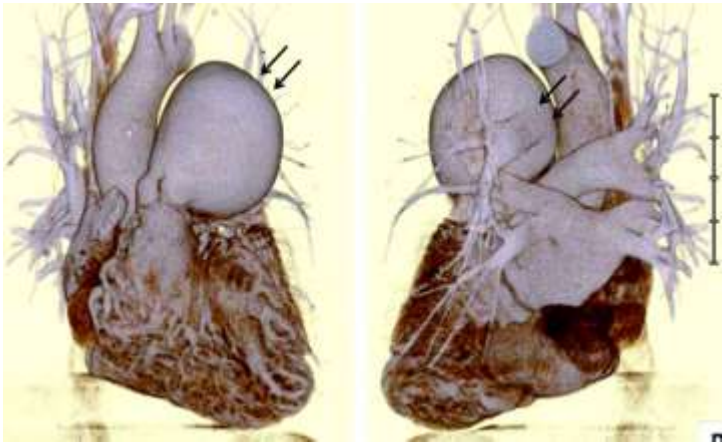
Most of the lesion in the inferior lobe similar to the arterial lesion

PULMONARY ANEURISM

- M>F
- Prevalence -1%
- The most common form of arterial involvement
- Wide range of parenchymal lesion

(nodule, consolidation and cavities) can be part of it as well

- Usually occurs at presentation or within 2 years
- Strongly associated with CNS veins involvement, DVT , and intra cardiac thrombosis
- Pulmonary artery involvement is usually multiple, and involves mostly descending branches of the pulmonary artery



“in situ “ pulmonary artery thrombosis observed in 1/3 of the patients, fever and high acute phase response are typical

TREATMENT OF PULMONARY ANEURISM

Pulse methylprednisolone for 3-5 days

Prednisone 1-2mg/kg tapering gradually for at least 6 month

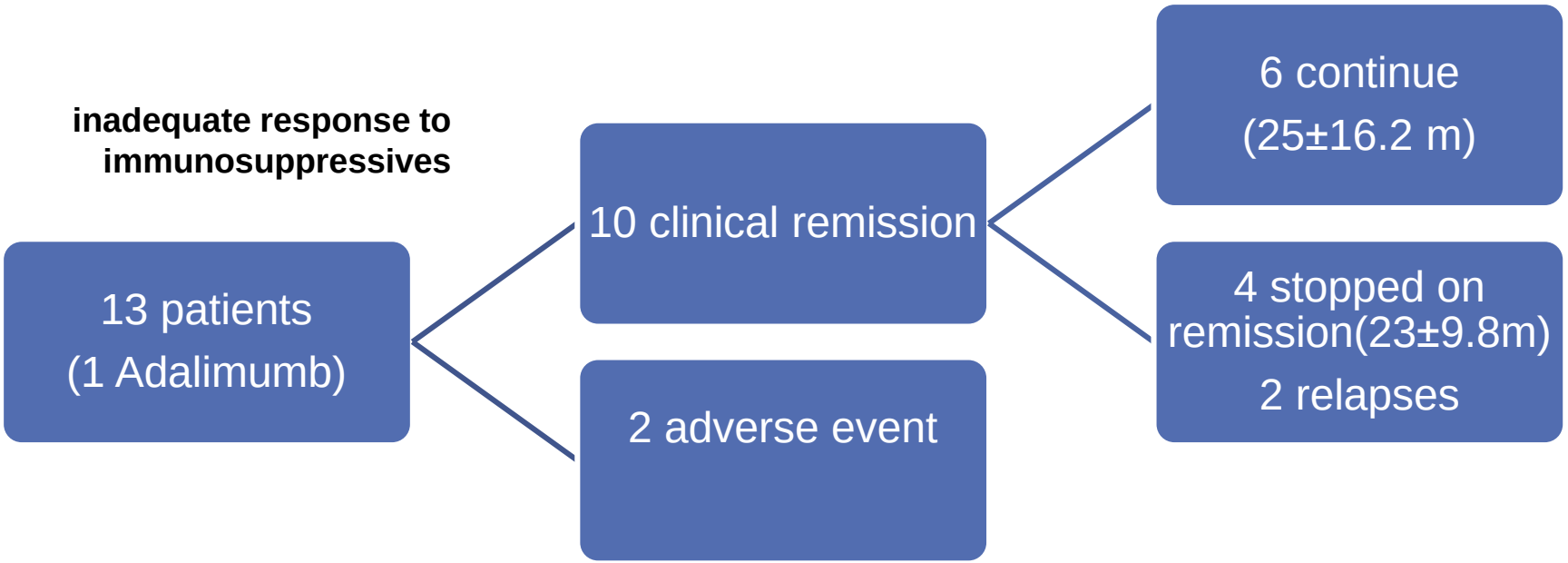
IV pulse cyclophosphamide 1gr/m^2 for 6-12 month

Remission maintained with Azathioprine 2.5mg/kg/d

Resistance cases anti TNF

Seyahi et al best practice and research clinical rheumaology 2016
Hamuryudan et al Seminar Arthritis & Rheum 2015

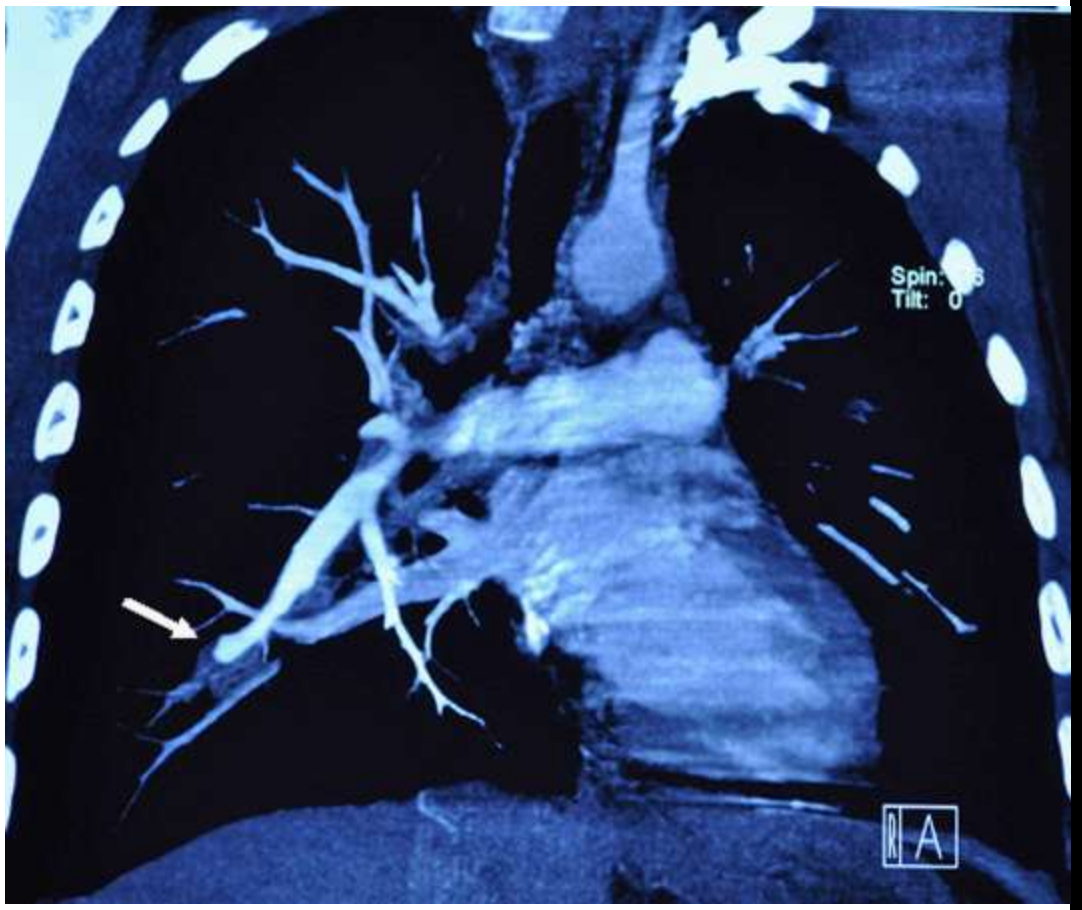
TREATMENT OF PULMONARY ANEURISM ANTI TNF



Pulmonary artery involvement in Behçet's syndrome: Effects of anti-Tnf treatment Vedat Hamuryudan Seminar in Arthritis and Rheum 2015

PROGNOSIS OF PULMONARY ANEURISM

- Mortality rate is 25%
- In up to 70% arterial lesion could disappear with immunosuppressive therapy
- Bronchial arterial collaterals could be a cause for hemoptysis on remission



PROGNOSIS OF PULMONARY ANEURISM

- 47 patients with pulmonary aneurism (41-M 6-F)
- Mean age at diagnosis was 29 ± 8 years
- Disease duration to the onset of pulmonary artery involvement was 3.6 ± 4.8 years
- Hemoptysis was the most common presenting symptom (79%)(massive 40%)
- Peripheral venous thrombosis was present in 36 of 47 (77%) patients, and intracardiac thrombi in 12 of the 36 (33%) patients

After a mean follow-up of 7 years

12 of 47 (26%) patients were dead; patients with larger aneurysms were more likely to die

16/35 (34%) of the remaining patients were symptom free, and the remaining 40% had mild dyspnea (13/47) and/or small bouts of hemoptysis (8/47).

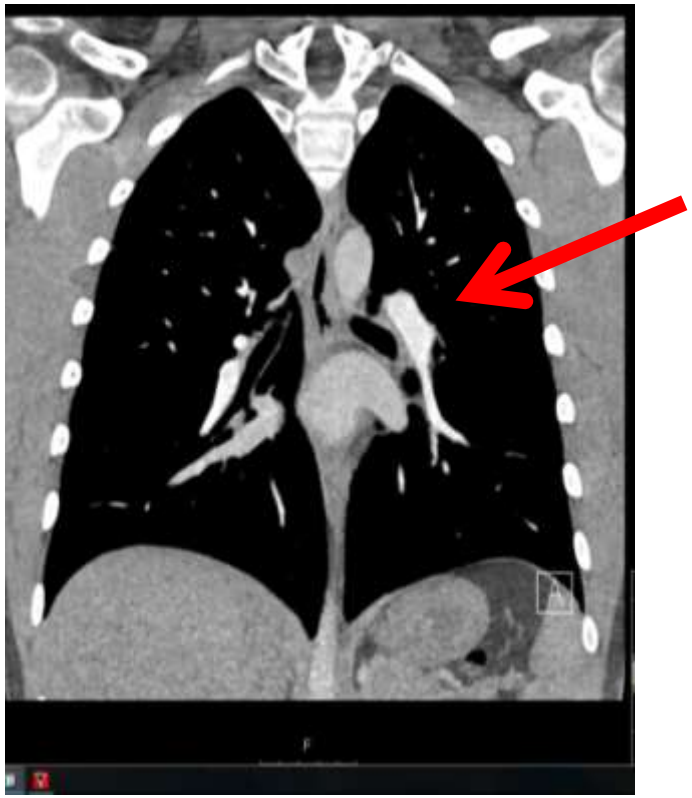
Pulmonary artery pressure may be elevated, and may indicate a poor prognosis.

Pulmonary artery involvement and associated lung disease in Behçet disease: a series of 47patients. Medicine Baltimor 2012 Seyahi et al

WRAP UP THE CASE

The patient was treated with 6 month of with pulse cyclophosphamide with good response

04/2017



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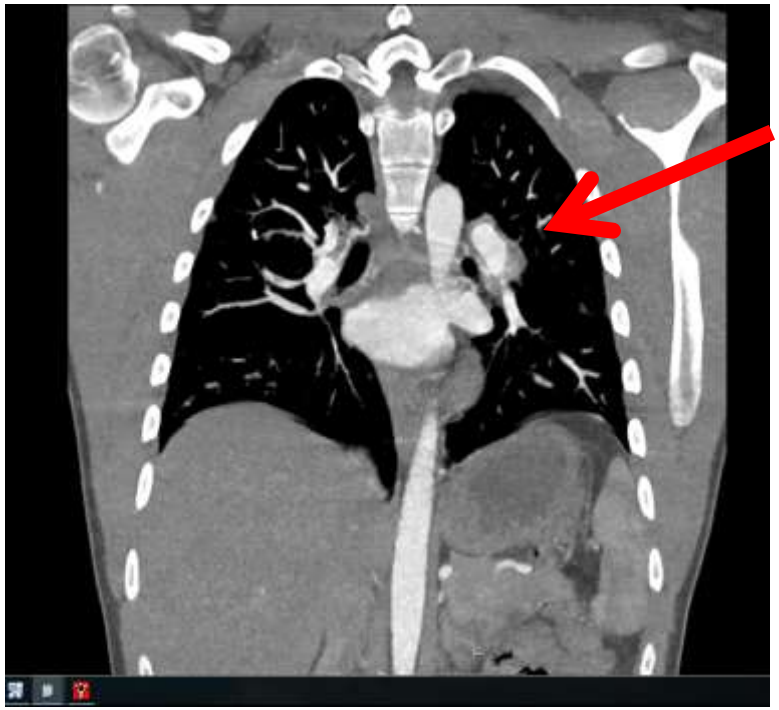

WRAP UP THE CASE

Currently on Adalimumab and Azathioprine