Interhospital

Pediatric Chest Conference

November 27, 2008

King Chulalongkorn Memorial Hospital

Case I

เด็กชายไทย อายุ 3 เดือน ภูมิลำเนา จ. สุรินทร์ refer จากรพ.สุรินทร์

CC ไข้ ไอ หอบเหนื่อยมากขึ้น 2 วัน PTA

PI 1 เดือน PTA มีอาการหายใจเร็ว มีเสียงครืดคราดในลำคอ มีไข้ มารดาพาไปรักษาที่โรงพยาบาลชุมชน แพทย์วินิจฉัยว่าเป็นหลอดลมอักเสบ ได้รับการรักษาด้วยยาปฏิชีวนะและยาขยายหลอดลมชนิดพ่นฝอยละออง ทุก 4-6 ชั่วโมง อยู่โรงพยาบาล 5 วัน อาการไม่ดีขึ้น แพทย์จึงส่งตัวไปรับการรักษาต่อที่รพ.สุรินทร์

PI ที่รพ.สุรินทร์นอนโรงพยาบาลนาน 14 วัน ระหว่างนอนรพ. ยังมีไข้ ไอเป็นช่วงๆ ผลการตรวจภาพถ่ายรังสีทรวงอกพบว่าผิดปกติ ได้รับการรักษาด้วยยาขยายหลอดลมชนิดพ่นฝอยละอองและยาปฏิชีวนะนาน 14 วัน อาการไข้ดีขึ้น จึงกลับบ้าน แต่ยังไอมีเสมหะ ไม่มีอาการหอบเหนื่อย แพทย์นัดติดตามอาการ และถ่ายภาพรังสีทรวงอกซ้ำหลังจากนั้นอีก 2 สัปดาห์ ยังพบความผิดปกติเหมือนเดิม จึงส่งตัวมารับการรักษาต่อที่รพ.จุฬาลงกรณ์

2 วัน PTA มีไข้ ไอ หายใจหอบเหนื่อยมากขึ้นไอมากเป็นชุดๆ

PH บุตรคนที่ 2 คลอดครบกำหนดปกติ น้ำหนักแรกเกิด 2,500 กรัม

หลังคลอดมีตัวเหลือง on phototherapy

Immunization ครบตามกำหนด

พัฒนาการปกติ

ไม่มีประวัติสัมผัสวัณโรค

Feeding นมแม่

Physical examination

GA A Thai male infant, active, BW 4 kg (P3),

HC 38 cm (P50)

V/S BT 37.8^{0}C, PR 148/min, RR 55/min,

BP 82/43 mmHg

HEENT mild pale conjunctiva, no icteric sclera,

no injected pharynx, anterior fontanelle 2x2 cm,

no bulging, posterior fontanelle closed

Chest	intercostal and subcostal retractions, coarse crepitations and expiratory wheezing both lungs
Heart	normal S1S2, no murmur
Abdomen	soft, liver just palpable, liver span 6 cm, spleen 1 cm below LCM
Neuro	normal

Initial investigations

CBC Hb 7.6 gm/dL, Hct 24%, MCV 62, MCH 22,

MCHC 35.5, RDW 22, WBC 21,500 /mm^3 ,

N 38%, L 56%, M 4%, E 2%, Plt 216,000/mm^3

Chest x-ray ที่ รพ.สุรินทร์

Chest x-ray แรกรับที่รพ. จุฬาฯ

Problem lists

- 3-month-old male infant with

-Recurrent/ persistent pneumonia

-Persistent RUL opacification

-Hepatosplenomegaly

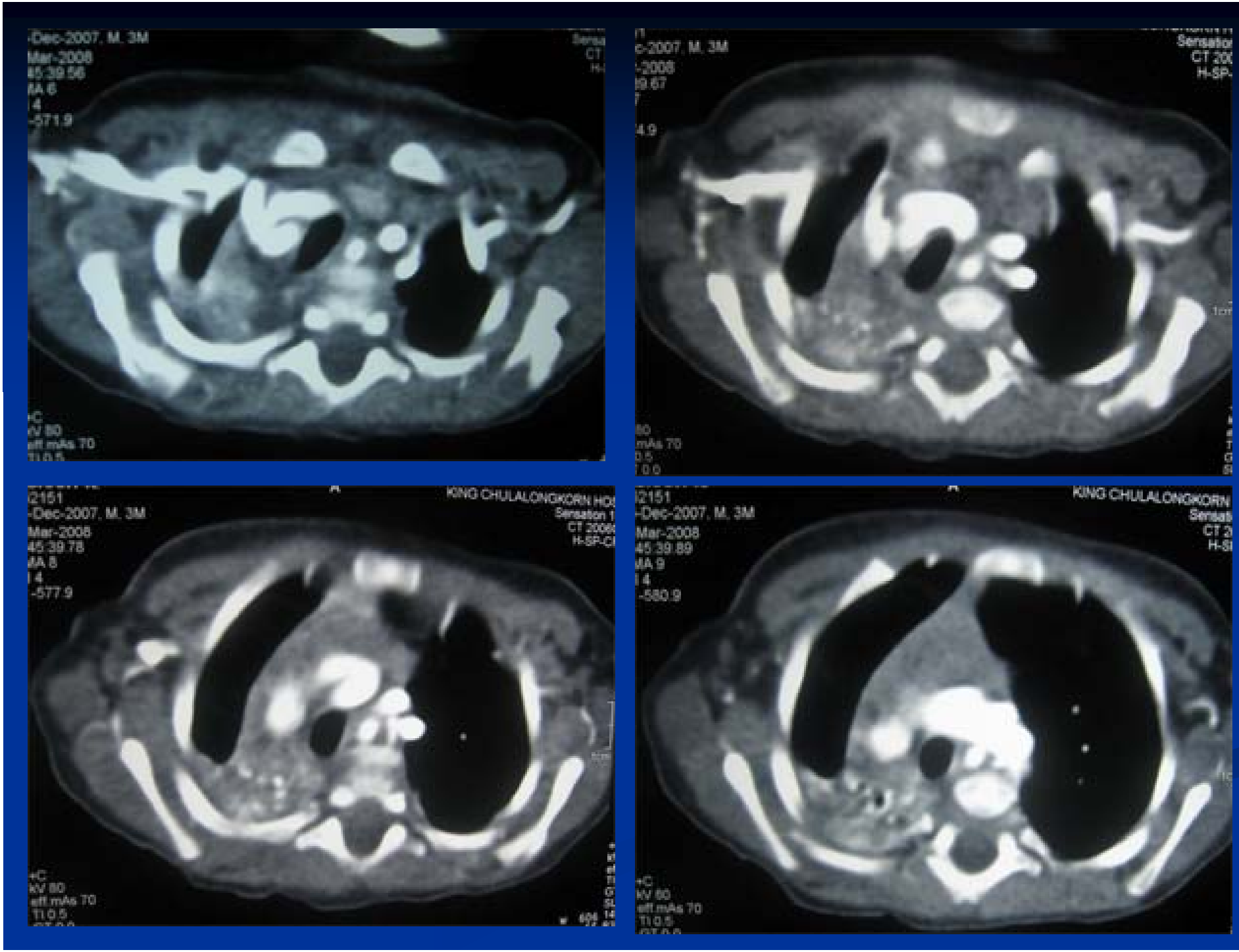
-Anemia

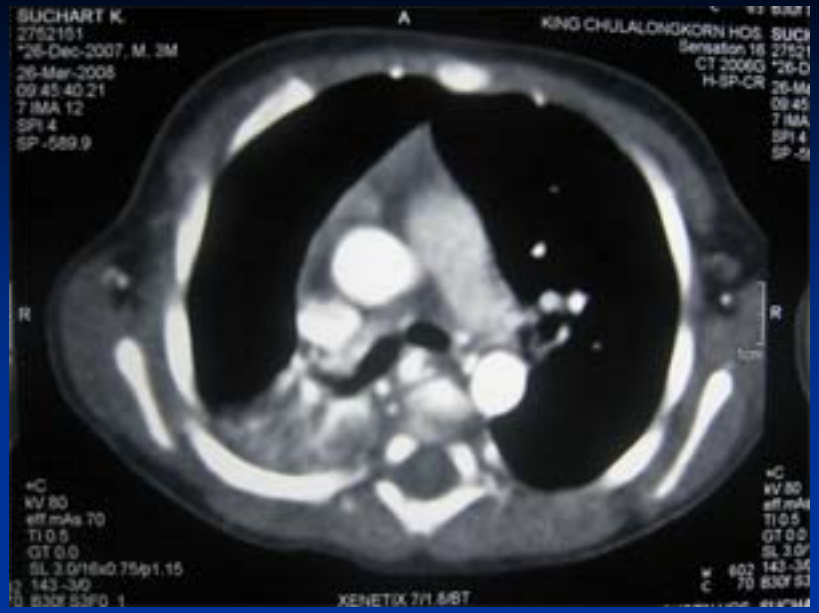
-Underweight

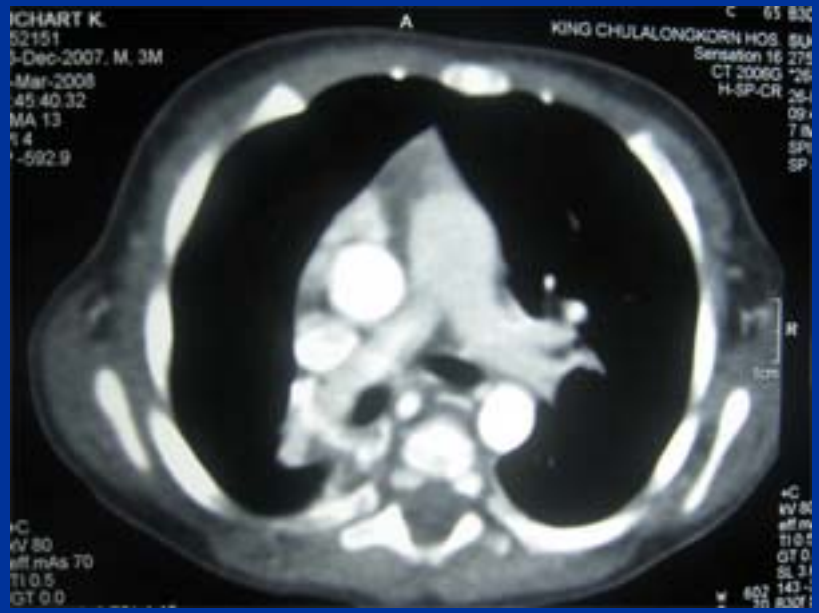
Chest x-ray

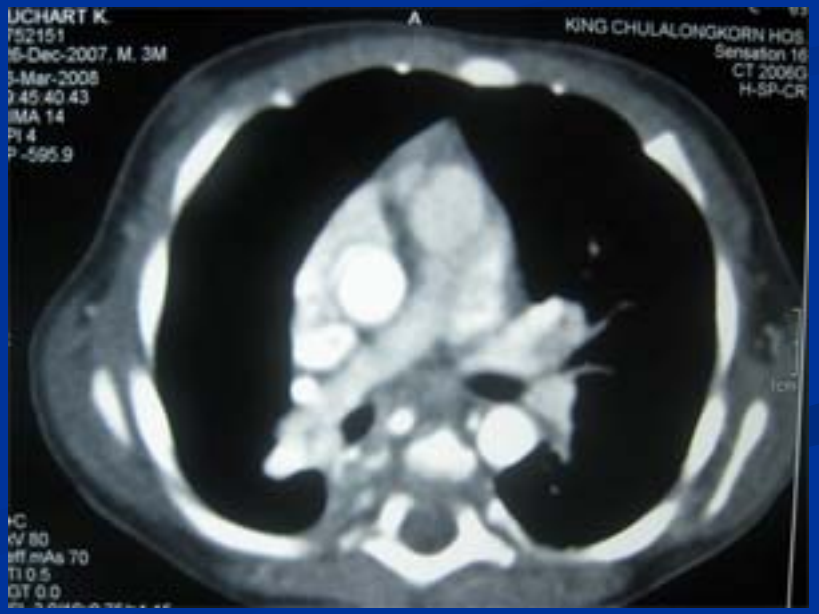
TB work up

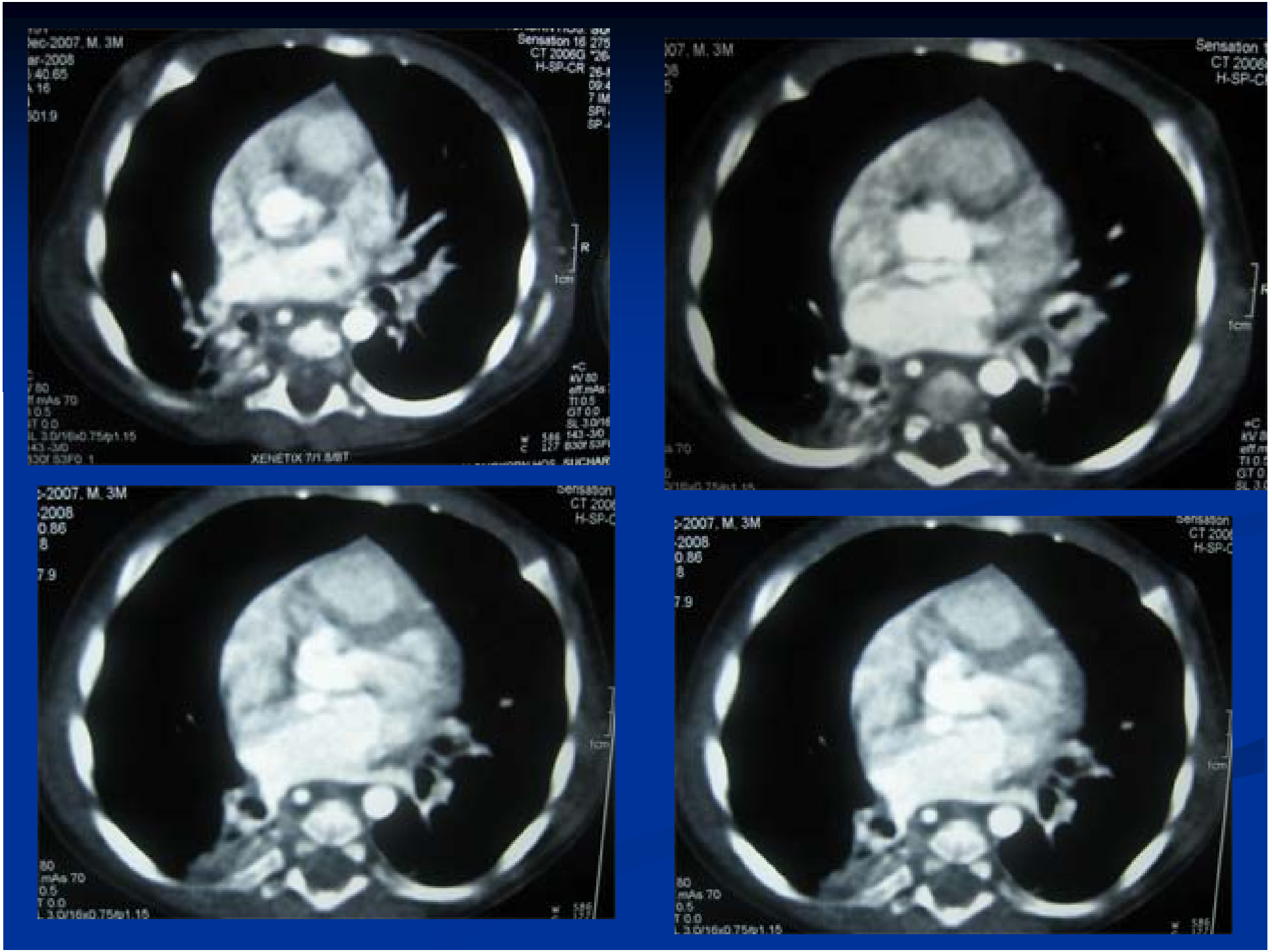
- PPD test: 3 mm
- Gastric wash for AFB stain: negative x 3 days
- Gastric wash for PCR TB: negative
- C/S TB: pending

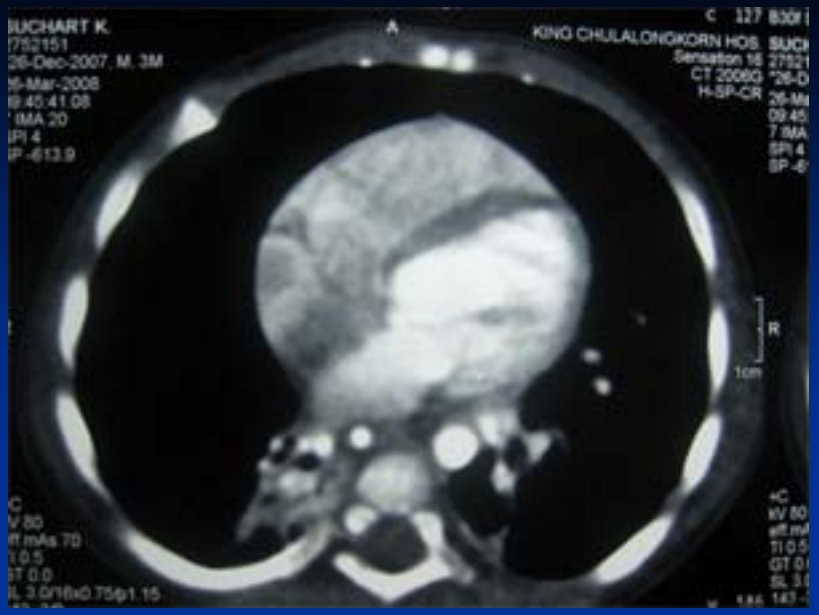

-Dec-2007, M, 3M
Mar-2008
-571.9
KING CHULALONGKORN
-577.9
-580.9

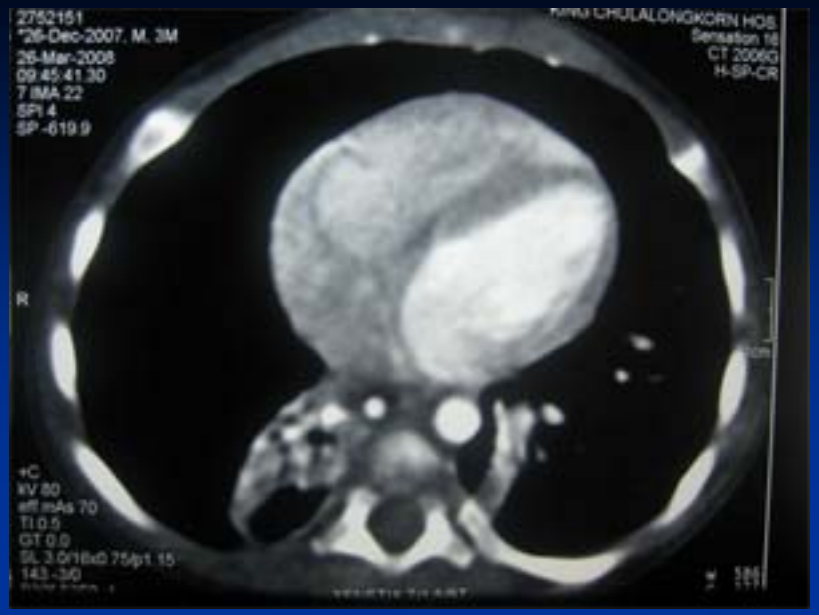









KING CHULALONGKORN HOS
Sensation 16
CT 2006G
H-SP-CR
R
1cm


2752151
26-Dec-2007, M, 3M
26-Mar-2008
09:45:41.30
7 IMA 22
SPI 4
SP -619.9
H-SP-CR
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H-SP-CR
5cm
XENETIX 7/1.8/BT


H-SP-CR
5cm
XENETIX 7/1.8/BT


26-Mar-2008
09:45:38.88
603 IMA 14
MIP 4
RA
1cm
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SL 10.0
XENETIX 7/1.8/BT


09:45:38.88
603 IMA 15
MIP 4
RA
A
SL 10.0
XENETIX 7/1.8/BT


26-Mar-2008
09:45:38.88
603 IMA 16
MIP 4
RA
cm
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XENETIX 7/1.8/BT
H


26-Mar-2008
09:45:38.88
603 IMA 17
MIP 4
RA
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SL 10.0
XENETIX 7/1.8/BT


XENETIX 7/1 8/BT
KING CHULALONGKORN HOS.


XENETIX 7/1 8/BT

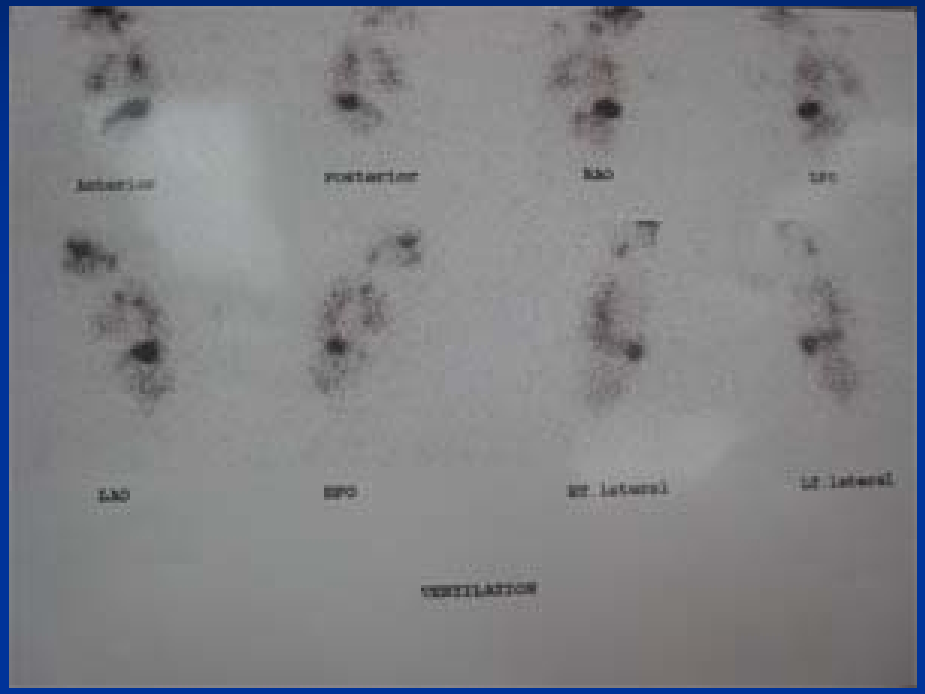

XENETIX 7/1 8/BT


XENETIX 7/1 8/BT

CT scan

- Presence of systemic arterial supply to RUL and pulmonary venous drainage; sequestration is suggested
- Stenosis or atresia of superior segment of RUL bronchus
- Near total atelectasis of RLL
- Small patchy infiltrate of anterior segment of right lung and lingular segment with feeding arteries from thoracic aorta
- Congenital dysplasia or acquired from repeated infection

V/Q scan


LAO
RPO
Rt. lateral
Lt. lateral
VENTILATION


LAO
RPO
Rt. lateral
Lt. lateral
PERFUSION

V/Q scan

- Ventilation study: fairly symmetrical without definite ventilation defect
- Perfusion study: perfusion defect at RUL
- IMPRESSION: Fairly symmetrical lung ventilation study with perfusion defect at RUL

Bronchoscopy

- Early opening of RUL bronchus
- Normal bronchus intermedius
- Hypersecretion

Immunology

- **Flow cytometry**

White blood count	16,000/ mm^3
Absolute total lymphocyte	7,721/ mm^3 (48%)
Absolute CD3 (Total T cell)	5,398 /mm^3 (70%)
Absolute CD4 (T helper cell)	383 /mm^3 (44%)
Absolute CD8 (Cytotoxic T cell)	1,774 /mm^3 (23%)
%CD19 (B cell)	15%
%CD 56 (NK cell)	3%

- **DHST** PPD 3 mm, candida 0 mm, measles 0 mm
- **Immunoglobulin level**
  - IgG 990 mg/dL (300-650)
  - IgM 263 mg/dL (16-64)
  - IgA 19 mg/dL (7-40)
- DHR normal

TORCH titer

- Anti HSV IgG: positive
- Anti CMV IgG: positive 198 (40)
- Rubella IgG: negative

Anti HSV IgM: positive

Anti CMV IgM: positive

Rubella IgM: negative

- PBS: hemoglobin leakaged cells, bite cells, microspherocyte 3+, anisocytosis 2+
- **G-6-PD:** deficiency

Operation

- **Operation** RUL lobectomy
- **Findings** Abnormal RUL with intraparenchymal mass, firm, size 2 cm

  Normal RML and RLL

  No emphysematous change

  Cannot identify feeding vessels

Pathology report

Gross examination:

- A piece of lung tissue, measuring 3.9 x 3.2 x 1.5 cm
- Rubbery whitish brown cut surfaces
- No abnormal insertion of blood vessel
- No cyst

Microscopic examination:

- Consolidated lung tissue with patchy areas of atelectasis
- Various degree of chronic inflammation of small to large bronchi associated with patchy alveolar interstitial lymphocyte infiltrations
- Several CMV inclusions identified in bronchial gland cells, pneumocytes and histiocytes

Diagnosis:

- Chronic bronchitis, bronchiolitis and patchy chronic interstitial pneumonitis
- Presence of CMV infected cells
- Atelectasis and alveolar accumulation of foamy histiocytes
- Evidence of sequestration is not definite

CMV viral load

- CMV viral load (before ganciclovir treatment): 1,390 copies/ml
- CMV viral load (after ganciclovir treatment): <600 copies/ml

Other investigations

- Ultrasound brain : normal study
- ABR audiometer : normal hearing both ears
- Eye examination : normal

Treatment

- Ganciclovir 5 mg/kg/dose q 12 hr x 6 wks

Post operation D 10

Cytomegalovirus

- A member of herpesvirus family, subfamily beta herpesviridae
- Ubiquitous virus, commonly infects people
- Most infections are asymptomatic or cause mild disease
- Can cause serious disease in newborns and immunocompromised children

Epidemiology

- Developing countries : most children are infected by 3 yrs
- Developed countries : 60-80 % infected by adulthood
- Classification of disease
  - Congenital
  - Perinatal
  - Acquired

Congenital CMV infection

- 0.2 - 2.2 % lived births
- 90 % asymptomatic
- 5 - 15 % have symptoms at birth

Rev Infect Dis 1991,13:315-29

- Primary maternal infection leads to fetal infection in 30-50%

  (10-15% have overt clinical disease)
- Secondary maternal infection less likely leads to fetal infection

  (1-2%) but may lead to severe disease

NEJM 2001, 344: 1366

Congenital CMV infection

- Clinical manifestations

  - Most are asymptomatic

  - 5-17% of asymptomatic cases develop neurological sequelae (esp. hearing loss)

  - 10 % of congenitally infected have symptoms at birth

    Jaundice, petechiae, hepatosplenomegaly, IUGR (33%), preterm, microcephaly, chorioretinitis, fatal outcome

J Pediatr 2005 ;146:817-23

Congenital CMV infection

- Abnormal blood counts (esp. thrombocytopenia), hemolytic anemia, ↑ transaminases, ↑ direct and indirect bilirubin
- CNS abnormalities: periventricular leukomalacia, cystic abnormalities, periventricular calcifications, ventriculomegaly, vasculitis, neuronal migration abnormalities, hydranencephaly
- Ocular abnormalities: chorioretinitis
- Sensorineural hearing loss: 2/3 of symptomatic congenital CMV infection

Perinatal infection

- Acquired during or shortly after birth

  - Maternal cervicovaginal secretions during delivery

  - Breast milk ingestion after delivery

  - Blood transfusion

Perinatal infection

- May occur in term and preterm infants
- May become apparent 3 weeks and as late as 3 to 6 mo of age
- Often asymptomatic, can produce a variety of clinical symptoms
- Sepsis-liked syndrome occurs most commonly (hepatosplenomegaly, abnormal blood counts, lymphopenia, neutropenia, thrombocytopenia, abnormal transaminases, pneumonitis)

Acquired CMV infection

- Most are asymptomatic in healthy child, 10 % produce symptoms
- Acquired during toddler and preschool years

  - Prevalence of active CMV shedding in saliva and urine in daycare centers varies from 10 to >80%

Acquired CMV infection

- Mononucleosis–liked syndrome (fever, fatigue, pharyngitis, adenopathy, hepatitis, headache, abdominal pain, diarrhea, arthralgia, rash)
- Unusual manifestations/complications : pneumonitis, myopericarditis, hemolytic anemia, viral hemophagocytic syndrome, granulomatous hepatitis, Guillain-Barré syndrome, meningoencephalitis

CMV infection in immunocompromised host

- Acquired serious CMV disease
- Hepatitis, colitis: liver transplant recipients
- Pneumonitis: lung, bone marrow transplant recipients
- Early myocarditis, atherosclerosis: heart transplant recipients
- Retinitis, colitis, encephalitis/encephalopathy

Laboratory diagnosis

- Congenital CMV infection:

  - Viral isolation in urine, saliva within 3 wks of life

  - May use PCR techniques to detect CMV DNA in urine and serum

- Acquired CMV infection in healthy child or adolescent :

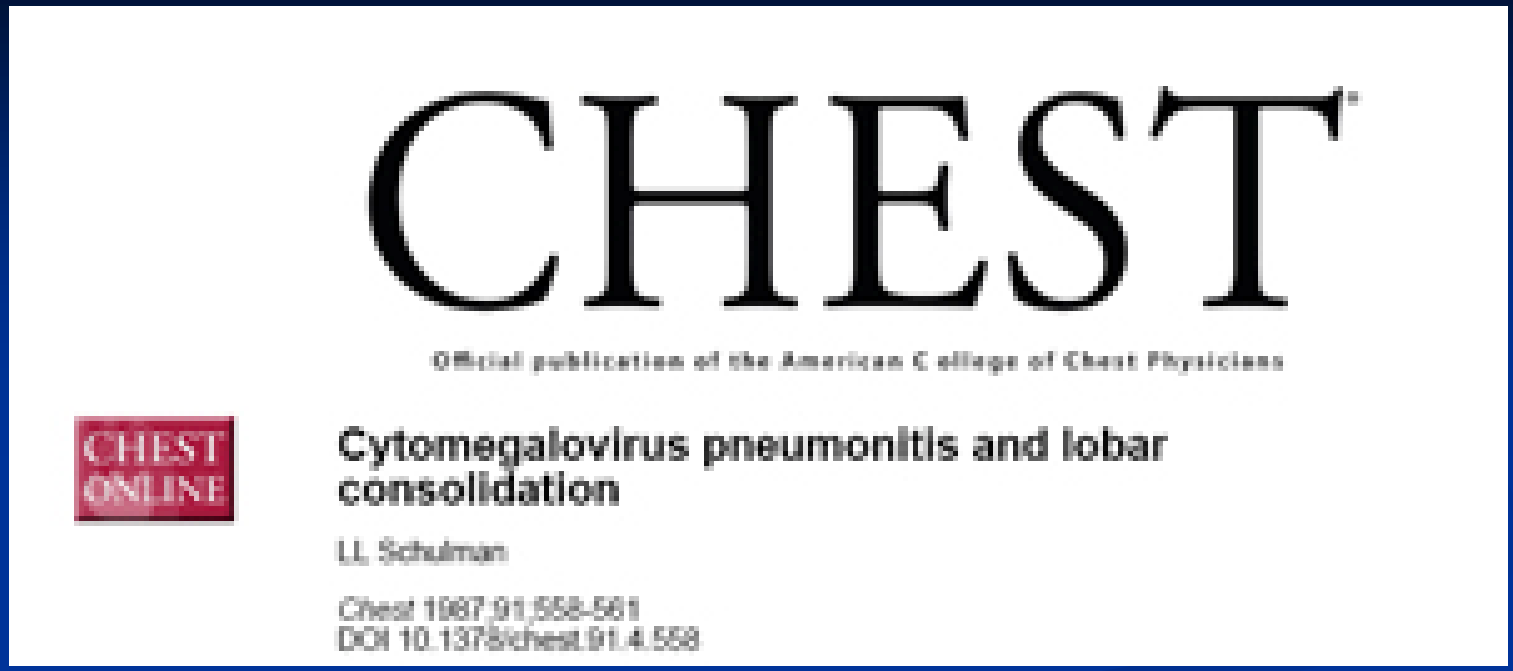
  - CMV IgG seroconversion plus CMV IgM + ve

  - CMV culture of urine, saliva, blood (may + ve in acute phase of infection)

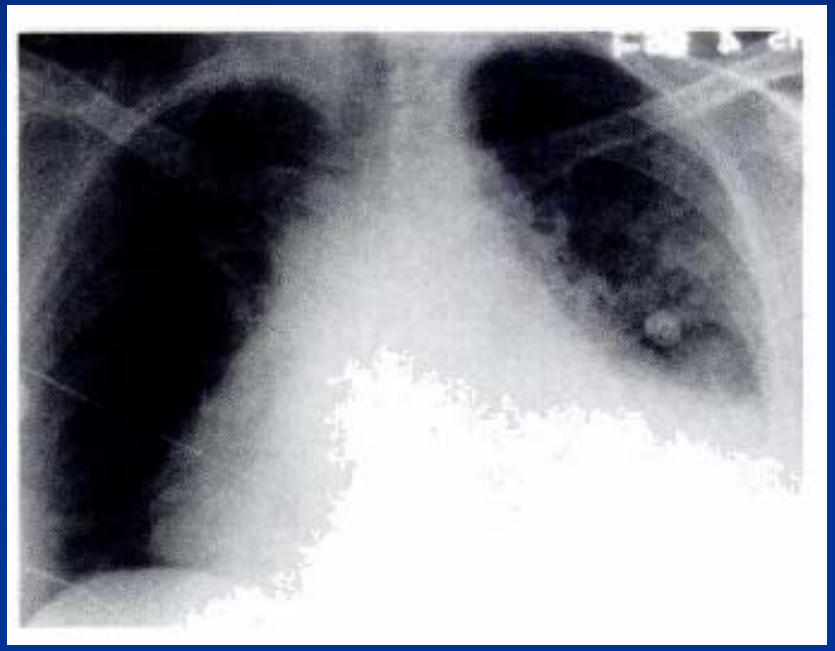
CMV pneumonia

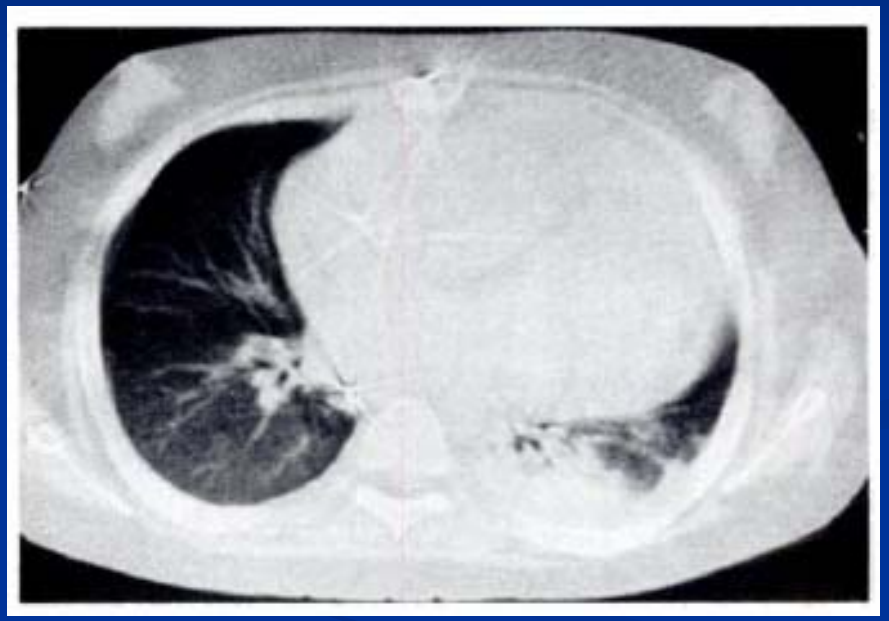
- Present with low-grade fever, shortness of breath, nonproductive cough, PFT changes
- Chest x-ray: diffuse reticulonodular densities, diffuse haze, dense areas of consolidation
- CMV pneumonitis and lobar consolidation: 2 case reports in heart transplant recipient

Chest 1987;91:558-61



The occurrence of localized lobar consolidation caused solely by CMV infection in two heart transplant recipients





CMV pneumonia

- CT findings:

  - Patchy areas of ground-glass opacity (most common)

  - Ill-defined centrilobular small nodules (90%)

  - Consolidation (70%)

  - Interlobular septal thickening

  - Pleural effusion

J Comput Assist Tomogr 1996; 20:295-9

CMV pneumonia

- Diagnosis: demonstration of typical inclusions in alveolar cells
- Pathology: small hemorrhagic nodules scattered throughout the lung, diffuse alveolar damage, chronic interstitial pneumonitis

Treatment

- Asymptomatic CMV infection in the normal host: no treatment
- CMV disease in normal child should be individualized, no clinical trials documenting the efficacy

- Neonates - remains controversial
- Ganciclovir is beneficial in

  -Viral sepsis-liked syndrome caused by CMV

  - Pneumonitis

  -Sight-threatening retinitis
- May benefit in :

  - Sensorineural hearing loss

  - Microcephaly

Pediatr Infect Dis J 1994;13:239-41

Trial of ganciclovir for congenital CMV disease

- Randomized trial of ganciclovir for symptomatic congenital CMV infection involving the CNS
- Neonates randomized to receive 6 wks of IV ganciclovir (6 mg/kg/dose q 12 hrs) or no therapy
- Primary endpoint of study was hearing test: BSER performed at baseline and at 6 mo

J Pediatr 2003; 143:16-25

Trial of ganciclovir for congenital CMV disease

- No significant difference in mortality (6% GCV vs. 12% untreated)
- Median head circumference growth at 6 wks was greater in the GCV group vs. the untreated group (3.5 vs 2.6 cm)
- Hearing improvement was more likely in the GCV group at 6 and 12 mo (OR 4.31, 4.03)
- Side effects of ganciclovir: neutropenia (transient), ↑ liver enz

Antiviral Px for congenital CMV?

- Current role for IV ganciclovir is uncertain: may be *considered* for patients with symptomatic congenital CMV disease involving the CNS

J Pediatr 2003; 143:16-25

- 2006 Red Book: not recommended routinely because of insufficient data of efficacy
- ?? Treatment of neonates with worsening retinitis or hepatitis, severe pneumonia, or persistent severe thrombocytopenia ?? Duration of therapy ??

Conclusions

- 3-month-old male infant presented with persistent pneumonia, persistent RUL opacification, hepatosplenomegaly, underweight
- Diagnosis of CMV pneumonitis: made by histopathology
- Treatment: RUL lobectony + ganciclovir 5 mg/kg/dose q 12 hr x 6 wks

Chest x-ray post op 4 mo

CT chest post op 4 mo

CT chest post op 4 mo

CT scan

- Thymus gland extending to posterior mediastinum
- Compensatory emphysematous change of RML
- Segmental atelectasis of posterior basal segment of LLL