Fever & Lymphadenopathy in a young CF patient

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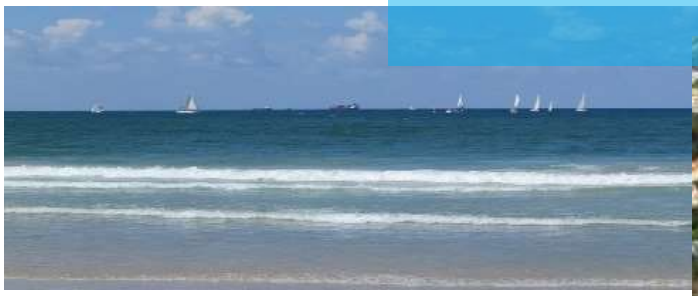


Preview

- Case presentation
- Diagnosis
- Literature review
- Summary & follow up
- Conclusions and take home message

Case Presentation

- 20 years old female
- CF diagnosis at birth (meconium ileus)
- Mutations: F508del/W1282X
- Hypothyroidism - 2008
- CFRD – 2013
- Microbiology: MRSA + *Alcaligenes xylosox* Pseudomonas (+/-)

Case Presentation

- **1/3/2015:** Fever, cough: ***influenza A*** (PCR pos), Rx oseltamivir, ciprofloxacin, rifampin
- **29/3/2015**: Hospitalization due to pulmonary exacerbation treated with: vancomycin & piperacillin/tazobactam
- Sputum cultures: MRSA & *Alcaligenes xyloxidans*

<u>Pre- discharge spirometry: **(9/4/15)**</u>

- FVC=2.95L (83%)
- FEV_1=2.24L (72%)
- FEF_{25-75}=1.68L (41%)

Case Presentation

- Three days after discharge: fever and cervical swelling. **Hospitalized 13/4/15**
- No cough or sputum production

PE: well appearing, no respiratory distress.

Vital signs: 38.2°C, HR:143, B.P: 100/66, SAT:97%

- Submandibular and cervical lymph node enlargement with mild tenderness
- Lungs were clear to auscultation

Case Presentation

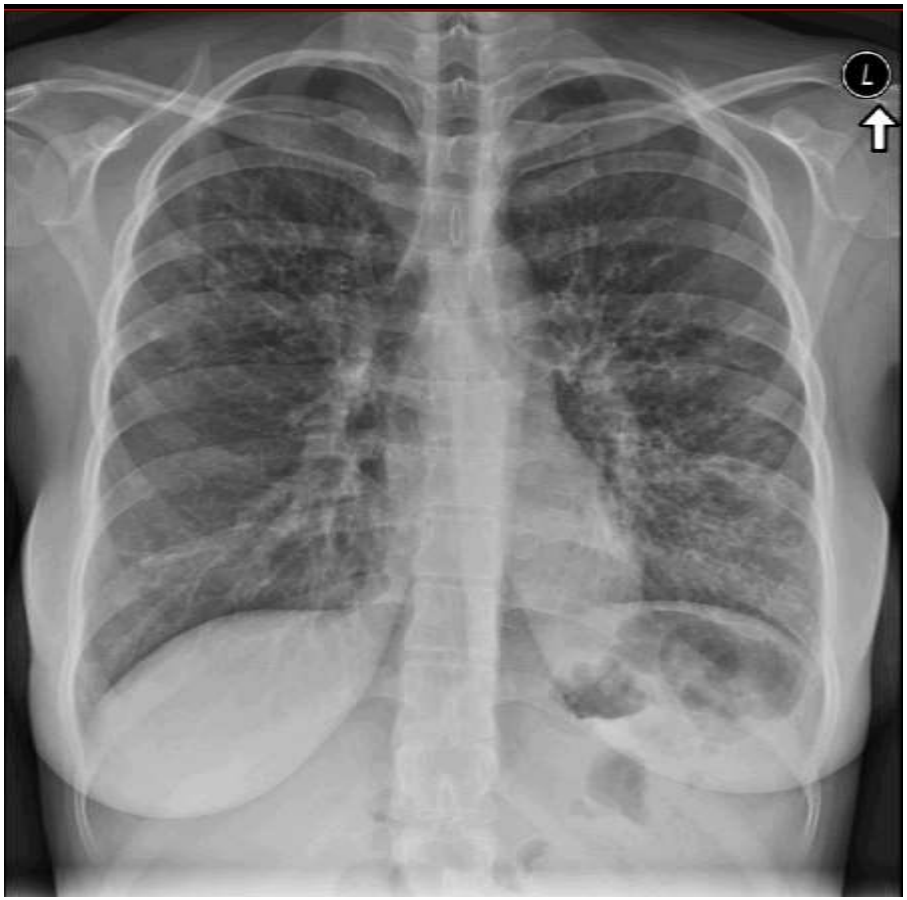
LAB:

- WBC=15400 /µl, PMN=85%
- Hemoglobin=12.6 g/dL, platelet-normal.
- CRP=13.5 mg/dL (normal 0-0.5)
- Electrolytes, kidney function- normal
- Lactate dehydrogenase (LDH)=294 U/L

Cervical US:

Enlarged irregular cervical lymph nodes

CXR 13/4/15



Case Presentation

Treatment: meropenem and linezolid

- During the next days: fever persists.

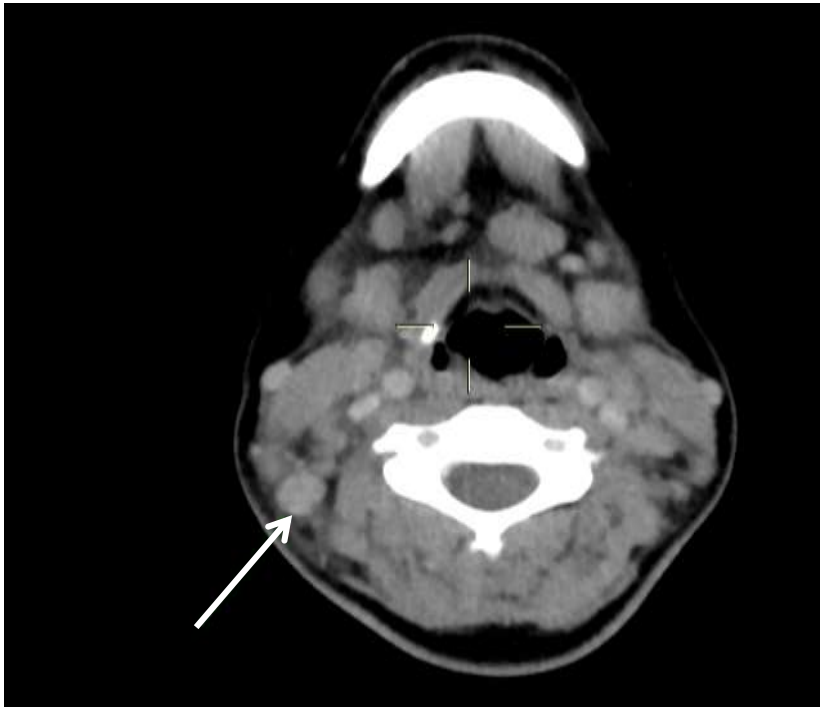
LAB: WBC↓= 5360 /µl, CRP= elevated (~10 mg/dL)

LDH↑↑= 1164 U/L

Sputum cultures (including mycobacterial): MRSA

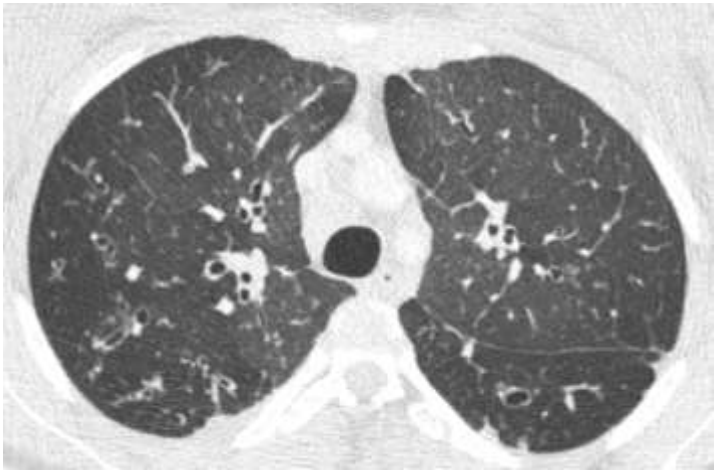
CT : neck & lung

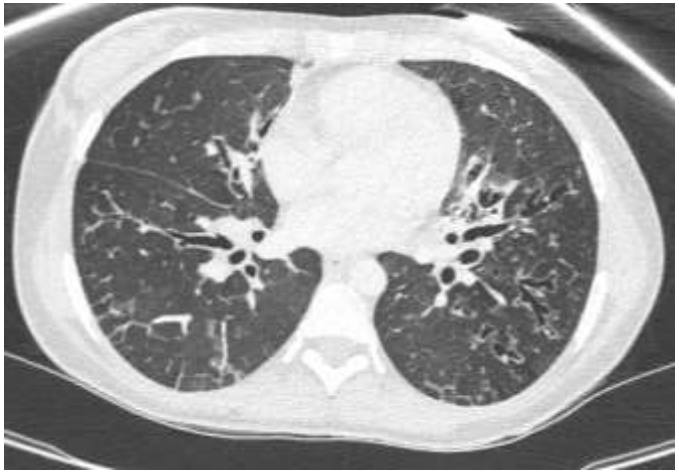
CT Neck 17/4/15

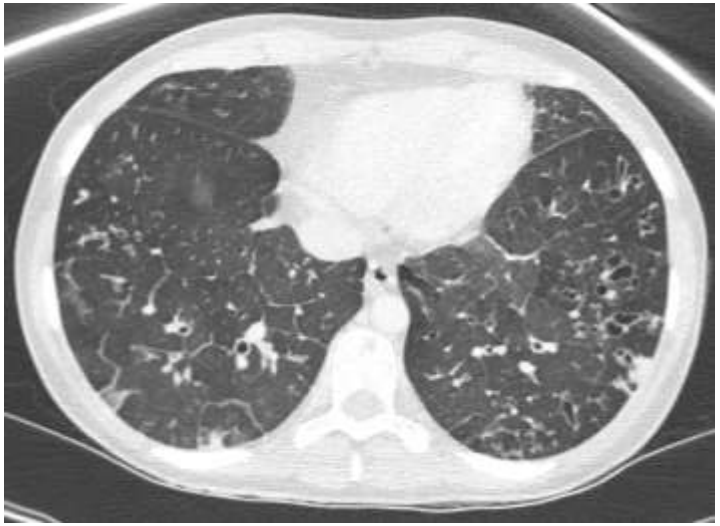


Neck CT scan demonstrating an enlarged cervical lymph node (arrow)

HRCT chest 17/4/15







Summary & Differential diagnosis

Fever, lymphadenopathy, CRP/LDH↑, Lungs: Ø
Infectious:

- Mycobacterial (TB, NTM)
- Viral infections (EBV, CMV, HIV)

Lymphoproliferative disorders:

- Lymphoma
- Acute Lymphoblastic Leukemia

Collagen vascular disorders

- Juvenile Idiopathic Arthritis
- Systemic Lupus Erythematosus

Case Presentation

Biopsy of cervical lymph node: cultures and gene amplification for bacteria, mycobacteria and fungi.

Deterioration: patient appeared ill, weakness, cough.

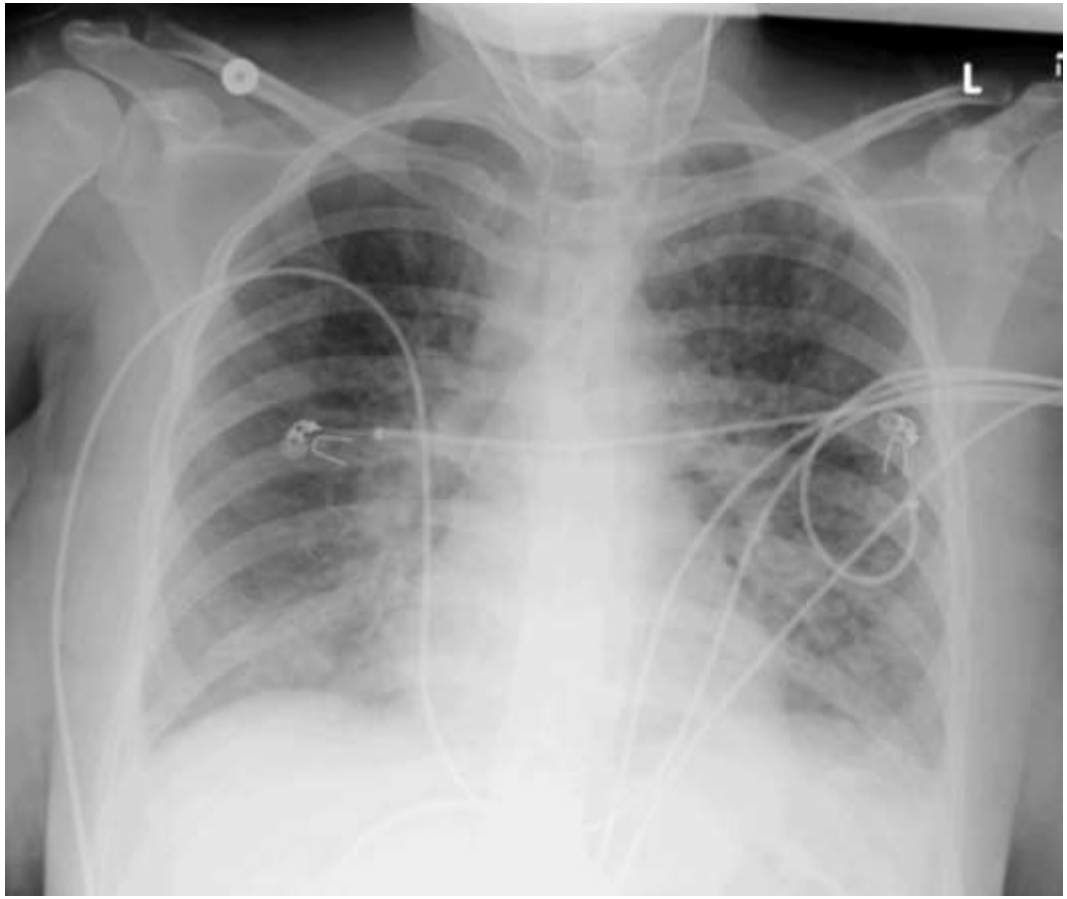
PE: tachypnea (30/min), tachycardia (124/min) hypotension (67/36 mmHg), and desaturation (84%)

- Lungs: new bilateral crepitation's

LAB:

- ABG: PH=7.53, PaC02=30, PaO2=46, HC03=27.3
- CBC: ↓Hb= 10.2 g/dL, ↓PLT = 75,000 /µl, WBC = 6000
- PT%=58 (70-140), PTT: 36.4 (22-36 sec), INR=1.44 (0.8-1.3) fibrinogen 195 (200-800mg%)
- Hypoalbuminemia -2.6 g/dL.

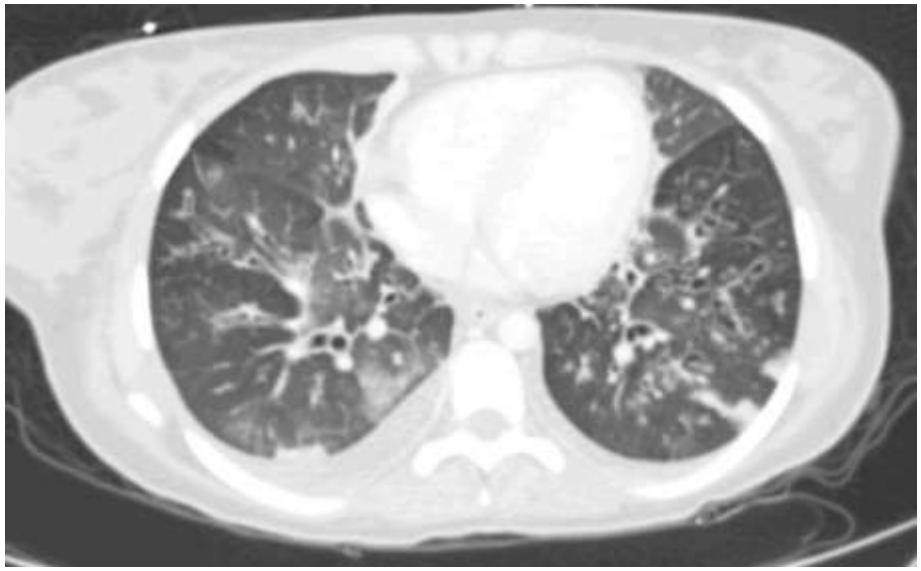
CXR-19/4/15

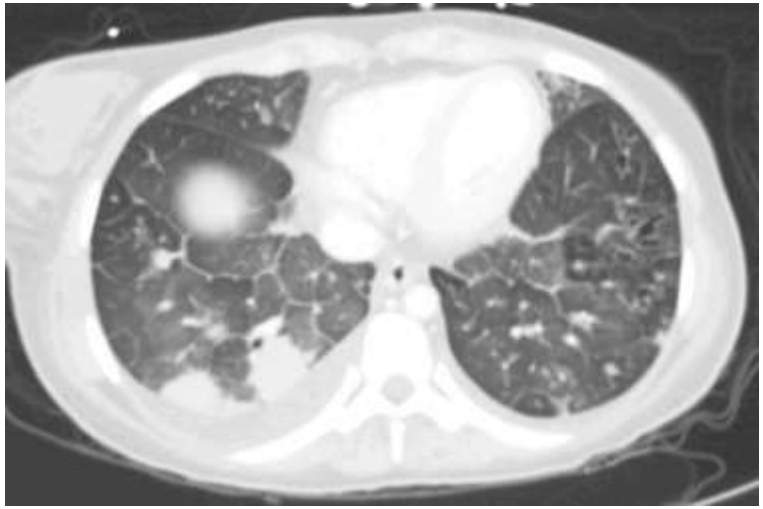


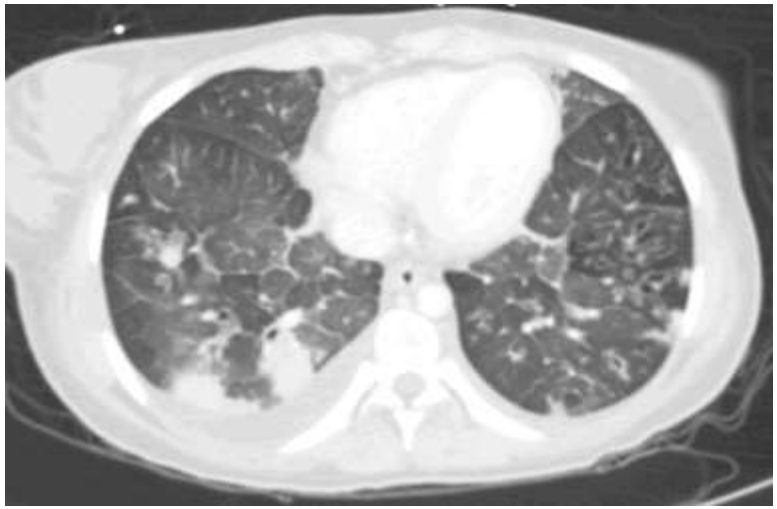
Case Presentation

- ~SIRS (Serious inflammatory response syndrome)
- ICU-24 hours
- Fluids, FFP, oxygen→ stabilization
- ECHO cardiogram: normal
- Abdominal CT: **moderate periportal lymph node enlargement** with new **bilateral pleural effusions** and **pulmonary infiltrates at the lung bases, not evident on chest CT three days earlier**

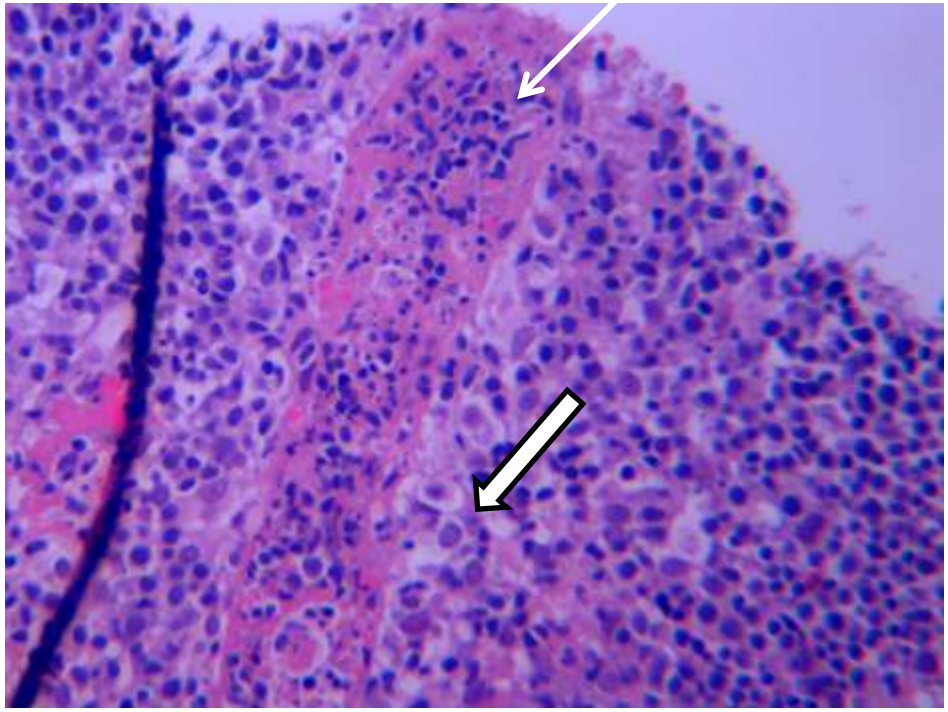
CT abdomen 20/4/15







Lymph node biopsy



Fibrinoid necrosis (white arrow) with nuclear dust and apoptotic cells with abundant histiocytes (outlined arrow)

Case Presentation

- The patient **recovered:** resolution of the fever and normalization of laboratory values
- During her illness: **lost 3** kilograms

Lung function dropped to **FEV1 of 55%**

Microbiologic workup:

- PCR of aspirated material (lymph node)- bacterial, fungal, mycobacterial were negative
- HIV serology-negative
- Antinuclear antibody (ANA): negative

Case Presentation summary

- Typical young CF patient
- 1.5 months after *influenza a* infection
- Prolonged fever + lymphadenopathy
- Anemia, thrombocytopenia, LDH↑
- ~SIRS → ICU
- Lungs: bilateral pleural effusion and pulmonary infiltrates
- Lymph node pathology: fibrinoid necrosis with nuclear dust and apoptotic cells with abundant histiocytes.

Case Presentation summary

Diagnosis: Kikuchi Fujimoto Disease (KFD)

Kikuchi Fujimoto Disease (KFD)

- Described by Kikuchi and Fujimoto in Japan (1972)
- Rare entity : lymph node enlargement (70%-90% cervical) with acute systemic illness
- Affects young people, female predominance
- Characterized by necrotizing lymphadenitis
- KFD is a self-limited disease with benign course
- **Lung involvement in KFD has rarely been reported and has not been described in CF**

Kikuchi-Fujimoto disease

Associated with:

- Viruses : parvovirus B19, HIV, EBV, CMV & herpes simplex virus type 6
- Microorganisms: Toxoplasma, Yersinia & Brucella
- Clear association between lupus and KFD
- Diagnosis by lymph node biopsy
- Treatment is not always indicated, although favorable responses to glucocorticoid & IVIG

Lin D et al. Severe Kikuchi's disease responsive to immune modulation. Singapore Med J. 2010
Jang YJ et al. Management of Kikuchi's disease using glucocorticoid. Journal of Laryngology & Otology. 2000

Kikuchi Fujimoto Disease in Israel More Than a Pain in the Neck

D. Rimar et al. Semin Arthritis Rheum 2010

Objective: characteristics of KFD in Israel.

Methods: retrospective analysis of all patients with KFD in seven medical centers in Israel

Results & Conclusions

- Nineteen patients, mean age 23y (range 9-50)
- Female/male ratio: 1.1:1
- **KFD in Israel:** systemic disease with fever (73%) leukopenia (72%), CRP↑(52%), night sweats (21%), weight loss (21%) & generalized or retroperitoneal lymphadenopathy

Kikuchi Fujimoto Disease in Israel More Than a Pain in the Neck

D. Rimar et al. Semin Arthritis Rheum 2010

- The histologic appearance and clinical manifestations are **not specific and mimic:** systemic lupus erythematosus (SLE) as well as infectious diseases (leprosy, cat scratch disease, HIV) and lymphoproliferative disorder
- Predisposing conditions : tonsillectomy and infectious etiologies

Rimar D et al. Kikuchi Fujimoto disease in Israel—more than a pain in the neck. Seminars in arthritis and rheumatism; Elsevier; 2010.

Kikuchi Fujimoto Disease and lungs

- 27-year-old woman, 3-months of fever, night sweats and maculopapular lesions
- CT: sub-pleural nodules in the right lung, enlarged subcarinal, paratracheal and bilateral hilar lymph nodes.
- Mediastinoscopy : lymph node conglomerate **Biopsy**: reactive lymphadenitis with non-neutrophilic necrosis suggestive of Kikuchi disease.

María Ramos Fernández et al. Kikuchi-Fujimoto Disease in an Atypical Site. Arch Bronconeumol. 2009

Bilateral pleural effusion and interstitial lung disease as unusual manifestations of kikuchi-fujimoto disease: case report and literature review

Garcia-Zamalloa et al. BMC Pulmonary Medicine 2010

Case Presentation: 32-year-old man, hypothyroidism.

- Fever and painful cervical lymphadenopathy.
  Biopsy: KFD
- Some days later → deterioration: generalized lymphadenopathy + bilateral pleural effusion and interstitial lung disease. Resolved with prednisone

Conclusion: Pleural effusion and interstitial lung disease are very uncommon manifestations of KFD. Treatment with oral prednisone was effective

Kikuchi Fujimoto disease associated with cryptogenic organizing pneumonia: case report and literature review

Hua and Zhu BMC Infectious Diseases 2010

- A 33-year-old male: 1-month cough and fever + cervical lymph node (5 days).
- **CXR:** bilateral lower lobe infiltrates → unresponsive to antibiotics.
- Bronchoscopy, BAL and lung biopsy: diagnosis of Cryptogenic Organizing Pneumonia
- **Lymph node biopsy** - consistent with **KFD.**
- The patient improved on steroids.

Conclusions: KFD and COP are possible part of a disease continuum, rather than separate entities.

Back to our patient

- Prolonged gradual recovery
- Anti Nuclear Ab (ANA): twice – negative
- Now what? - CT? Bronchoscopy with BAL?
- Clinic visit 22/10/15:

Healthy (back to her baseline)!

FVC= 2.91L (78%)

FEV_1= 2.22L (68%)

FEF_{25-75} =1.78 (43%)

Summary & take home message

- This is the first case of KFD described in a patient with CF.
- Lymphadenitis occurred after *influenza A*
- Lung: bilateral pleural effusion with pulmonary infiltrates + PFT↓
- Lung involvement could result from either severe systemic illness with hypoalbuminemia or direct involvement of the lung with KFD.

Thank you

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