ESIM Winter School 2014
Case Presentation

Hacettepe University School of Medicine
Ankara/Turkey

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Patient

- T.K., 59 years old, male, married with one child, unemployed, place of birth/ residence: Karaman (Central Turkey)
- Chief complaints: Chest pain, shortness of breath, periorbital edema

History

February 2013

- Chest pain-> A cardiology center
- Angina, acute coronary syndrome
- Coronary angiography: Multivessel disease, giant aneurysms in coronary arteries
- Coronary CT angiography: Thrombosed aneurysms in each three major coronary arteries and contrast enhancement in their walls, compatible with vasculitic involvement
- Patient was referred to our rheumatology clinic.

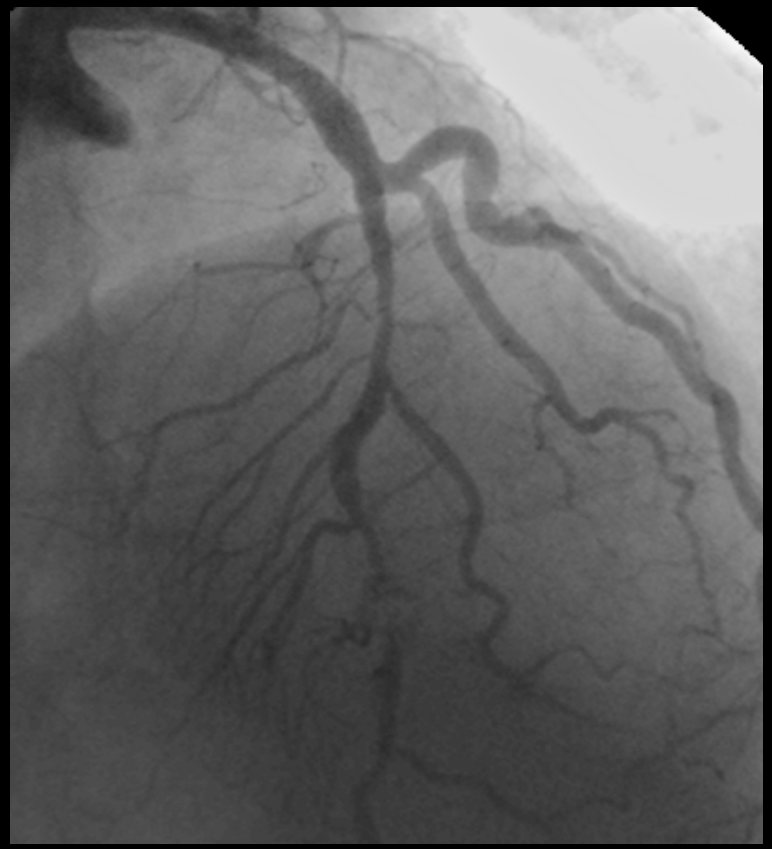
History of previous diseases

- Since 1995 followed as Graves' ophtalmopathy
- Received corticosteroids on demand, with irregular dosing schemes

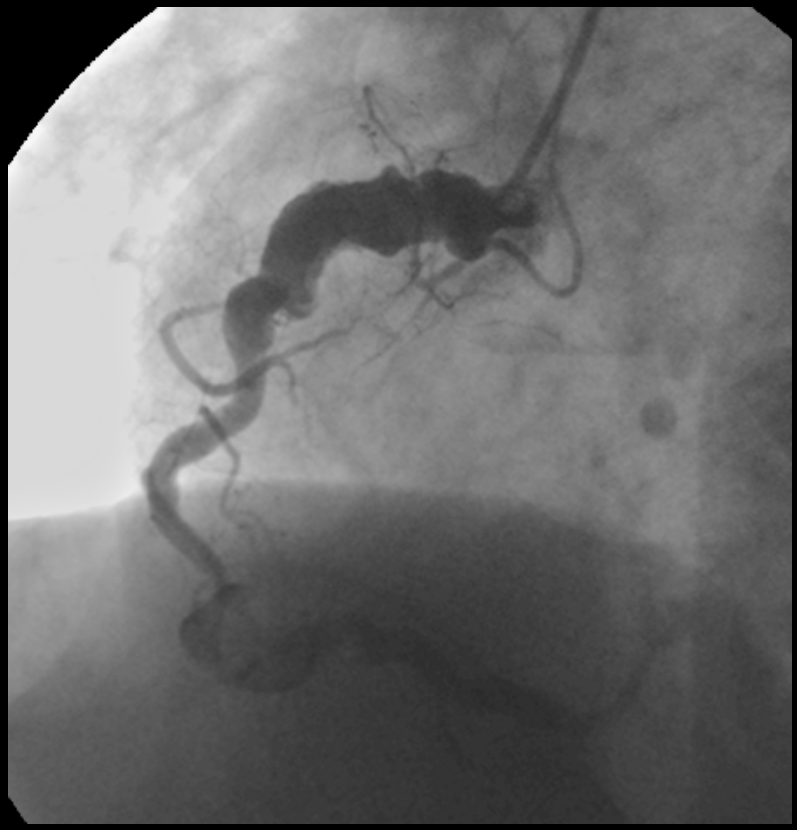
October 2012

- Orbital MRI: pseudotumor orbita? Ocular myositis?
- Pulse steroid 1 g/day for 3 days
- Euthyroid, thyroid autoantibodies unknown
- Ex-smoker

Coronary angiography

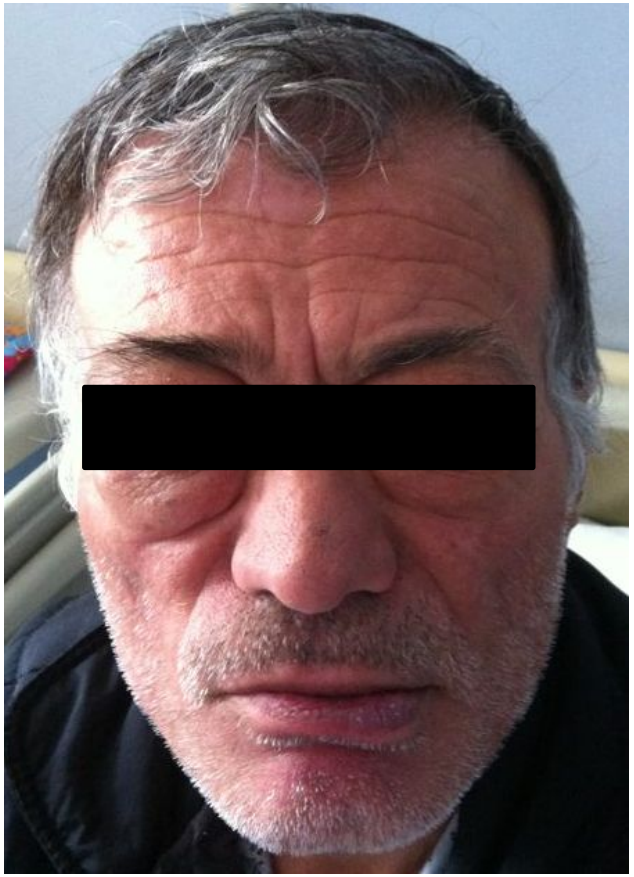


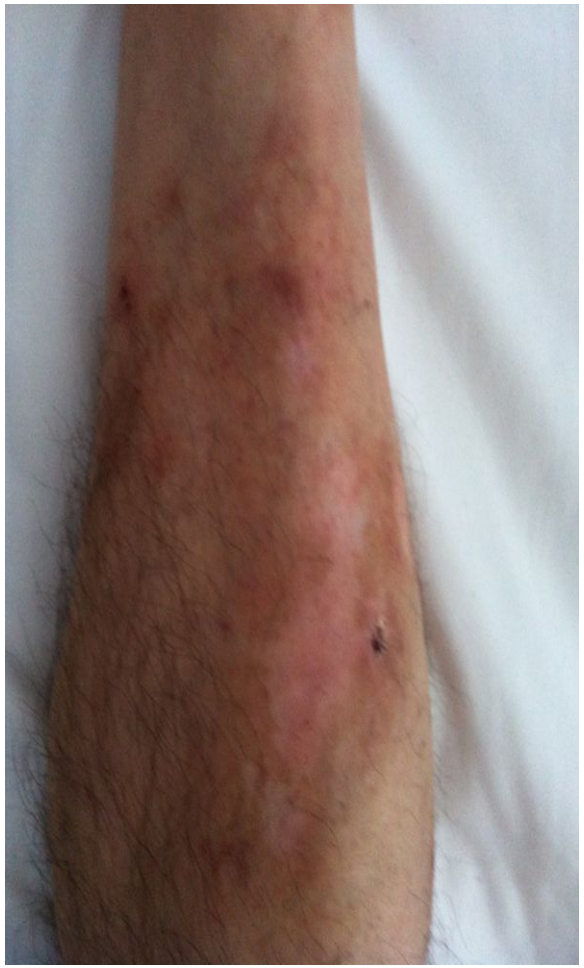
Aneurysms on circumflex and left anterior descending arteries



Giant aneurysm on right coronary artery

Physical examination





Other system examinations were in normal range

Differential diagnosis

- Atherosclerotic disease
- Prior cardiac surgery
- Behcet's disease
- Tertiary syphilis
- Eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss' disease)
- Antiphospholipid syndrome
- Takayasu arteritis
- Adult Kawasaki disease
- HIV related vasculitis

Laboratory

- Hemogram, peripheral smear, C-reactive protein, procalcitonin : Normal,
- Erythrocyte sedimentation rate: 40 mm/h

- Anti-nuclear antibody titer: 1/160, homogenous-granular
- Extractable nuclear antigens: negative, ANCA profile: negative

- Antiphospholipide/cardiolipin antibodies/lupus anticoagulant: negative

- Serum biochemistry: Normal except for albumin: 3,3 (3,5-5,5 g/dL)

- Anti-thyroid peroxidase: positive, anti-TSHreceptor antibody: negative (Thyroid USG: NO thyroiditis)

- Veneral disease research laboratory test: negative

- Creatine kinase: Normal, LDH: Normal, Ferritin: Normal

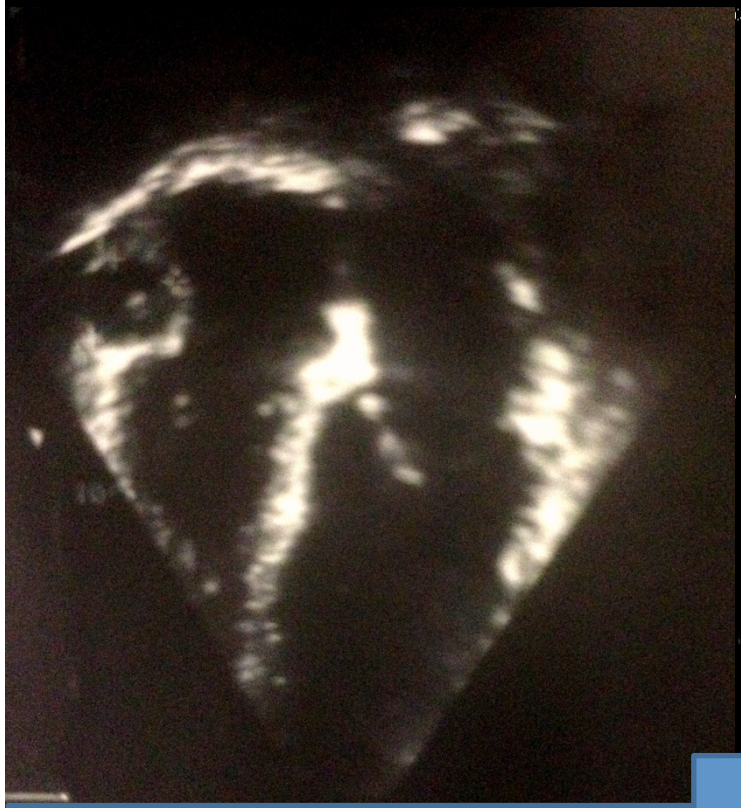
- Borrelia serology: negative , Beta2microglobulin: Normal

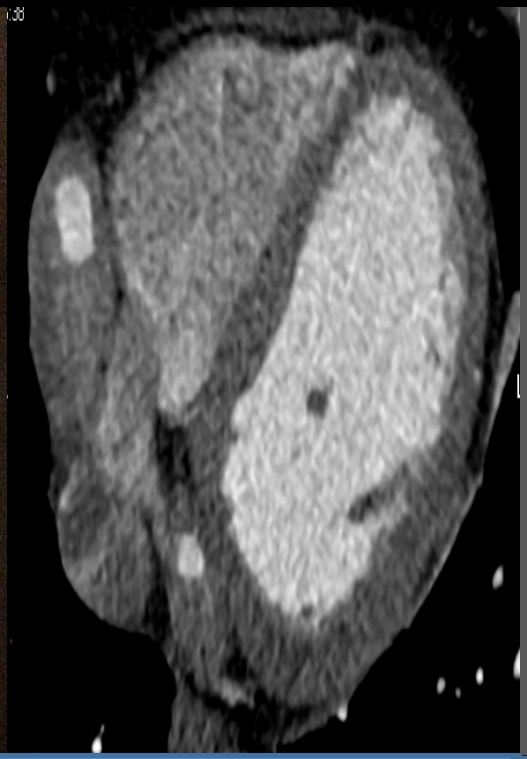
- Angiotensin converting enzyme levels: Normal

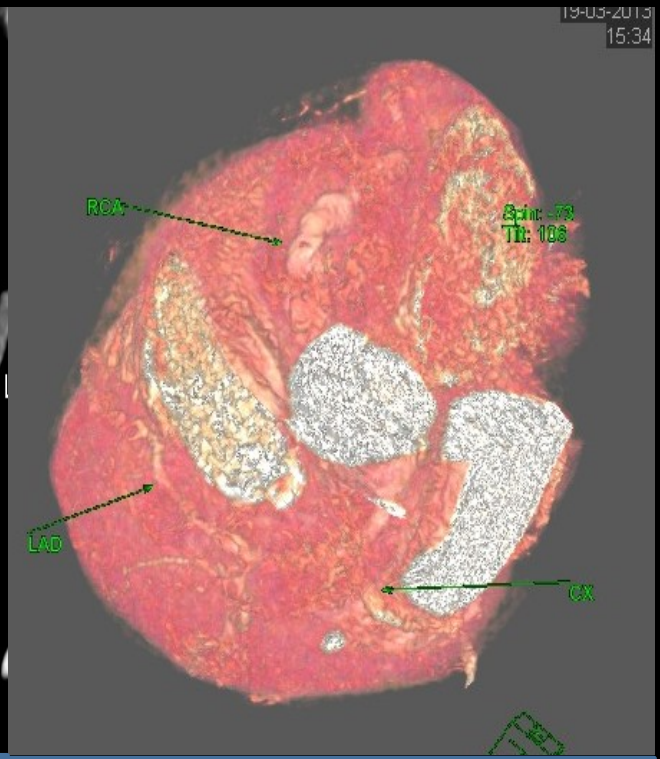
- No anomaly in urine sediment, no proteinuria

- PPD: 5 mm , Quantiferon assay: negative

Radiology





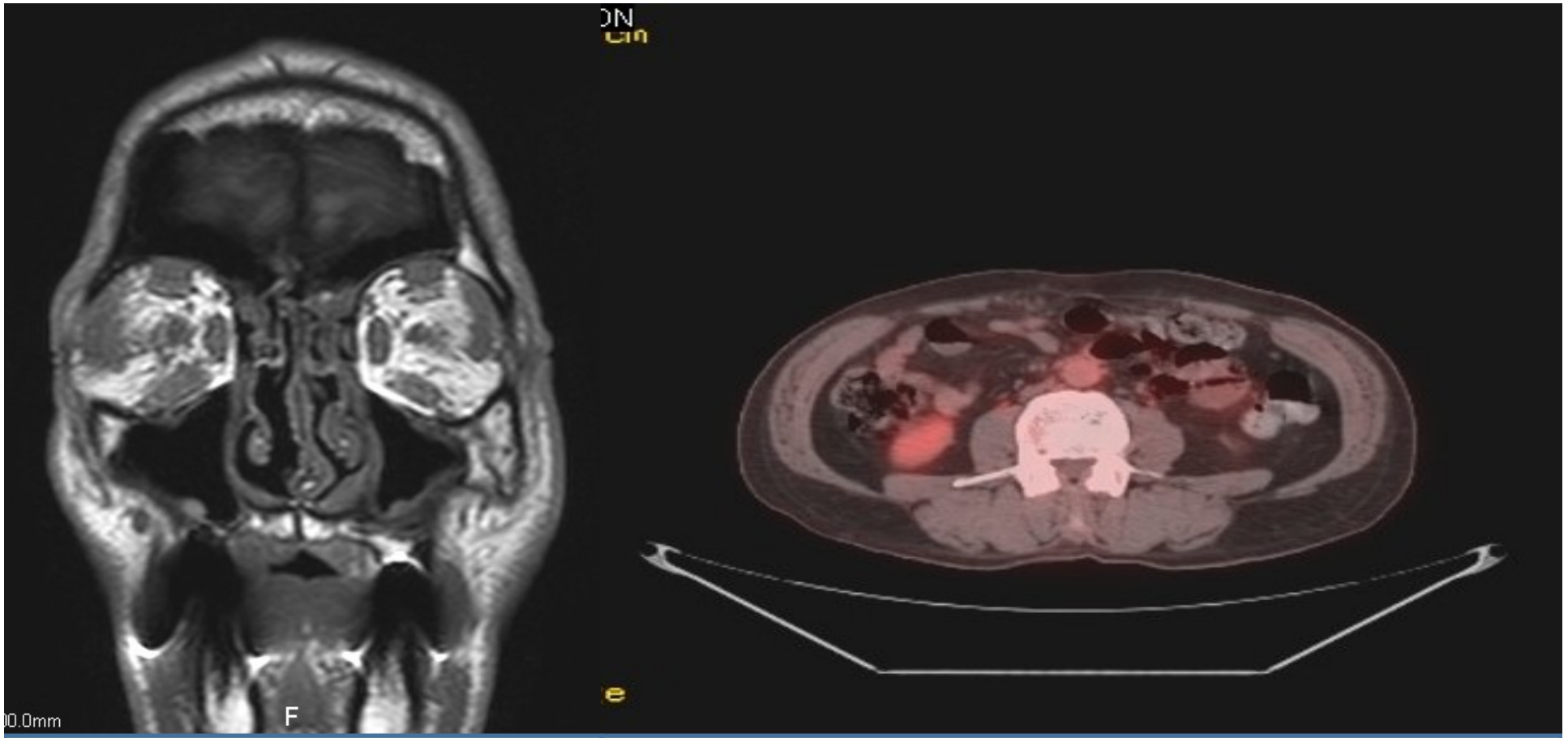


Echocardiography: Inferior and posterior wall hypokinesia, ejection fraction: %45-50, 23x25 mm cystic structure in right atrial groove

CT angiography: Contrast enhancement in aortic root

3D reconstruciton of CT angiography: Aneuyrsms and strictures in coronary arteries

Whole thoracic and abdominal aorta shows contrast enhancement, and walls are thickened, soft tissue mass like appearance around abdominal aorta (retroperitoneal fibrosis ? Periaortitis ?) mediastinal and parailiac lymphadenopathies (not shown)



Orbita MRI: Thickened extraoculer muscles, soft tissue around right optic nerve	**PET: FDG uptake alongside whole aorta, incresad FDG uptake on extraoculer eye muscles, low FDG uptake on lymphadenopathies (SUV max: 3,9 and below),**

Summary; A 59 years old male with coronary aneurysms, pseudotumor orbita, generalized lymphadenopathies, rashes

New differential diagnoses ?

- Sarcoidosis
- Multicentric Castelman Disease

Biopsies

- **Skin:** Changes compatible with vasculopathy, lymphocyte infiltration
- Lymph nodes unreachable with lesser invasive method
- High risk for general anesthesia
- No consent for bronchoscopy
- **Minor salivatory gland:** Atrophy, lymphocyte infiltration

Diagnosis

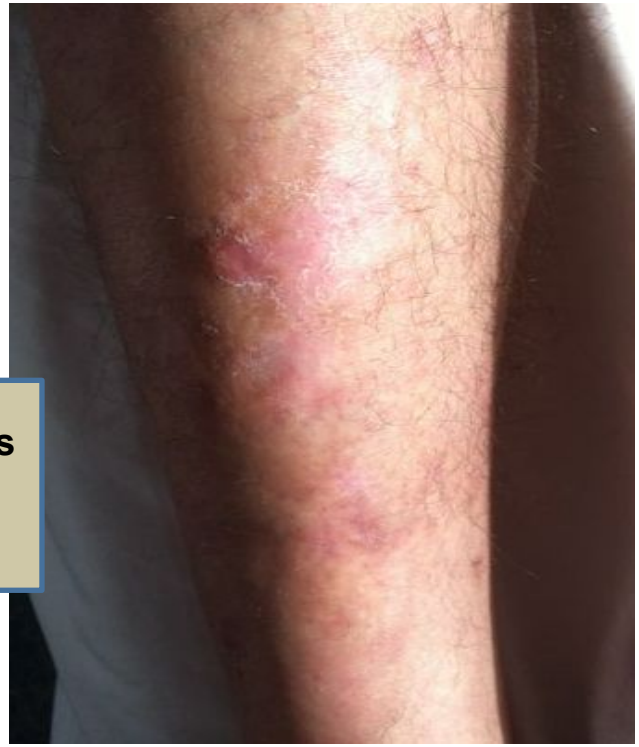
- **Total Ig G levels: 2700 mg/dL (upper 1590)**
- **Ig G4: 3300 mg/dL (upper: 126)**
- **Coronary arteritis, aortitis, pseudotumor orbita, skin and salivatory gland involvement, retroperitoneal fibrosis, generalized lymphadenopathies**

Ig G4 related disease

- Treatment regimen
  - Pulse corticosteroids + Cyclophosphamide
  - Oral corticosteroids

After treatment

Two weeks after treatment



Six months after treatment: CT angiography; stable disease
Orbita MRI: Nearly complete regression

Ig G4 related disease

- **Newly recognized disease (around 1980's)**

- **Many names;**

- **IgG4-related disease**
- IgG4-related systemic disease
- IgG4-syndrome
- IgG4-associated disease
- **IgG4-related sclerosing disease**
- IgG4-related systemic sclerosing disease
- IgG4-related autoimmune disease
- IgG4-positive multiorgan lymphoproliferative syndrome
- Hyper-IgG4 disease
- Systemic IgG4-related plasmacytic syndrome
- Systemic IgG4-related sclerosing syndrome
- Multifocal fibrosclerosis
- Multifocal idiopathic fibrosclerosis

Ig G4RD; Answer to many «idiopathic diseases of past»

- Type 1 autoimmune pancreatitis (IgG4-related pancreatitis)
- IgG4-related sclerosing cholangitis
- Mikulicz's disease (IgG4-related dacryoadenitis and sialadenitis)
- Sclerosing sialadenitis (Küttner's tumor, IgG4-related submandibular gland disease)
- Inflammatory orbital pseudotumor (IgG4-related orbital inflammation or orbital inflammatory pseudotumor)
- Chronic sclerosing dacryoadenitis (lacrimal gland enlargement, IgG4-related dacryoadenitis)→ PITFALL
- A subset of patients with "idiopathic" retroperitoneal fibrosis (Ormond's disease) and related disorders (IgG4-related retroperitoneal fibrosis, IgG4-related mesenteritis)
- Chronic sclerosing aortitis and periaortitis (IgG4-related aortitis or periaortitis)
- Riedel's thyroiditis (IgG4-related thyroid disease)
- IgG4-related interstitial pneumonitis and pulmonary inflammatory pseudotumors (IgG4-related lung disease)
- IgG4-related kidney disease (including tubulointerstitial nephritis and membranous glomerulonephritis secondary to IgG4-RD)
- IgG4-related hypophysitis
- IgG4-related pachymeningitis

It is much more important to know what sort of a patient has a disease than what sort of a disease a patient has.

William Osler

Ig G4RD; Pathology and other features

IgG4-related disease is a newly recognized fibro-inflammatory condition characterized by several features: a tendency to form tumefactive lesions at multiple sites; a dense lymphoplasmacytic infiltrate rich in IgG4$^+$ plasma cells; storiform fibrosis; and—often but not always—elevated serum IgG4 concentrations.

Consensus statement on the pathology of IgG4-related disease *(Modern Pathology* (2012) 25, 1181–1192)

- **Excellent response to steroids**
- **Relapses common with decreasing steroids**
- **Many steroid sparing drugs used; azathiopurine, cyclophosphamide, mycofenolate, RITUXIMAB**


Thank you…