What was Her Deficiency?

RHTSK CICU

Case Presentation

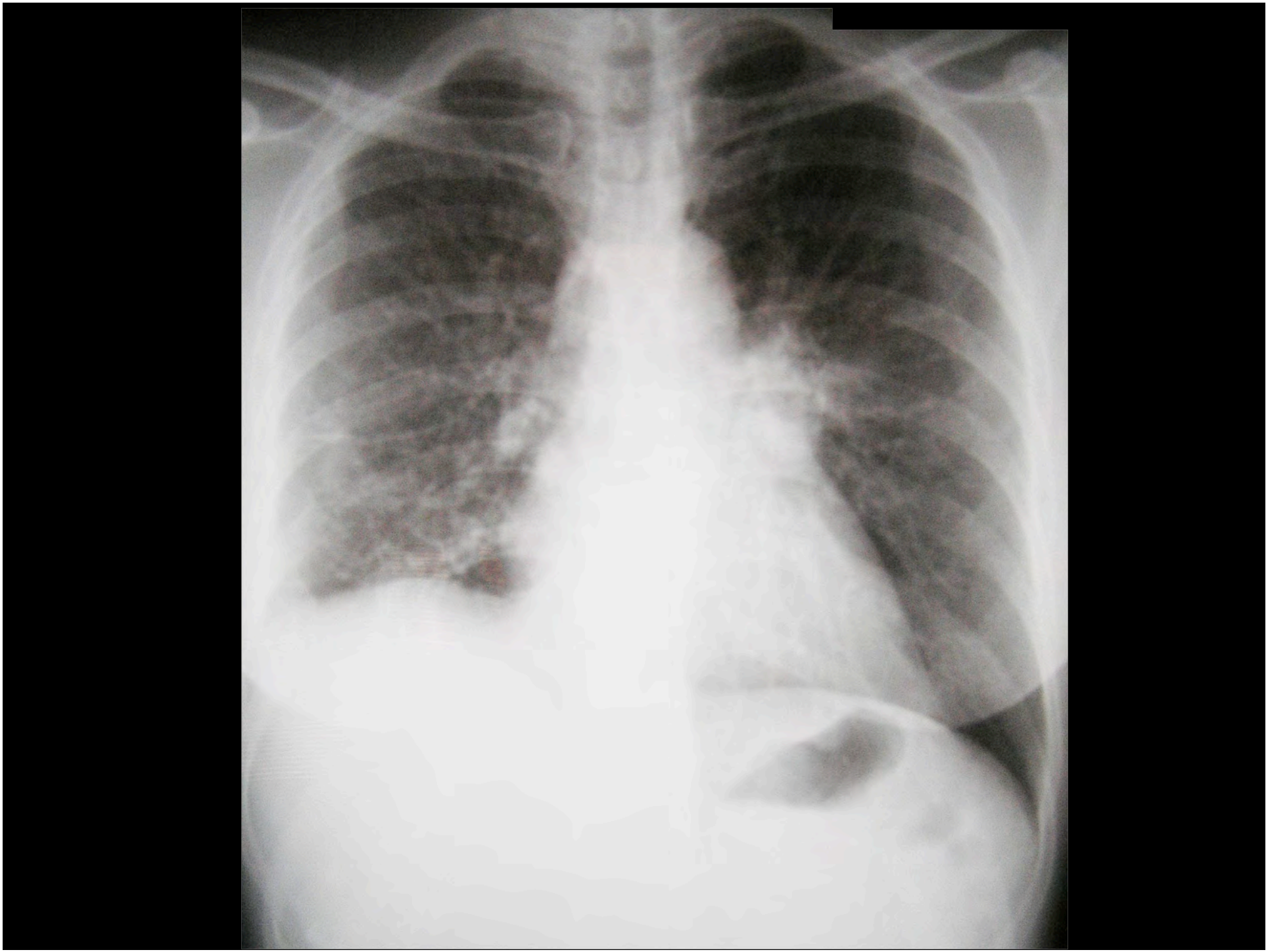
- F/51, housewife, NSND, NKDA
- Admitted to RH chest ward through chest clinic
- c/o blood stained sputum, increased cough x 1/12
- PMH:
  - G6PD deficiency, screened in 1993
  - Mild pancytopenia, ?BM exam done years ago in PWH, claimed to be normal
  - Old endobronchial PTB RLL 1993, completed 6-month treatment
  - Post TB bronchiectasis

Case Presentation

- PMH (con't) :
  - Malabsorption; presented in 1989 with steatorrhea with numerous Ix done in PWH including normal OGD/colonoscopy, fecal fat, jejunal Bx, small bowel enema, rectal biopsy, -ve Schilling test
  - Liver hemangioma
  - Anal wart with cauterization
  - Left conjunctiva papilloma with excision Bx showing squamous cell CA in situ
  - Cervical intraepithelial neoplasia
- FU PYNEH O&G and Eye, Wan Chai Chest Clinic

Case Presentation

- P.E. afebrile, unremarkable
- CXR : Left hilar shadow and RLZ hazziness

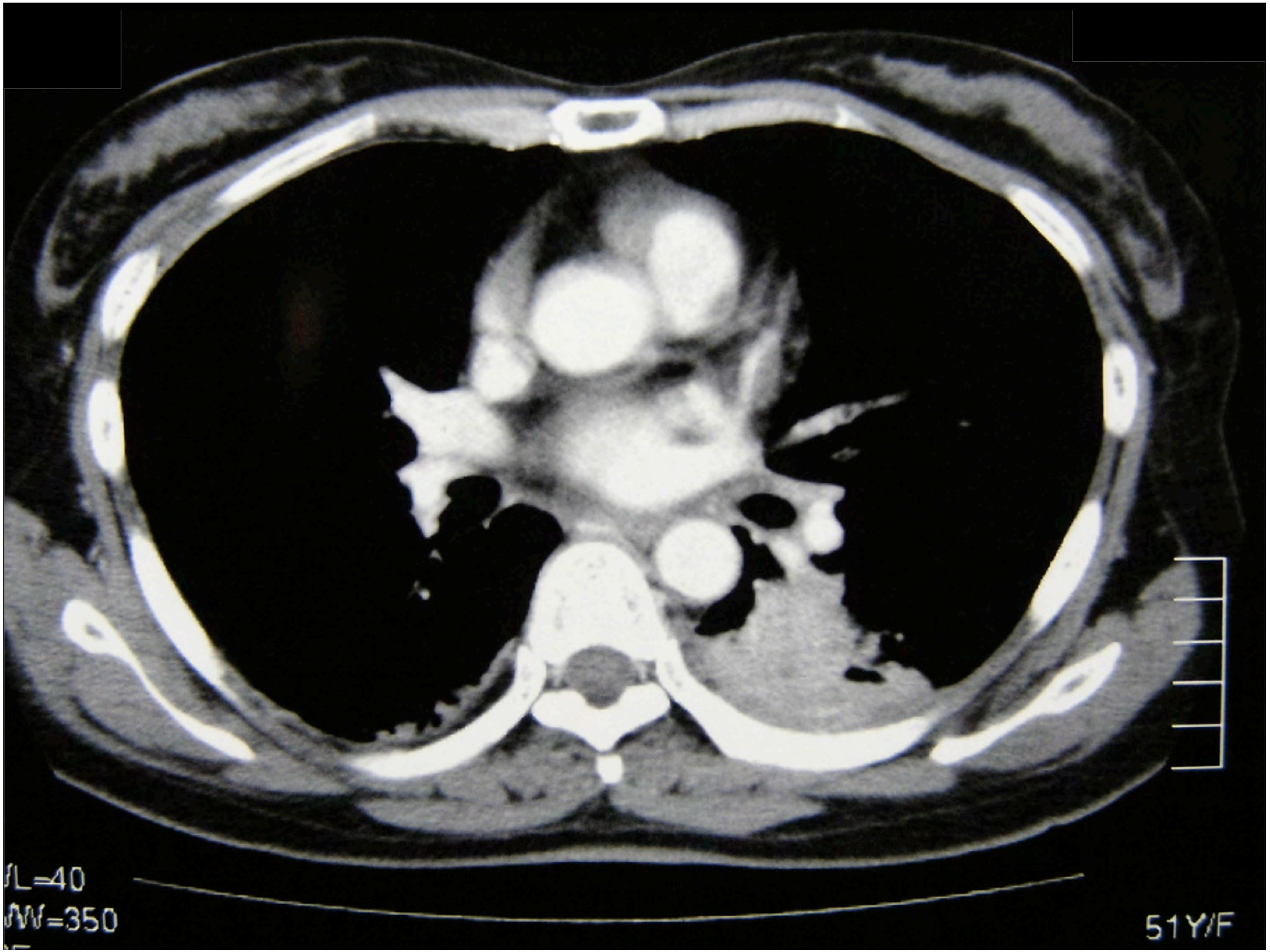


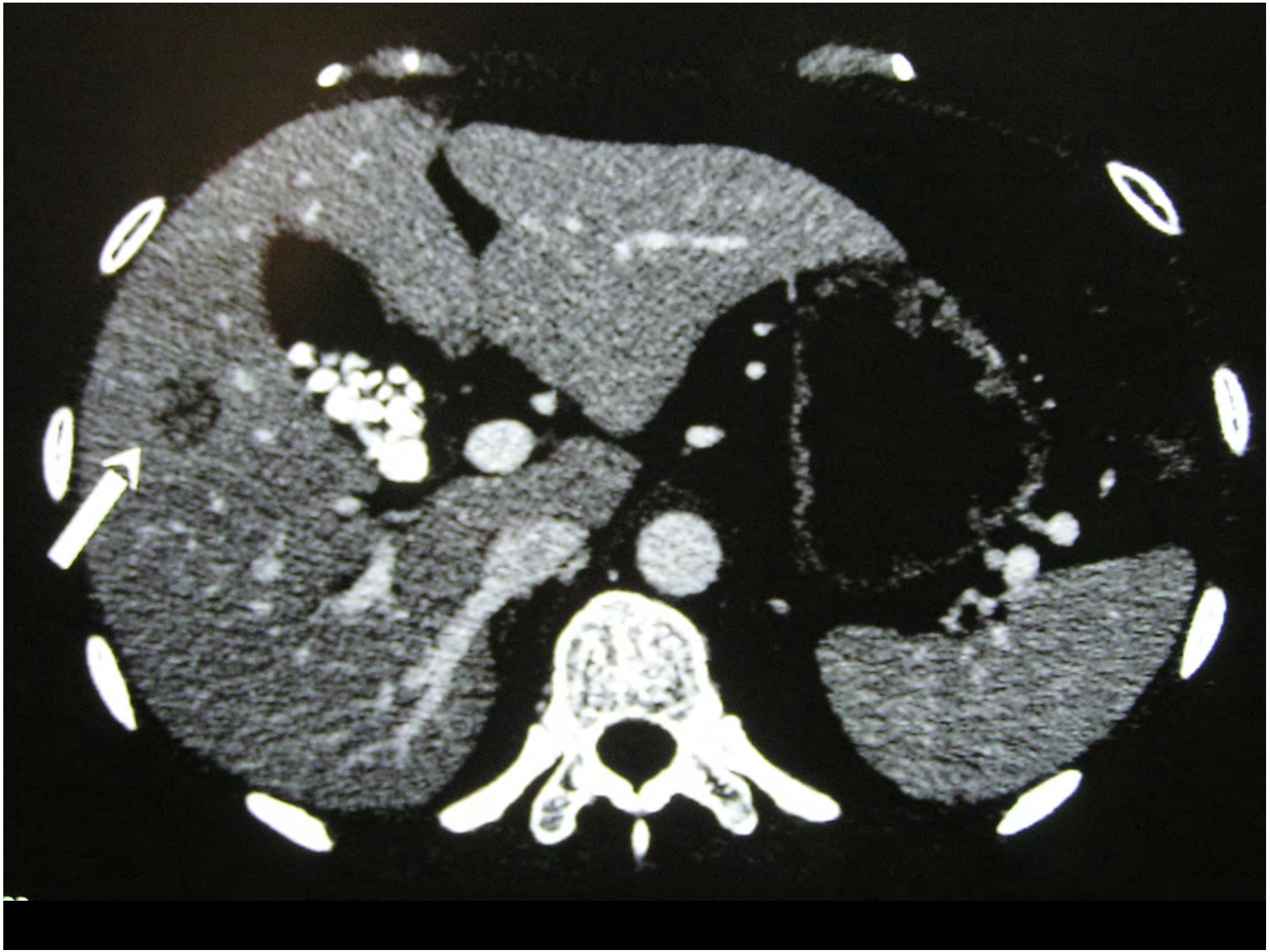
Case Presentation

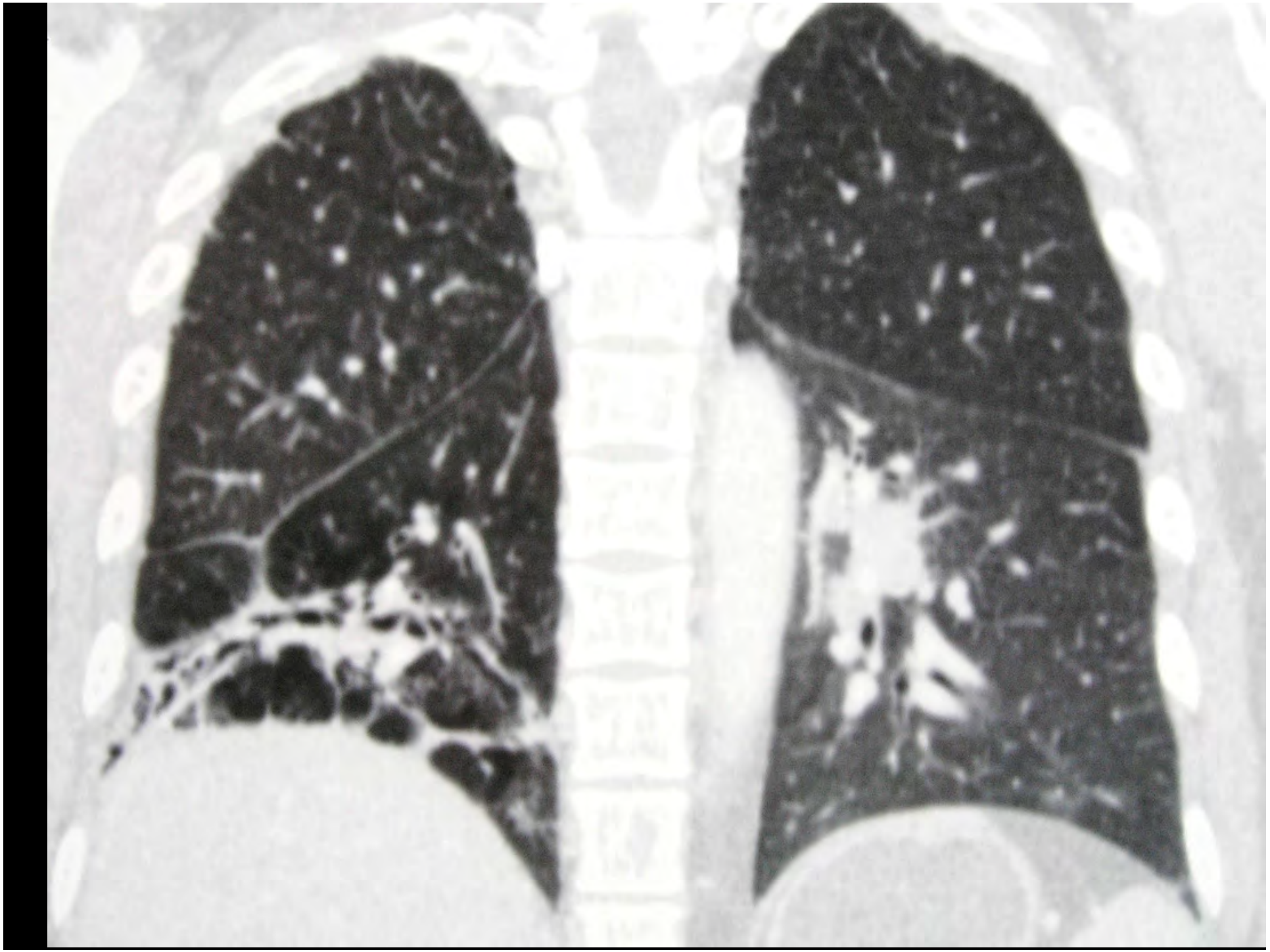
- Initial Ix :
  - CBC WBC 5.2 Hb 10.5 NcNc platelet 77
  - Clotting normal
  - LRFT normal
  - Sputum C/ST oral flora; AFB smear –ve, cytology saliva only

Case Presentation

- Bronchoscopy : no endoscopic abnormality or bleeding site
- Bronchial aspirate : AFB smear –ve, cytology –ve
- CT thorax
  - LLL posterior subpleural lesion ?malignancy
  - RLL bronchiectatic change
  - Right hepatic lesion ?atypical hemangioma


L=40
W=350
51Y/F





Case Presentation

- Clinically readmitted for CT guided lung biopsy
- Thrombocytopenic and anemic
  - PYNEH hematologist consulted over phone
  - Thrombocytopenia likely due to chronic ITP in view of –ve autoimmune markers
  - Hb dropped to ~5.6, NcNc
    - not Fe def
    - haptoglobin ↓
    - indirect antiglobulin test –ve
    - direct antiglobulin test weakly +ve
    - anti-IgG weakly +ve
    - anti-C3d –ve
    - Imp: ?hemolysis due to oxidative stress ?infection ?drug related
- Pack cell and platelet conc transfusions given

Case Presentation

- CT guided lung biopsy: granulomatous inflammation, ZN stain and fungal stain both –ve; no evidence of malignancy
- Readmitted for empirical trial of antituberculous treatment

Case Presentation

- Persistent low grade fever
- Given Naprosyn for ?TB fever, unresponsive
- Stop all anti-tuberculous treatment 10/10 – 12/10 ?drug fever
- Still swinging fever, not septic looking

Case Presentation

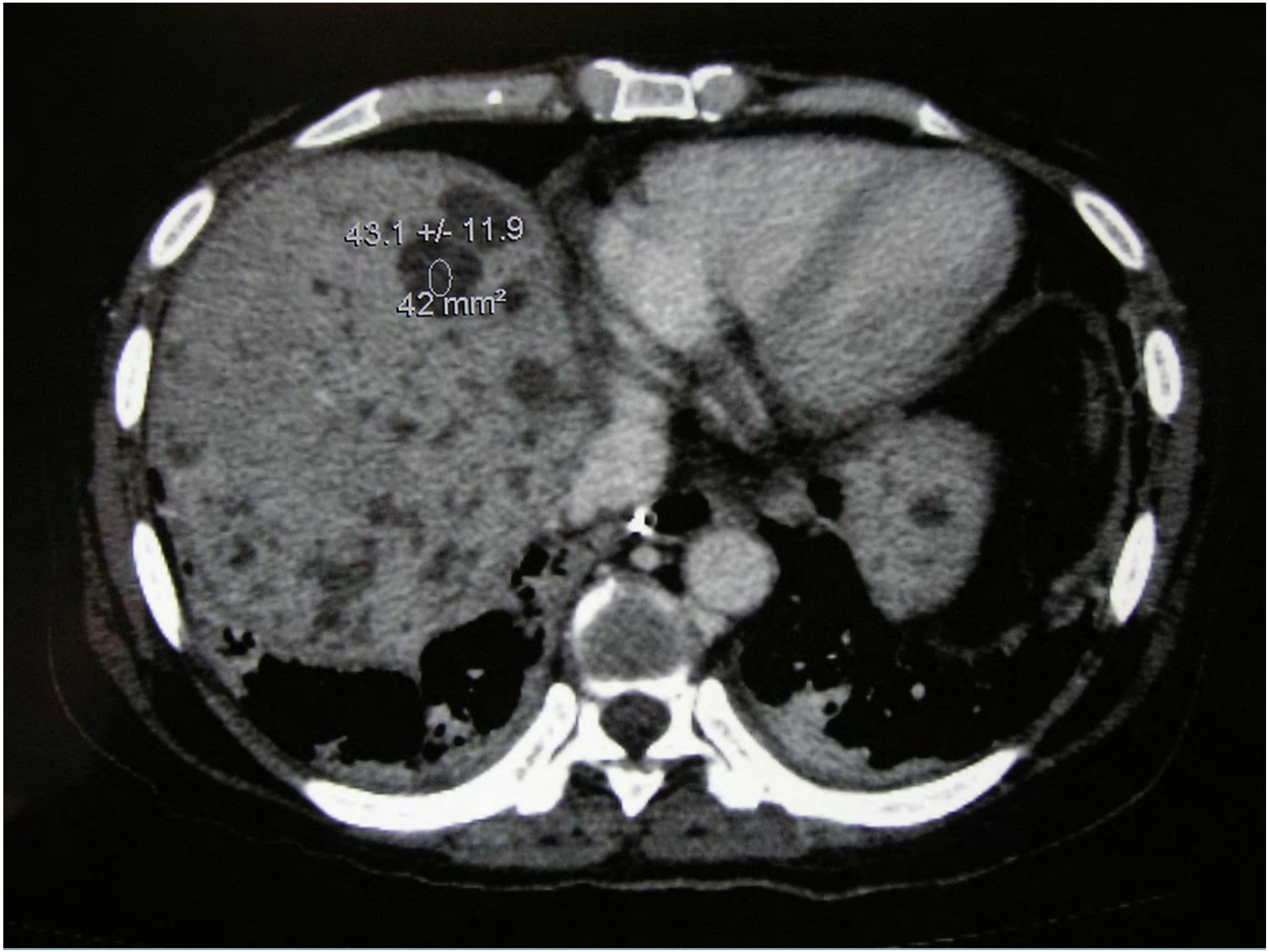
- Other Ix
  - ESR > 100
  - HBsAg –ve
  - HCV –ve
  - HIV –ve
  - TSH normal
  - All along all blood C/ST, CSU/MSU C/ST, sputum C/ST and AFB smear results all –ve
- Pyrexia due to ?TB (not on full regimen), ? underlying malignancy, ?other causes of granulomatous inflammation

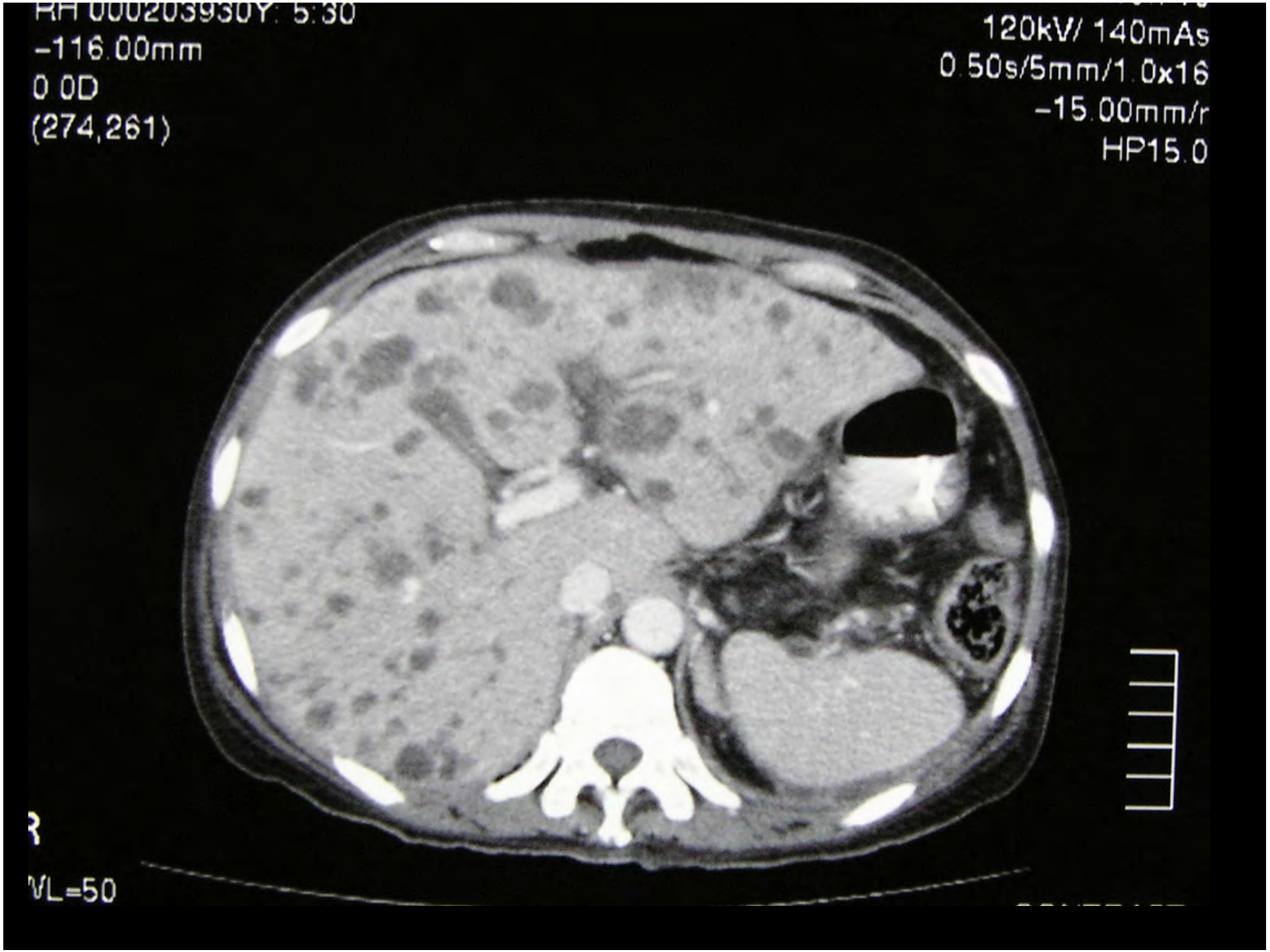
Case Presentation

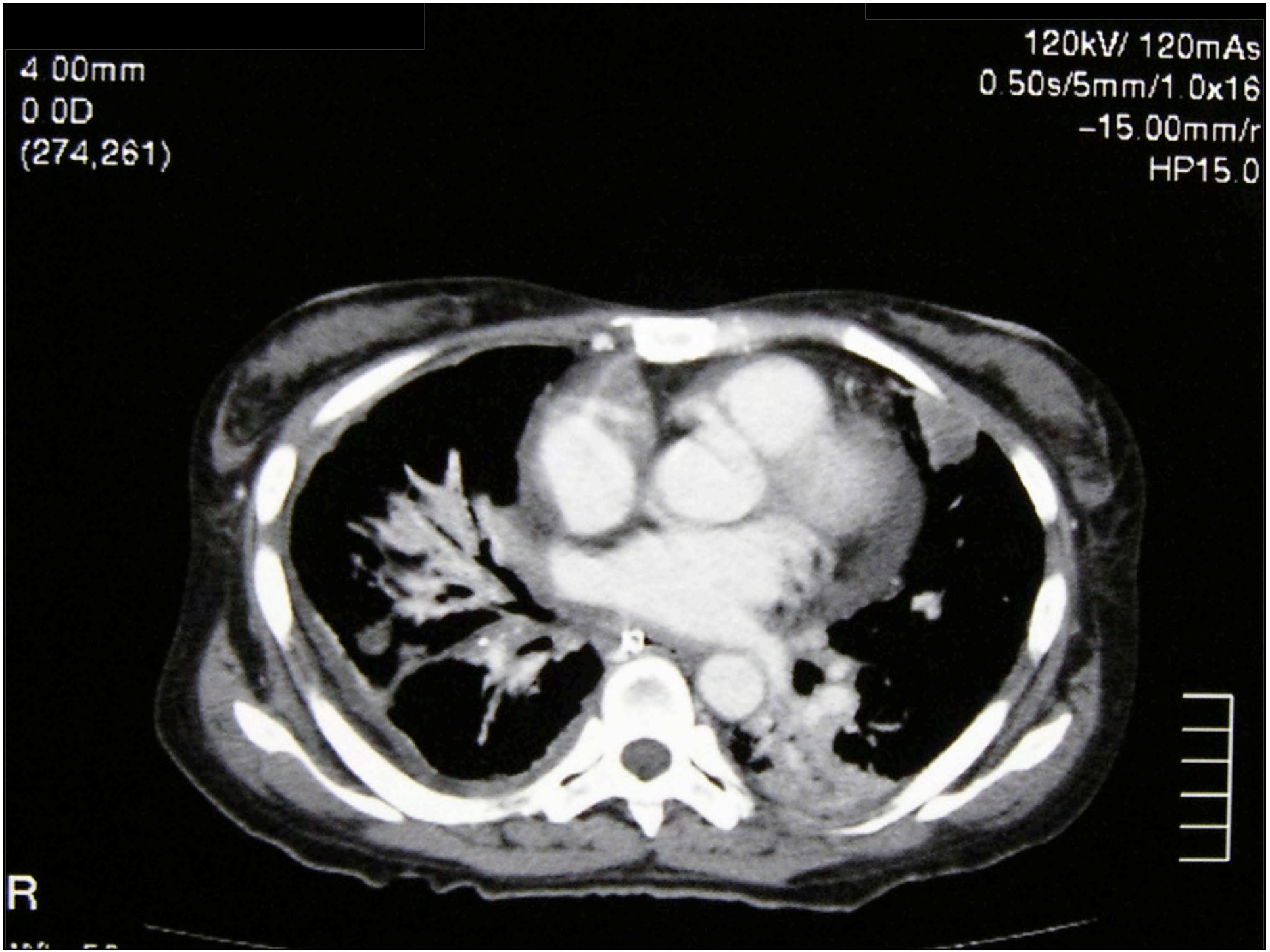
- Resumed rifampicin and EMB 12/10 – 17/10
- While adding on isoniazid, ↓general condition with ↑fever, ↑SOB and septic shock

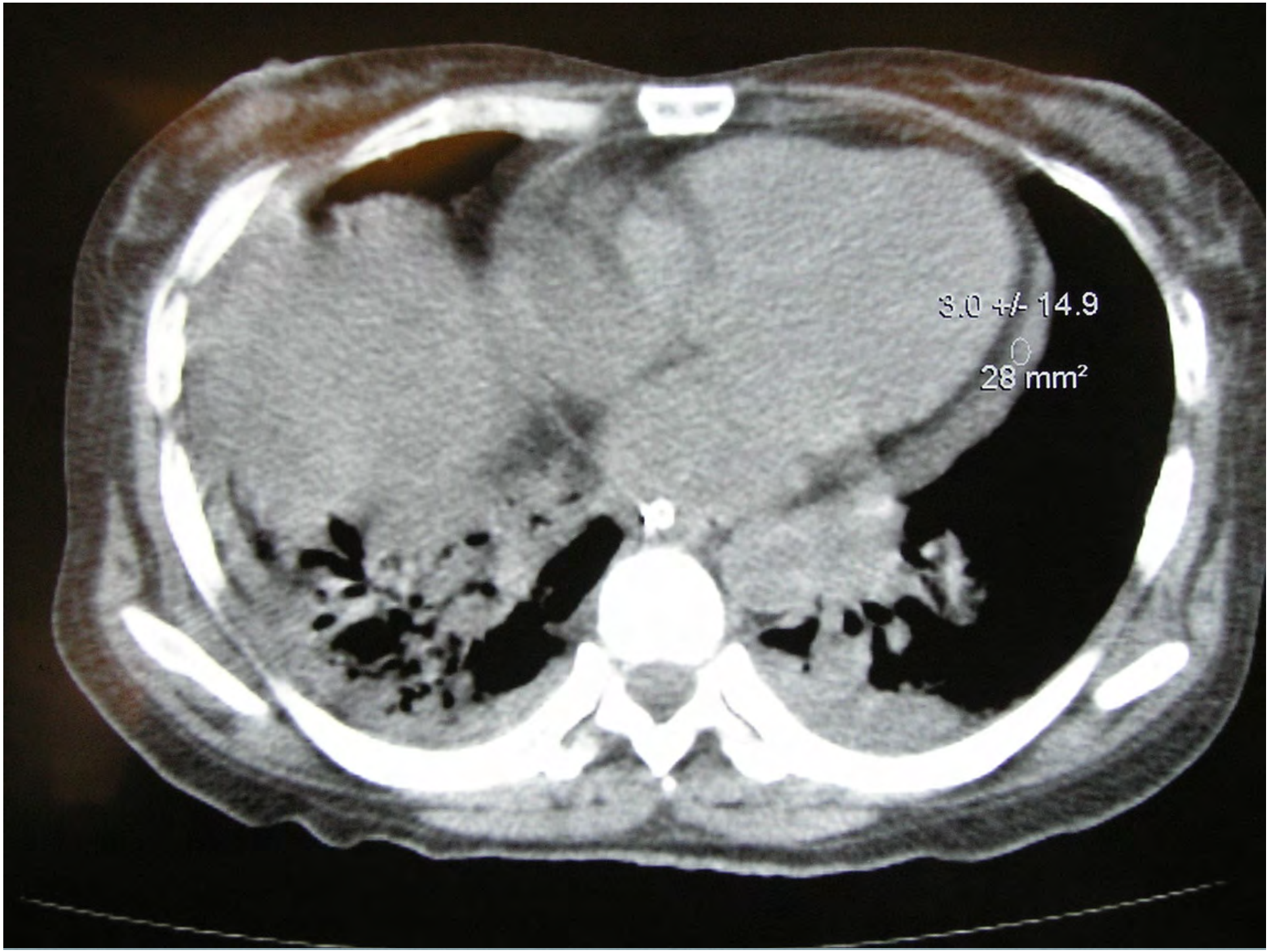
Case Presentation

- Transferred to ICU
- Intubated and mechanically ventilated
- Given IV Meropenem and Flagyl empirically
- Urgent CT abd/pelvis done


43.1 +/- 11.9
42 mm²


RH 0002039301Y: 5:30
-116.00mm
0 0D
(274,261)
120kV/ 140mAs
0.50s/5mm/1.0x16
-15.00mm/r
HP15.0
R
WL=50


4.00mm
0.0D
(274,261)
120kV/ 120mAs
0.50s/5mm/1.0x16
-15.00mm/r
HP15.0
R


3.0 +/- 14.9
28 mm²

Case Presentation

- Bedside bronchoscopy with bronchial aspirate :
  - Aspergillus species scanty +ve
  - AFB/parasite/PCP/influenza A & B/adenovirus/RSV/HSV/CMV all –ve
  - Viral culture –ve
- Blood tests:
  - Aspergillus Ab +ve
  - Legionella pneumophilia titre <32
  - CMVpp65 Ag –ve
  - Crytococcus Ag –ve
  - Penicillium marneffei Ab <1:40
  - Blood C/ST for AFB and fungus –ve
  - Entamoeba hisolytica IgG –ve
  - ANCA –ve

Case Presentation

- Treated as invasive pulmonary aspergillosis
- Given Amphotericin B initially then switched to Voriconazole

Case Presentation

- Septic shock requiring high dose vasopressors, CVVHDF
- Newly developed right thigh abscess with bedside aspiration : Nocardia species (scanty)

Case Presentation

- Changed to IV Imipenem and Amikacin for better coverage of Nocardia
- Finally passed away despite maximal support

Case Presentation

- Immunodeficiency workup before death
  - HIV –ve
  - Severe lymphopenia but no particular subset remarkably affected
  - Weak MPO positivity

Case Summary

- A middle aged lady with G6PD deficiency and a number of premalignant conditions, dying from disseminated nocardiosis and probable invasive pulmonary aspergillosis
- ?Underlying immunodeficiency
  - ?Myeloperoxidase deficiency
  - ?Other occult immunodeficiency

Discussion

Pulmonary Aspergillosis
Nocardiosis
MPO Deficiency
G6PD Deficiency in Female

Pulmonary Aspergillosis

- A mould
- Widespread in the environment
- Most cases due to Aspergillus fumigatus
- A few cases due to A. flavus or niger

Spectrum of Pulmonary Aspergillosis

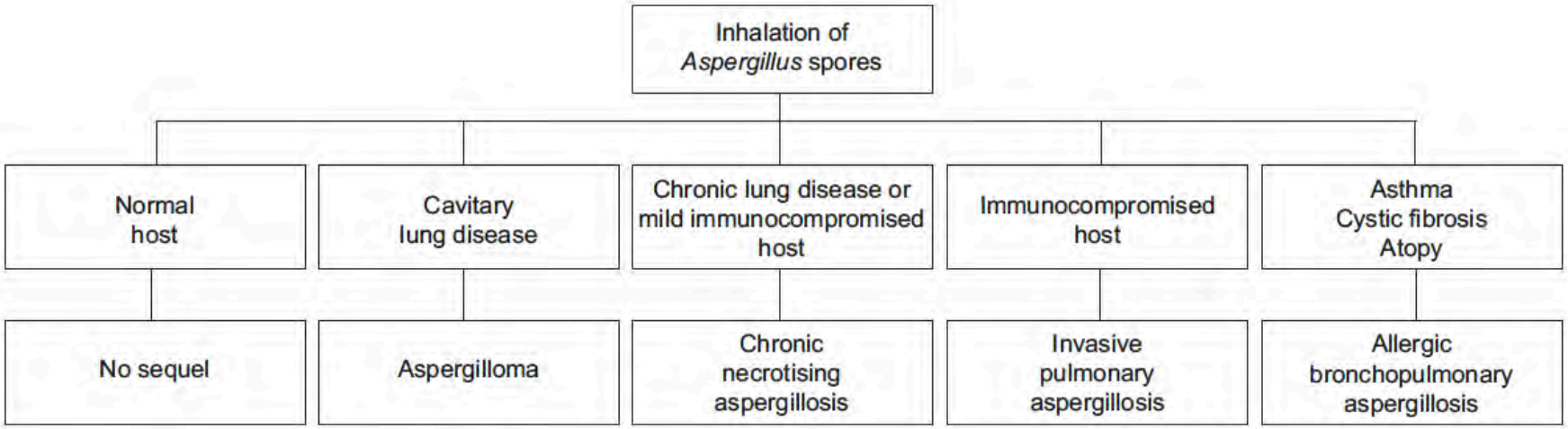


TABLE 1 Classical risk factors for invasive pulmonary aspergillosis

Prolonged neutropenia (<500 cells·mm^{-3} for >10 days) [10]
Transplantation (highest risk is with lung transplantation and HSCT) [11–14]
Prolonged (>3 weeks) and high-dose corticosteroid therapy [10, 15, 16]
Haematological malignancy (risk is higher with leukaemia) [5, 7]
Chemotherapy [5, 7, 17]
Advanced AIDS [18–21]
Chronic granulomatous disease [22]

HSCT: haematopoietic stem-cell transplantation.

Eur Respir Rev 2011; 20: 121, 156–174

TABLE 2 Diagnostic criteria for invasive pulmonary aspergillosis

Diagnosis	Criteria
Proven	Histopathological or cytopathological examination of lung tissue showing hyphae from needle aspiration or biopsy specimen with evidence of associated tissue damage OR positive culture result for *Aspergillus* from a sample obtained by sterile procedure from the lung AND clinically or radiologically abnormal site consistent with infection
Probable	Host factor (table 1) AND mycological evidence (positive *Aspergillus* microscopy or culture from the sputum or BAL or positive antigen assay[#]) AND clinical criteria consistent with infection[¶]
Possible	Host factor (table 1) AND clinical criteria consistent with the infection[¶]

TABLE 3 Treatment recommendations for pulmonary aspergillosis

Disease	Primary treatment	Other treatments
Invasive pulmonary aspergillosis	Voriconazole [119–123]	Alternative therapy: liposomal amphotericin B [124] Continuation therapy: voriconazole or itraconazole [122, 123] Salvage therapy: echinocandin or posaconazole [125–127]
Chronic necrotising aspergillosis	Voriconazole [120, 123]	Alternative therapy: itraconazole [128, 129] Severe cases: intravenous voriconazole or liposomal amphotericin B [123, 128, 130] Consider surgical resection [130]
Aspergilloma	Observation [123]	Bronchial artery embolisation [131] Surgical resection [132–135] Consider itraconazole [136–138]
Allergic bronchopulmonary aspergillosis	Corticosteroids [139–142]	Itraconazole or voriconazole as steroid-sparing agents [143–146]

Nocardiosis

- Genus *Nocardia*
- Aerobic gram-positive bacillus with branching hyphae; varying degress of acid-fastness
- Environemntal bacteria
- Opportunistic infections, especially in patients with depressed cell-mediated immunity

Nocardiosis

- Pulmonary nocardiosis is the most common clinical presentation
- Extrapulmonary nocardiosis can occur through hematogenous dissemination or contiguous spread
  - CNS is the most common extrapulmonary site
- Primary cutaneous and soft tissue nocardiosis from traumatic injury that involves soil contamination

Treatment of Nocardiosis

Mayo Clin Proc. ■ April 2012;87(4):403-407

- Lack of prospective controlled trials
- TMP-SMX
- Alternative agents :
  - Amikacin
  - Imipenem
  - Ceftriazone
  - Cefotaxime
  - Minocycline
  - Moxifloxacin
  - Amoxcillin-clavulanic acid
  - Tigecycline
  - Linezolid
- Combination therapy up to 6-12 months

TABLE 2. Select *Nocardia* Species and Corresponding Antimicrobial Susceptibility Patterns[a]

Species	Antimicrobial susceptibility patterns									
	Sulfamethoxazole	Ampicillin	Amoxicillin-clavulanate	Ceftriaxone	Linezolid	Amikacin	Imipenem	Fluoroquinolone	Clarithromycin	Other[b]
Nocardia asteroides complex[c]										
N abscessus	+	+	+	+	+	+	–	–	–	
N asteroides	+	–	+/–	+	+	+	+	–	–	
N brevicatena and *N paucivorans*	+	+	+	+	+	+	–	+	–	
N cyriacigeorgica	+	+/–	+/–	+	+	+	+	+/–	–	[d]
N farcinica	+/–	–	+/–	–	+	+	+	+	–	[e]
N nova complex	+	+/–	–	+	+	+	+		+	
N transvalensis complex	+		+/–	+	+	–	+	+	–	[f]
Other *Nocardia* species										
N brasiliensis	+	–	+		+		–	–	–	
N otitidiscaviarum	+/–	–	–	–	+	+	–	+		
N pseudobrasiliensis	+	–	–		+			+	+	

[a] + = active; – = less active or inactive; +/– = may be active, but resistance is common; no entry = variable susceptibility results or insufficient information.

[b] Minocycline, moxifloxacin, and tigecycline are active against selected *Nocardia* species.

[c] *Nocardia asteroides* complex is a group of bacteria that have a heterozygous pattern of antimicrobial drug susceptibilities and are responsible for the majority of clinical human *Nocardia* infections.

[d] *N cyriacigeorgica* may be reported as *N asteroides* by some laboratories unless additional testing is performed.

[e] Usually susceptible to amikacin; resistant to other aminoglycosides.

[f] Usually resistant to amikacin and other aminoglycosides.

Myeloperoxidase Deficiency

- Myeloperoxidase (MPO) → a human enzyme found in azurophilic granules of neutrophils and lysosomes of monocytes
- Major role → aids microbial killing, removing foreign cells and tumour surveillance
- Prevalence of total or subtotal MPO deficiency : 1 per 2727

Kutter D. Prevalence of myeloperoxidase deficiency: population studies using Bayer-Technicon automated hematology. J Mol Med. Sep 1998;76(10):66975.

Myeloperoxidase Deficiency

- Hereditary
  - *The gene is located on chromosome 17q22-23*
  - *Autosomal recessive*
  - *Most patients are compound heterozygotes*
- Acquired → usually transient and reversible
  - *Pregnancy*
  - *Lead intoxication*
  - *Iron deficiency*
  - *Severe infection → due to PMN activation and MPO consumption*
  - *Thrombotic disease*
  - *Renal transplantation*
  - *Drugs esp. cytotoxic agents*
  - *Disseminated cancers*
  - *Severe hematologic disorders and neoplasms*

Complete Myeloperoxidase Deficiency

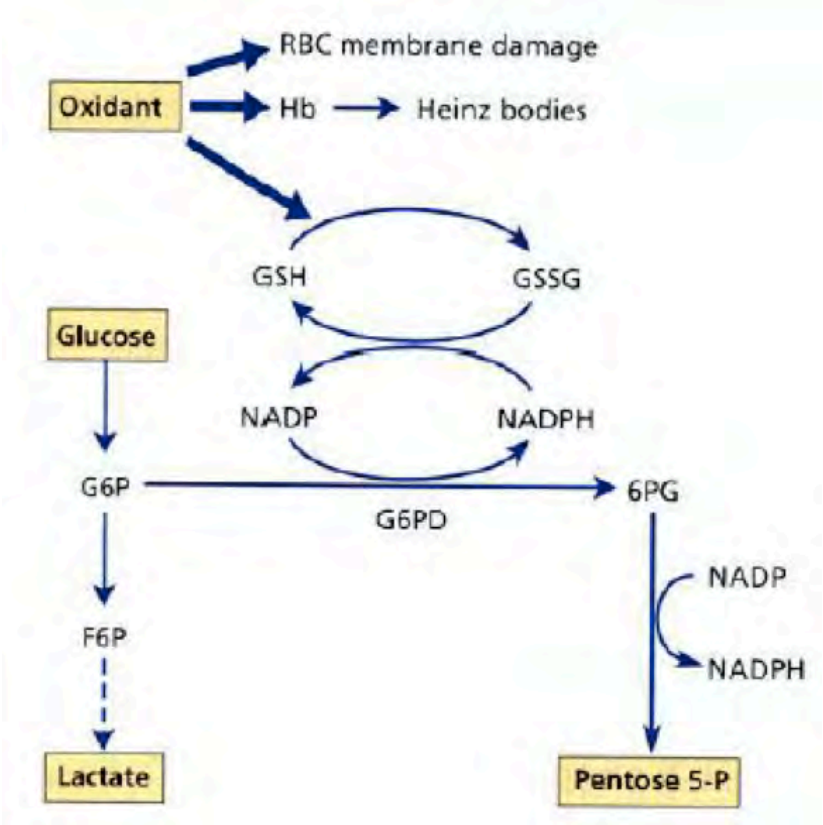
- Most are asymptomatic because of the presence of MPO-independent killing mechanisms
- Some have infectious complications
  - ~10% life threatening
  - Usually fungal infection, particularly Candida infection, in association with DM
  - ?MPO deficiency becomes clinically significant only in the presence of an additional defect in host defense
- A strong association with malignancies including leukemia, lymphoma

G6PD Deficiency in Female

G6PD

- Glucose-6-phosphate dehydrogenase
- Maps to Xq28
- 515 amino acid

Metabolic Role of G6PD



G6PD Variants

- >127 mutations identified
  - Missense
  - Frame deletions
  - Splice site mutations
  - Nonsense

WHO Classification of G6PD Variants

TABLE 1
Classes of G6PD Enzyme Variants

Class	*Level of deficiency*	*Enzyme activity*	*Prevalence*
I	Severe	Chronic nonspherocytic hemolytic anemia in the presence of normal erythrocyte function	Uncommon; occurs across populations
II	Severe	Less than 10 percent of normal	Varies; more common in Asian and Mediterranean populations
III	Moderate	10 to 60 percent of normal	10 percent of black males in the United States
IV	Mild to none	60 to 150 percent of normal	Rare
V	None	Greater than 150 percent of normal	Rare

G6PD = glucose-6-phosphate dehydrogenase.

Information from references 1 and 7.

Diagnosis of G6PD Deficiency

- Fluorescent spot test – “absent”, “intermediate”, “present”
  - Screening test
  - Detects the generation of NADPH from NADP. The test is positive if the blood spot fails to fluoresce under ultraviolet light
- Quantitative spectrophotometric analysis of G6PD activity
  - Based on reduction of NADP as measured spectrophotometrically when hemolysate is incubated with G6P
  - Limitations : reticulocytosis and recent blood transfusion
  - Reference range : 6.35-10.33 IU/gHb
- PCR to detect specific mutations

G6PD Deficiency

- In HK, G6PD deficiency found in 4.47% of male newborn, 0.27% of female newborn

Data from Lo KK et al: Neonatal screening for G6PD deficiency in Hong Kong. In Lam STS, Pang CCD (eds): Neonatal and Perinatal Screening - the Asian Perspective, CUHK press, 1996, pp 33 - 35.

G6PD Deficiency in HK

- 3 commonest variants Canton, Kaiping and Gaohe accounts for 70 - 80% of cases in HK

  Canton 1376 G→T
  Kaiping (Anant) 1388 G→A
  Gaohe 95 A→G

- No class I variants

Dr SK Ma. G6PD deficiency in Hong Kong: diversity and clinical relevance. Retrieved August 25, 2013, from http://www.fmshk.com.hk/hkabth/ss/G6PD%20HKABTH.ppt

G6PD Deficiency in Females

- Compound heterozygous or homozygous
- XO
- Clonal hemopoiesis
- Extreme lyonization

Lyonization

- The process by which one of the two copies of the X chromosome present in female is inactivated
- The inactive X chromosome is silenced by being packaged in such a way that it has a transcriptionally inactive structure called heterochromatin
- To achieve dosage compensation with males. This event is random for each cell and is passed on to the progeny of the cell in a stable manner

American Journal of Medical Genetics 129A:208–211 (2004)

Research Letter

Glucose 6-Phosphate Dehydrogenase (G6PD) Deficiency in Elderly Chinese Women Heterozygous for G6PD Variants

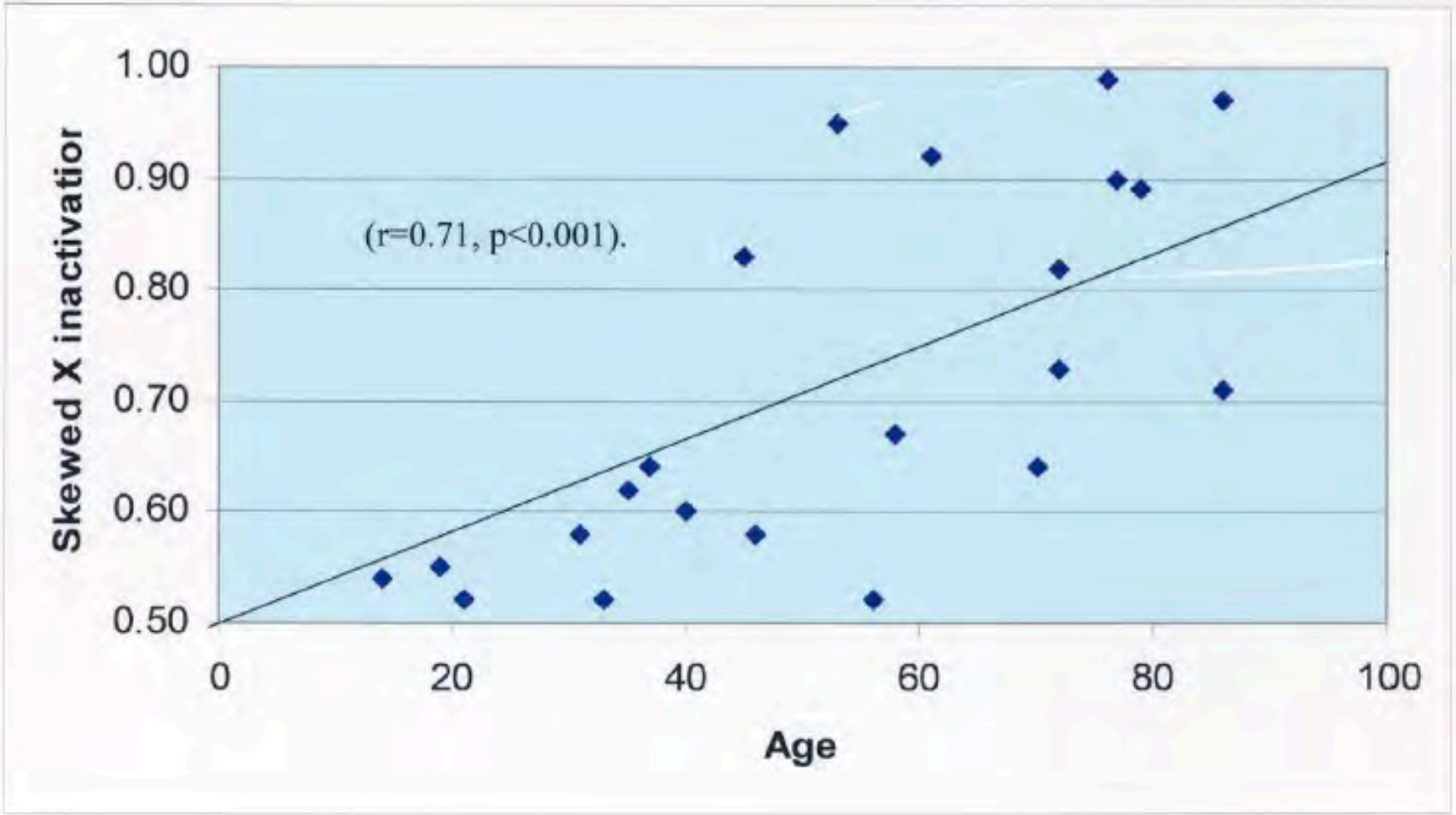
Wing-Yan Au, Edmond S.K. Ma, Veronica M.S. Lam,
Jess L.C. Chan, Annie Pang, Yok-Lam Kwong

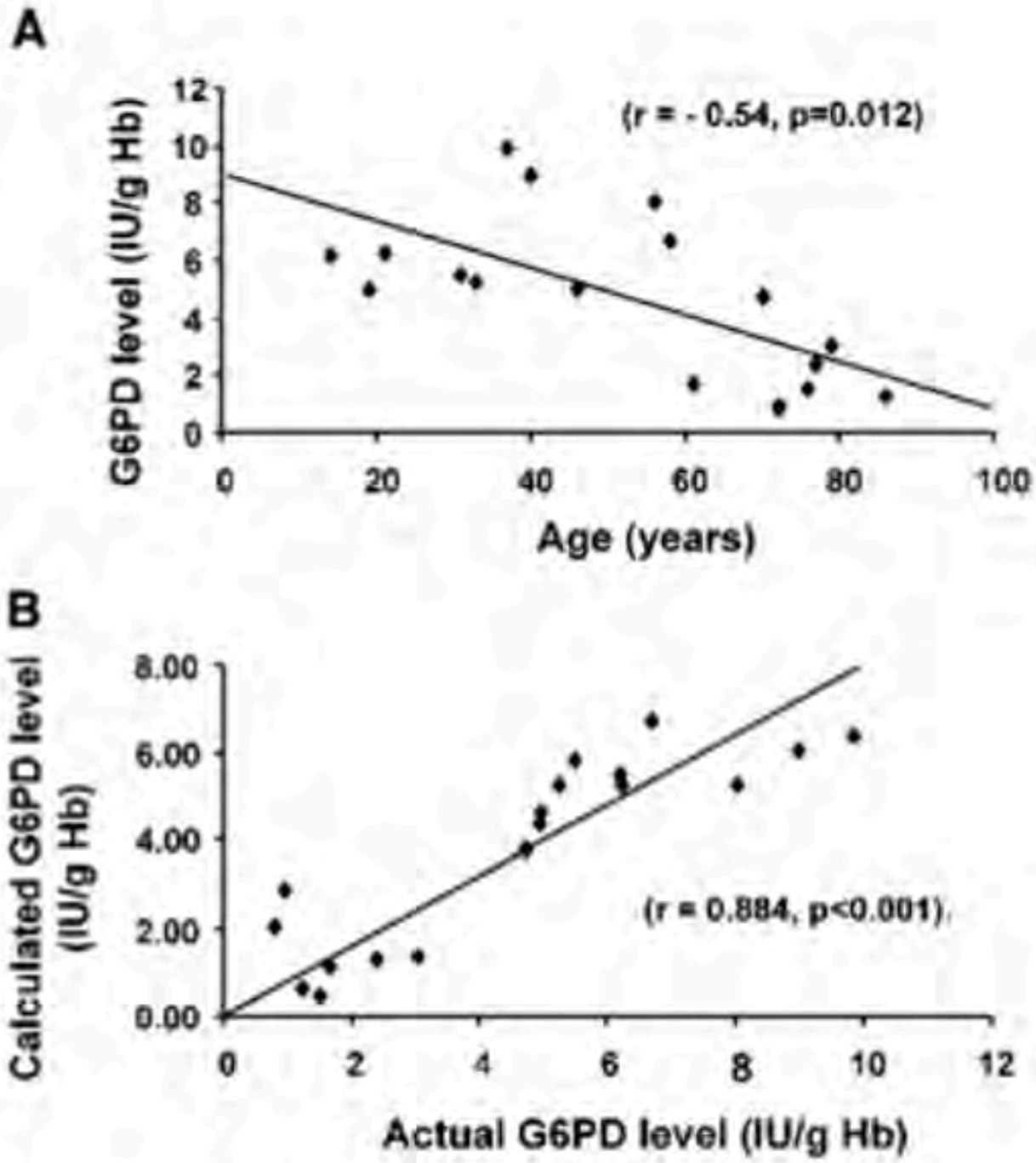
- 160 female BMT donors
  - Median age: 32 years (range: 15 - 58)
  - No G6PD deficiency identified
- 132 elderly females screened for G6PD deficiency
  - Median age: 80 years (range: 71 - 101)
  - G6PD deficiency = 7 (5.3%)
    - Median enzyme activity = 1.57 IU/gHb (range 0.51 - 4.73)
    - G6PD variant:
      - Canton = 2; Kaiping = 2; Goahe = 2;
      - Canton + 871 = 1

Hardy-Weinberg Law

- In the absence of evolutionary influences including non-random mating, mutation, selection, genetic drift, gene flow
  - Take
    - Gene frequency of normal allele (p) = 95.53%
    - Gene frequency of mutant allele (q) = 4.47%
      - Note : prevalence in male = 4.47% on neonatal screening
  - Proportion of females
    - Homozygous normal (p^2) = 91.26%
    - Heterozygous (2pq) = 8.54%
    - Homozygous mutant (q^2) = 0.2%
      - Note : prevalence in female = 0.27% on neonatal screening

Increased skewed Lyonization with age




A
G6PD level (IU/g Hb)
(r = - 0.54, p=0.012)
Age (years)
B
Calculated G6PD level (IU/g Hb)
(r = 0.884, p<0.001)
Actual G6PD level (IU/g Hb)

Effect of Lyonization on G6PD Level

- In female heterozygote carriers, the G6PD level negatively correlate with increasing age
- G6PD level shows close correlation with that predicted from degree of lyonization

Their Conclusion…

Secondly, our results showed that the frequency of G6PD deficiency in elderly Chinese females approached that in males (4.1%). Therefore, it might be prudent to screen for G6PD activity before prescribing oxidative drugs to elderly Chinese females.

J Gerontol A Biol Sci Med Sci. 2006 Oct;61(10):1086-9.

Glucose-6-phosphate dehydrogenase deficiency in female octogenarians, nanogenarians, and centenarians.

Au WY, Lam V, Pang A, Lee WM, Chan JL, Song YQ, Ma ES, Kwong YL.

Department of Medicine, Professorial Block, Queen Mary Hospital, Pokfulam Road, Hong Kong.

Abstract

BACKGROUND: Age-related skewing of X-chromosome inactivation leading to glucose-6-phosphate dehydrogenase (G6PD) deficiency in elderly women in a population with prevalent G6PD gene mutations was investigated.

METHODS: G6PD activity was measured biochemically. G6PD mutations were detected by polymerase chain reaction (PCR) and allele-specific extension, and analyzed by matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry and Sequenom MassARRAY. X-chromosome inactivation was quantified by semiquantitative PCR for the HUMARA gene, before and after HpaII digestion.

RESULTS: In 173 women (median age: 90 years; range, 80-107 years), 18 heterozygotes for G6PD mutations were identified. Three heterozygotes were G6PD deficient, owing to skewed X-chromosome inactivation affecting the wild-type allele. Fifteen heterozygotes, with skewing apparently affecting the mutant alleles, had normal but significantly lower G6PD levels. At 1.73%, G6PD deficiency was significantly more frequent than expected from population screening at birth.

CONCLUSION: Due to skewed X-chromosome inactivation, elderly women in populations with prevalent G6PD mutations are at risk of G6PD deficiency.

blood 1996 88: 59-65

Nonrandom X-inactivation patterns in normal females: lyonization ratios vary with age

L Busque, R Mio, J Mattioli, E Brais, N Blais, Y Lalonde, M Maragh and DG Gilliland

blood 1995 85: 599-600

A skewed lyonization phenomenon as cause of hemophilia A in a female patient [letter]

M Acquila, D Caprino, P Bicocchi, PG Mori and AR Tagliaferri

Bone Marrow Transplantation (2007) 40, 677–681

www.nature.com/bmt

ORIGINAL ARTICLE

G6PD deficiency from lyonization after hematopoietic stem cell transplantation from female heterozygous donors

W-Y Au[1], A Pang[1], KKY Lam[1], Y-Q Song[2,3], W-M Lee[4], JCC So[4] and Y-L Kwong[1]

[1]*Department of Medicine, University of Hong Kong, Hong Kong, China;* [2]*Department of Biochemistry, University of Hong Kong, Hong Kong, China;* [3]*Genome Research Center, University of Hong Kong, Hong Kong, China and* [4]*Department of Pathology, University of Hong Kong, Hong Kong, China*

Usual Clinical Manifestations of G6PD Deficiency

- Drug-induced hemolytic anemia
- Infection-induced hemolysis
- Favism
- Neonatal jaundice
- Chronic “non-spherocytic” hemolytic anemia

The Question is…

- Any association with immunodeficiency ?

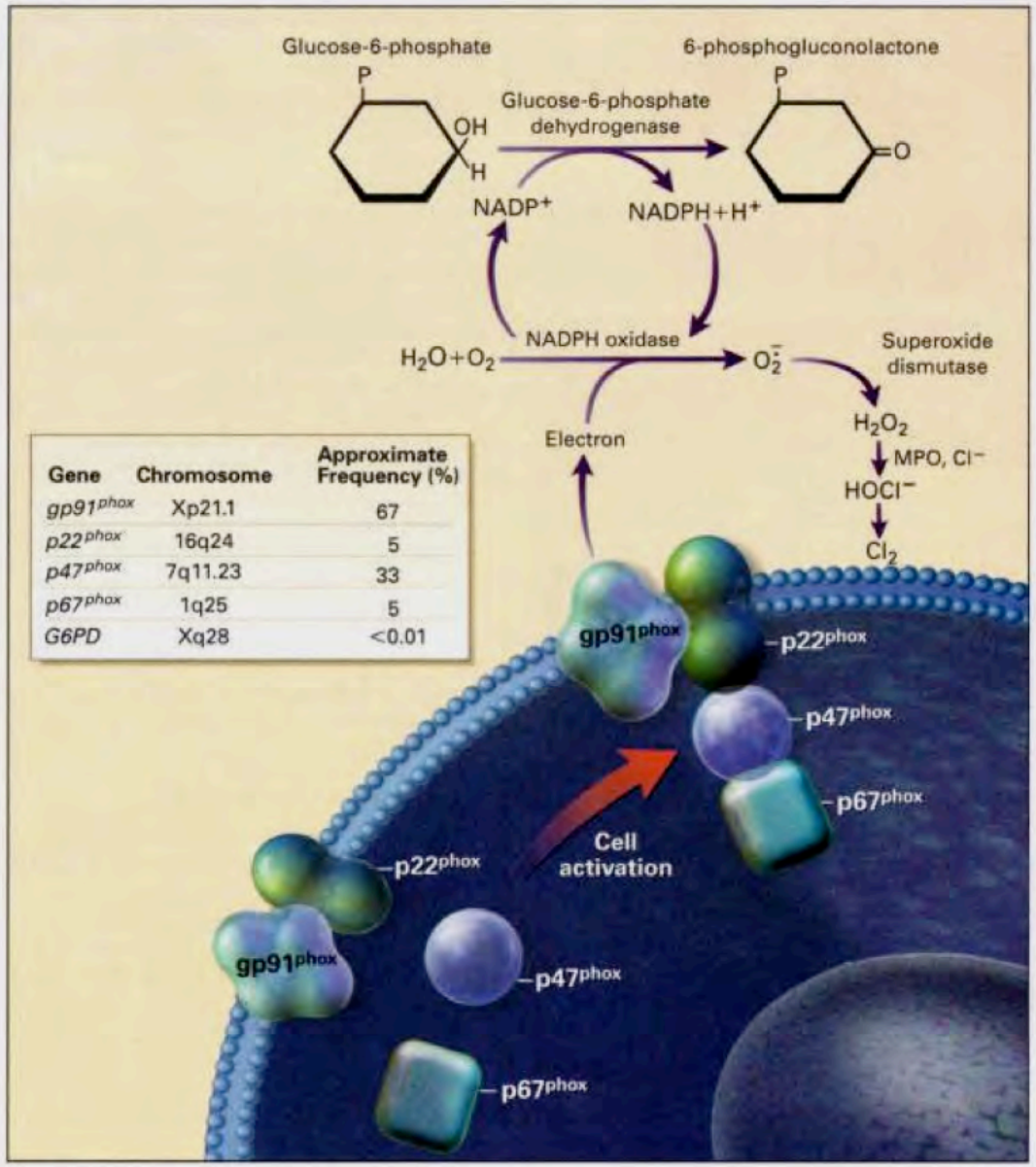


Figure 3. Relation among the Components of NADPH Oxidase That Are Affected in Patients with Chronic Granulomatous Disease.

The membrane-bound phagocyte oxidase components, the 91-kd glycoprotein (gp91^{phox}) and the 22-kd protein (p22^{phox}), interact with the cytoplasmic components, the 47-kd protein (p47^{phox}) and the 67-kd protein (p67^{phox}). Glucose-6-phosphate dehydrogenase (G6PD) converts glucose-6-phosphate to 6-phosphogluconolactone, generating NADPH and a hydrogen ion from $NADP^+$. NADPH oxidase catalyzes the monovalent reduction of O_2 to superoxide anion (O_2^-), with the subsequent conversion to hydrogen peroxide (H_2O_2) by superoxide dismutase. Neutrophil-derived myeloperoxidase (MPO) converts hydrogen peroxide to hypochlorous acid ($HOCl^-$ [bleach]), which is then converted to chlorine (Cl_2). The genes for the components of NADPH oxidase, their chromosomal locations, and the frequency of mutations as a cause of chronic granulomatous disease are indicated in the box.

BACTERICIDAL ACTIVITY OF POLYMORPHONUCLEAR NEUTROPHILS IN INDIVIDUALS SEVERELY DEFICIENT IN GLUCOSE-6-PHOSPHATE DEHYDROGENASE

Atif H. Asghar, MS; Kasim O. Ardati, MD;
Khaled S. Tabbara, PhD; Koharik M. Bajakian, BSc

Annals of Saudi Medicine, Vol 18, No 4, 1998

FEBS 20934 FEBS Letters 436 (1998) 411–414

Impaired production of nitric oxide, superoxide, and hydrogen peroxide in glucose 6-phosphate-dehydrogenase-deficient granulocytes

Kan-Jen Tsai[1,a], Iou-Jih Hung[b], Ching Kwong Chow[c], Arnold Stern[d], Sin Sin Chao[a], Daniel Tsun-Yee Chiu[a,*]

[a] *Graduate Institute of Basic Medical Sciences and School of Medical Technology, Chang Gung University, 259 Wen-Hua 1st Road, Kwei-san, Tao-yuan, Taiwan*
[b] *Department of Hematology, Chang Gung Children's Hospital, Kwei-san, Tao-yuan, Taiwan*
[c] *Department of Nutrition and Food Science, University of Kentucky, Lexington, KY, USA*
[d] *Department of Pharmacology, New York University Medical Center, New York, NY, USA*

Received 4 September 1998

THE LANCET

Volume 302, Issue 7828, 8 September 1973, Pages 530–534

Originally published as Volume 2, Issue 7828

NEUTROPHIL DYSFUNCTION, CHRONIC GRANULOMATOUS DISEASE, AND NON-SPHEROCYTIC HÆMOLYTIC ANÆMIA CAUSED BY COMPLETE DEFICIENCY OF GLUCOSE-6-PHOSPHATE DEHYDROGENASE

G.R. Gray, G. Stamatoyannopoulos, S.C. Naiman, M.R. Kliman, S.J. Klebanoff, T. Austin[1], A. Yoshida[2], G.C.F. Robinson

[a] Departments of Medicine, Pœdiatrics, and Surgery, University of British Columbia, United Kingdom

[b] Department of Pathology, Vancouver General Hospital, Vancouver, Canada

[c] and Department of Medicine, University of Washington School of Medicine, Seattle, Washington, U.S.A..

Abstract

A syndrome characterised by complete absence of erythrocyte and leucocyte glucose-6-phosphate dehydrogenase (G.-6-P.D.) activity, chronic non-spherocytic hæmolytic anæmia, and decreased leucocyte bactericidal and metabolic activity has been observed in three male siblings of a Canadian family. The oldest patient had episodes of recurrent granulomatous lymphadenitis, the second sibling had a single episode of cervical lymphadenitis, while the youngest has been free of infection. An intermediate defect in leucocyte microbicidal and metabolic activity and red and white blood-cell mosaicism was detected in the mother. The findings support the concept that complete or severe deficiency of G.-6-P.D. may affect both red-blood-cell survival and white-blood-cell function and express with the combined picture of hæmolytic anæmia and mild chronic granulomatous disease.

Journal of Pediatric Hematology/Oncology:
February 2002 - Volume 24 - Issue 2 - pp 164-165
Letters to the Editor

Neutrophil Dysfunction in a Case of Glucose-6-Phosphate Dehydrogenase Deficiency

Costa, Elísio B.Sc.; Vasconcelos, Júlia M.D.; Santos, Eugénia M.D.; Laranjeira, Armando M.D.; Melo, João Castroe M.D., Ph.D.; Barbot, José M.D.

blood 1982 59: 428-434

Severe-glucose-6-phosphate dehydrogenase (G6PD) deficiency associated with chronic hemolytic anemia, granulocyte dysfunction, and increased susceptibility to infections: description of a new molecular variant (G6PD Barcelona)

JL Vives Corrons, E Feliu, MA Pujades, F Cardellach, C Rozman, A Carreras, JM Jou, MT Vallespi and FJ Zuazu

J Pediatr. 1987 Dec;111(6 Pt 1):852-4.

Glucose-6-phosphate dehydrogenase deficiency, neutrophil dysfunction and Chromobacterium violaceum sepsis.

Mamlok RJ, Mamlok V, Mills GC, Daeschner CW 3rd, Schmalstieg FC, Anderson DC.

Department of Pediatrics, University of Texas Medical Branch, Galveston 77550.

Glucose-6-phosphate dehydrogenase deficiency with recurrent infections: case report

Abertina Rosa-Borges, Márcia G. Sampaio, Antônio Condino-Neto, Orlando C.O. Barreto, Victor Nudelman, Magda M.S. Carneiro-Sampaio, Susie A. Nogueira, Thalita F. de Abreu, Jussara Rehder, Beatriz T. Costa-Carvalho

J Pediatr (Rio J) 2001;77(4):331-6

Increased incidence of sepsis and altered monocyte functions in severely injured type A− glucose-6-phosphate dehydrogenase-deficient African American trauma patients

Zoltán Spolarics, MD, PhD; Muhammad Siddiqi, MD; John H. Siegel, MD; Zenaida C. Garcia, BS; Dana S. Stein, BS; Hortencia Ong, BS; David H. Livingston, MD; Thomas Denny, BS; Edwin A. Deitch, MD

Crit Care Med 2001 Vol. 29, No. 4

Song et al. Clinical and Molecular Allergy 2011, 9:10
http://www.clinicalmolecularallergy.com/content/9/1/10

CMA CLINICAL AND MOLECULAR ALLERGY

REVIEW Open Access

Chronic granulomatous disease: a review of the infectious and inflammatory complications

EunKyung Song[1], Gayatri Bala Jaishankar[1], Hana Saleh[3], Warit Jithpratuck[3], Ryan Sahni[3] and Guha Krishnaswamy[1,2,3*]

Table 5 Infectious Consequences of CGD

Type	Organ System	Manifestations	Etiology	Diagnosis
Infectious				
	Blood stream	Sepsis	B Cepacia Pseudomonas Serratia Staphylococcus Salmonella	Blood cultures Echocardiogram
	Pulmonary	Pneumonia	Aspergillus Nocardia Serratia Pseudomonas Staphylococcus Klebsiella Candida Others	Radiolology Cultures Biopsy
	Cutaneous	Impetigo Abscess	Staphylococcus Klebsiella Aspergillus/Candida Serratia	Aspirate cultures Biopsy
	Lymph node	Adenitis Adenopathy	Candida/Nocardia Aspergillus Serratia/Klebsiella	Fine needle aspirate Cultures Biopsy
	Liver	Abscess	Staphylococcus Streptococcus Aspergillus/Nocardia Serratia	Ultrasound or CT Aspirate Biopsy
	Bone	Osteomyelitis	Serratia, Aspegillus Staphylococcus Pseudomonas/Nocardia	Bone scan CT/Biopsy
	GI Tract	Perirectal abscess Fistulae	Enterobacteriaceae Staphylococcus	Biopsy Cultures
	Urinary	Pyelonephritis	Enterobacteriaceae	Cultures IVP/CT etc
	CNS	Meningitis Brain abscess	Candida, Haemophilus Aspergillus Staphylococcus	LP, cultures CT/MRI Biopsy

Take Home Messages

- In a patient with numerous premalignant conditions, think of occult immunodeficiency
- G6PD deficiency is not an “all-or-none” condition
- Biochemical G6PD deficiency is not that uncommon among elderly females due to skewed lyonization
- A very low level of G6PD can be associated with increased risk of sepsis, the clinical picture of which may resemble that of chronic granulomatous disease

The End

Thank you