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Dengue case vignettes

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Case 1

- 69 year old Indian female
- No drug allergy
- Medical history:
  - Hyperlipidaemia
  - Glaucoma

Presentation

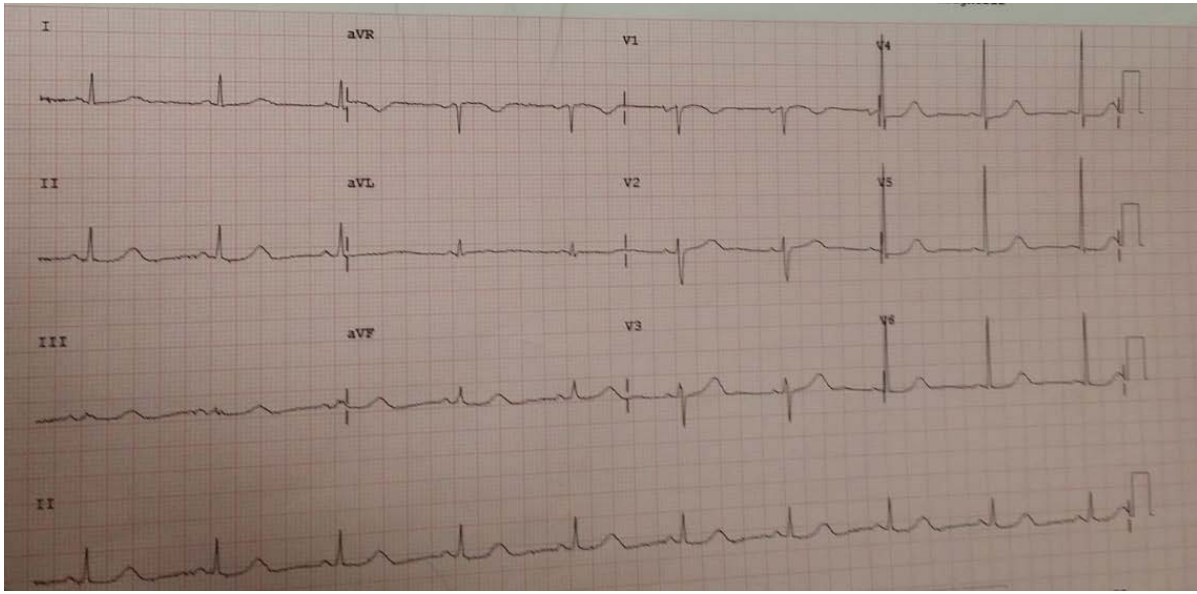
- Fever for 4 days
  - Headache, myalgia, generalised malaise
  - Giddiness on standing for 2 days
- Vomiting for 2 days
  - Small amounts with oral intake
  - Mild abdominal pain and nausea
- Chest pain for 1 day
  - Dull in nature, at rest, no radiation
  - First episode
  - Worsened with sour taste when supine or after eating

Examination

- 37.8°C, 56/min, 146/71mmHg, no postural drop
- Oximetry 98% room air
- Alert, oriented
- Dual heart sound, no murmur
- Lungs clear
- Abdomen soft, non-tender, no hepatomegaly
- No rash
- No gum bleeding

Investigations

- WCC 3.8, HB 11.7, HCT 34.4, PLT 129
- CR 47
- ALT 67, AST 160
- Dengue Duo
  - NS1 positive
  - IgM/IgG negative
- Troponin I 0.01
- CXR no focal consolidation



Decision

- Admission?
- Reason for decision?
- Na 126, K 4.6
- Urea 3.9, albumin 43

Dengue in elderly

Am. J. Trop. Med. Hyg., 79(2), 2008, pp. 149–153

Clinical and Laboratory Characteristics and Risk Factors for Fatality in Elderly Patients with Dengue Hemorrhagic Fever

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Abstract. To better understand the clinical and laboratory characteristics and to identify risk factor(s) for fatality in elderly patients with dengue hemorrhagic fever (DHF), 66 elderly (age ≥ 65 years) and 241 non-elderly adults (age, 19–64 years) with DHF were retrospectively analyzed. Compared with non-elderly adults, elderly individuals had significantly lower incidences of fever ($P = 0.002$), abdominal pain ($P = 0.003$), bone pain ($P < 0.001$), and skin rashes ($P = 0.002$); higher frequencies of concurrent bacteremia ($P = 0.049$), gastrointestinal bleeding ($P = 0.044$), acute renal failure ($P = 0.001$), and pleural effusion ($P = 0.010$); higher incidence of prolonged prothrombin time ($P = 0.025$); lower mean hemoglobin level ($P < 0.001$); longer hospitalization ($P = 0.049$); and a higher fatality rate ($P = 0.006$). Five elderly patients with DHF died. When compared with non-fatal elderly patients with DHF, a significant higher frequency in men ($P = 0.019$), those with chronic obstructive pulmonary disease ($P = 0.008$), those with dengue shock syndrome (DSS; $P < 0.001$), and those with acute renal failure ($P < 0.001$) was found in the elderly counterparts that died. Multivariate analysis showed that only DSS (odd ratio = 77.33, $P = 0.001$) was an independent risk factor for fatality in elderly patients.

Elderly: less fever, abdominal pain, bone pain, rash; more bacteraemia, GIT bleeding, acute kidney injury, pleural effusion; higher APTT, lower HB, longer hospital stay, higher mortality

The benign nature of acute dengue infection in hospitalized older adults in Singapore

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Objectives: In Singapore, dengue primarily affects adults. This study aimed to determine if older dengue patients in Singapore have greater morbidity and mortality.

Methods: All laboratory diagnosed dengue patients admitted to Tan Tock Seng Hospital in 2004 were retrospectively reviewed. Cases were re-classified into dengue fever and dengue hemorrhagic fever based on World Health Organization criteria. Demographic, clinical, laboratory, and outcome data of patients aged ≥60 years and <60 years were collected.

Results: Of 1971 laboratory confirmed dengue cases, 66 were aged ≥60 years. Older patients were significantly less likely to be male (44% vs. 64%), and more likely to have diabetes (17% vs. 2%), hypertension (48% vs. 4%), ischemic heart disease (6% vs. 0.1%), hyperlipidemia (18% vs. 1%), and secondary dengue infections (64% vs. 34%). Clinical features were similar except older patients were significantly less likely to report fever (92% vs. 99%), or have leukopenia (32% vs. 51%) or hemoconcentration (0 vs. 5%) on admission. Older patients had similar dengue hemorrhagic fever, bleeding, hypotension, severe thrombocytopenia, and elevated transaminase rates. Length of hospital stay, risk of intensive care unit admission, and outcome of death were not statistically different.

Conclusions: Despite greater co-morbidity and secondary dengue infection, older dengue patients in Singapore did not have greater morbidity or mortality.

Elderly: More co-morbidity, secondary dengue infection; less fever, leukopenia, haemoconcentration; similar risk of DHF, bleeding, low platelet, raised AST, hospital stay, ICU and death

Overnight after admission

- Found by nurse to be non-responsive with eyes open
- GCS 8 (E4V1M3)
- No seizure
- Afebrile, 89/min, 166/79mmHg
- Oximetry 77% room air → 100% on Fi02 100%
- Capillary blood glucose 8.6

On review

- Right gaze preference
- Bilateral limb movement equal
- Power upper limb >3/>3, lower limb 2/2
- Right pupil 4mm non-reactive (previous eye surgery), left pupil 4mm brisk reaction
- Bilateral Doll's eye reflexes intact
- Neck soft and supple
- Right plantar reflex extensor

Questions

- Differential diagnoses?

- Diagnostic investigations?

Investigations

- WCC 11.4, HB 14.9, HCT 44.7, PLT 137
- Na 113, K 3.1, CR 36
- Albumin 42, bilirubin 18, ALT 167, AST 227
- CRP 2.9
- ABG: pH 7.47,pC02 32, p02 122

Body Fluid M'scopy				
Sample	CSF			
Appearance	Clear and colourless			
Cell Count				
RBC, Fluid	23 (Ref Range: < 1 cell/ul)		cells/ul	
Nucleated Cell	2 (Ref Range: 0 - 5 cells/ul)		cells/uL	
Differential, Fluid	Low cell count, no differential count done			
Differential comment	Occasional monocytes and lymphocytes seen			
CLINICAL CHEMISTRY				
Protein Glucose,csf				
Sample	CSF			
Protein, csf	0.18	N	g/L	0.10 - 0.40
Glucose, csf	4.1	N	mmol/L	2.5 - 5.5

Blood culture 3 sets negative
CSF bacterial culture negative
CSF Dengue PCR negative
CSFHSV, VZV, CMV PCR negative

There is no restricted diffusion to suggest an acute infarct or abnormal susceptibility to suggest intracranial haemorrhage. Small focal subcortical and deep white matter T2 hyperintensities are non-specific, but may be related to small vessel disease. Age-related involutional changes are present. No mass effect, hydrocephalus or midline shift is seen. The basal cisterns are preserved.

There is no abnormal parenchymal or leptomeningeal enhancement.

The major dural venous sinuses demonstrate normal signal voids. A left maxillary sinus mucus retention cyst, mild sphenoid sinus and bilateral frontal sinus mucosal thickening are noted.

Dengue encephalitis or encephalopathy

- Solomon Lancet 2000
  - Prospective, 4.2% of 378 suspected encephalitis, and 1% of 1681 suspected dengue
  - N=21, virologically proven in blood 7, 1 of whom in CSF
    - Evidence of CSF dengue in 6
  - ↑opening pressure=3, pleocytosis=3, ↑CSF protein=7
  - CT normal in 2/2
  - No death, coma resolved 3.5d, neurological sequalae on discharge in 6

- Cam AJTMH 2001
  - Prospective, 0.5% of 5400 DHF
  - N=27, CSF PCR=1, CSF IgM=14/22
  - CSF normal cell count, protein and glucose
  - MRI (n=18): encephalitis=2, oedema=12, bleed=1
  - Cases vs. controls:
    - ↑leukocyte count, sodium, urea, AST, ALT, bilirubin, ALP, D-dimer
    - ↓haematocrit, glucose, prothrombin time
  - Mortality=22%, complete recovery within 7d

Dengue
encephalitis or encephalopathy

- Malavige IJMM 2007
  - N=15, dengue and encephalopathy, serology
  - DSS=14, death= 7 (47%)
  - Gastrointestinal illness=53%, acute liver failure=73%
  - Pleural effusion and ascites=100%, pulmonary oedema=53%
  - Myocarditis=27%
  - Bacteraemia=4 (all *E coli*)

- Wasay CNN 2008
  - N=16, retrospective, serology, DHF
  - CSF mean leukocyte 61, predominant lymphocyte
  - Abnormal CT/MRI=5, oedema=3
  - EEG generalised slowing 2/4
  - Death 2 (32%)

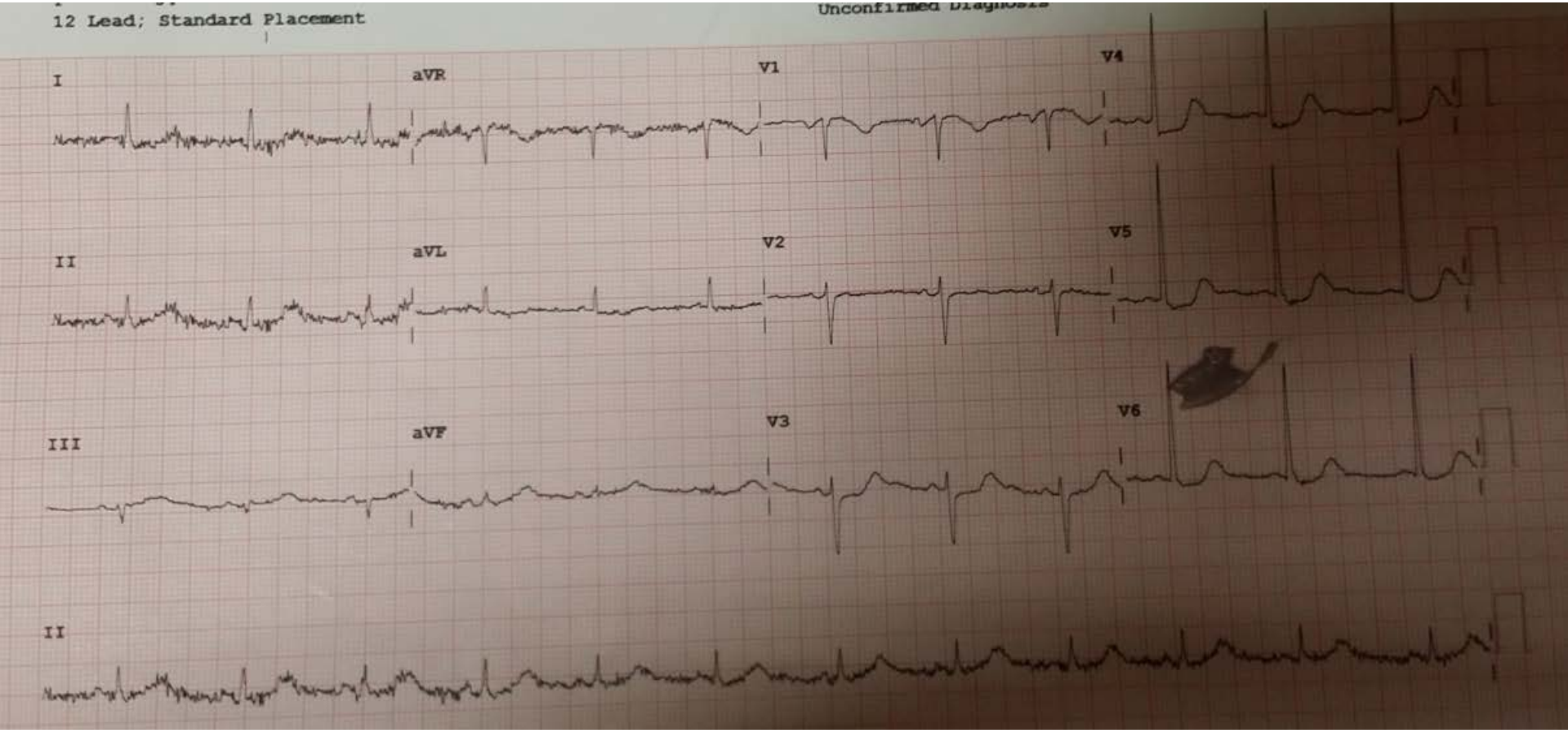
Dengue
encephalitis or encephalopathy

- Garcia-Rivera PRHSJ 2009
  - Enhanced prospective surveillance in response to West Nile
  - N=11, DHF=2, encephalitis=9, motor=2
    - 26% of all encephalitis
  - Suspected=4, death=2
  - Serology=8, isolation=2, CSF IgM=1
  - CSF raised protein 4/5, normal glucose 3/5, pleocytosis 3/5

Further progress

- After return from MRI brain
  - GCS 8 (E2V1M5)
  - Gaze central transiently then right gaze preference
- Rubbing chest wall

ECG

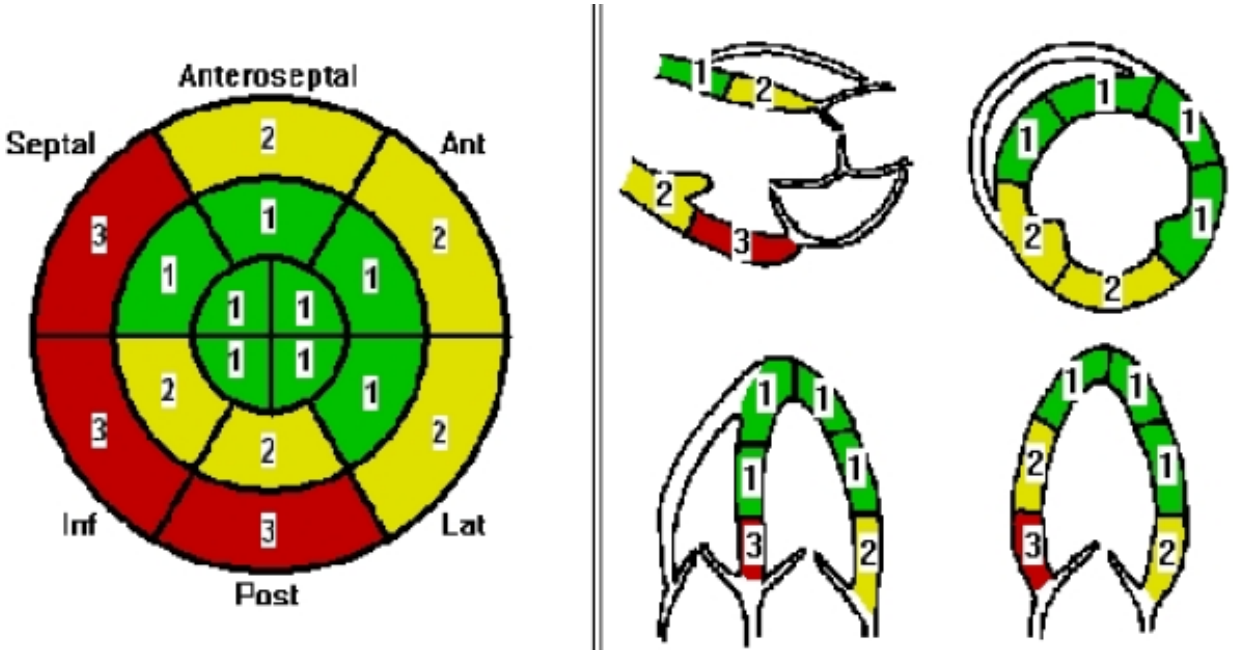


ST depression V2-V6

Trop I 3.39 → 7.87 → 6.69

Echocardiogram

Patient is in sinus rhythm. LVEF 45%. Mildly impaired LV systolic function. Impaired left ventricular diastolic relaxation with elevated left ventricular filling pressure. No left ventricular hypertrophy. Multiple wall motion abnormalities not particularly in keeping with coronary artery disease territories (see diagram below). Normal chamber sizes. Moderate eccentric mitral regurgitation. Normal sized right



2=hypokinesia, 3=akinetic

Dengue myocarditis

- Obeyesekere AHJ 1973
  - Retrospective, Sri Lanka, n=35
    - Age 5-58y, male 17
    - Gallop rhythm 12, pan-systolic murmur 7, cardiac failure 6, pericardial rub 2
    - Arrhythmia=25
  - Monthly follow-up
    - Death=3
    - Complete recovery=4
    - Asymptomatic, normal chest XR, T wave change=2
    - Persistent cardiomegaly, abnormal ECG=26
    - Cardiac failure 3, constrictive pericarditis 1

Reversible impaired cardiac function in dengue

- Wali Int J Cardiol 1998
  - DEN2, 1996, New Delhi
  - Consecutive DHF/DSS=17
  - Radionuclide ventriculography
    - Mean LVEF 42%, 7 <40%, 12 global hypokinesia
  - Echocardiography
    - Mean EF 40%, 5 <40%
  - 99m Tc pyrophosphate for myocardial necrosis in 4 → negative
  - ECG ST and T changes in 5
  - No abnormality after 3 weeks, EF>50% all cases, global hypokinesia improved, ECG normalised within 3 weeks

Acute myocarditis in dengue hemorrhagic fever: a case report and review of cardiac complications in dengue-affected patients

Ing-Kit Lee [a], Wen-Huei Lee [b], Jien-Wei Liu [a,*], Kuender D. Yang [c]

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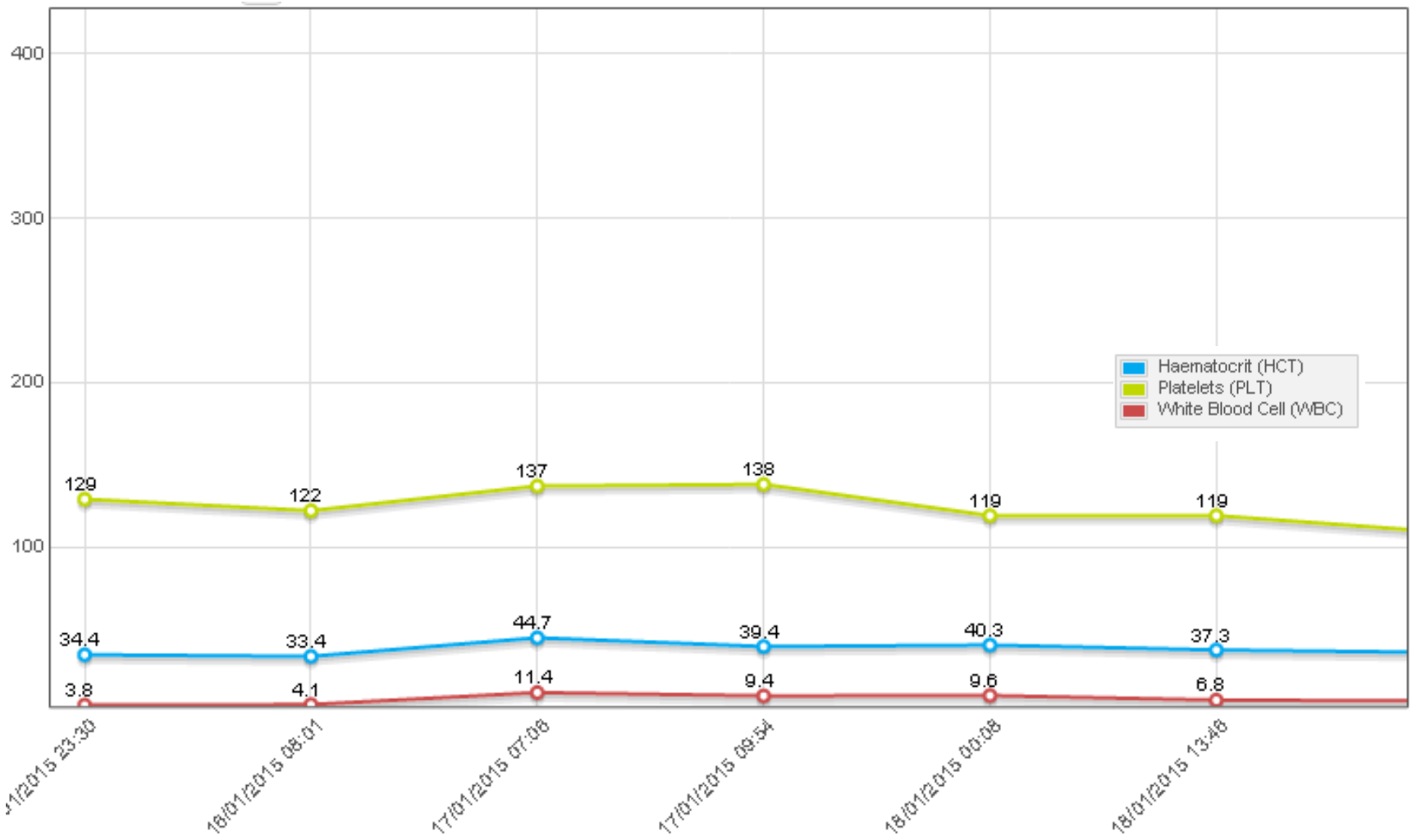
Summary of demographic details, cardiac manifestations, and outcomes in dengue-affected patients with cardiac manifestations reported in the English-language literature

Author(s), year of publication [Ref.]	No. patient(s)	Gender or sex ratio/age (years)[a]	Cardiac manifestations[b] (*n* [%])	Dengue serotype	Outcome
Present case	1	F/65	Myocarditis, LVEF <62%	DEN-3	Survived
Lee et al., 2008 [23]	1	M/25	Myocarditis, pulmonary congestion and hypotension	ND	Died
Kularatne et al., 2007 [3]	75	M:F = 25:50/ median 34	Tachy–brady arrhythmia (58 [77%]), hypotension (17 [23%]), and LVEF <55% (5 [6.7%])	DEN-3 infection in three patients and DEN-2 in one with data available	All survived
Ravindral et al., 2007 [2]	61	ND/ND	Tricuspid regurgitation (35 [57%]), left ventricular dilatation (13 [21%]) and dual chamber dilatation (10 [16%])	DEN-2	Not reported
Khongphatthanayothin et al., 2007 [21]	30 DF, 36 DHF, 25 DSS	ND/mean 9.6 ± 2.8 (patients with DF); ND/mean 11.4 ± 2.7 (patients with DHF); ND/mean 10.3 ± 3.1 (patients with DSS)	LVEF <50% in two (6.7%) patients with DF, five (13.8%) with DHF and nine (36%) with DSS	ND	All survived
Lateef et al., 2007 [20]	50	M:F = 39:11/mean 32.8 ± 10.8	Relative bradycardia	ND	ND
Malavige et al., 2006 [19]	2	ND/ND	Low LVEF, pulmonary edema, hypotension and tachycardia	ND	Died
Promphan et al., 2004 [8]	1	M/13	Hypotension with junctional rhythm and bradycardia and LVEF <40%	ND	Survived
Horta Veloso et al., 2003 [6]	1	M/61	Acute atrial fibrillation	ND	Survived
Khongphatthanayothin et al., 2003 [15]	24	M:F = 13:11/mean 10.8 ± 2.8	Mean LVEF 53.3 ± 9.0%	ND	ND
Khongphatthallayothin et al., 2000 [5]	1	M/7	Mobitz type I 2nd degree atrioventricular block	ND	Survived
	1	F/7	Mobitz type I 2nd degree atrioventricular block	DEN-2	Survived
Wali et al., 1998 [4]	17	M:F = 12:5/mean 29.76	Mean LVEF, 41.69 ± 5.04% with global hypokinesia in 12 patients (70.59%) (detected by radionuclide ventriculography) and 47.06 ± 3.8% (detected by echocardiogram)	DEN-2	All survived
Kabra et al., 1998 [7]	9	ND/<12	LVEF <50%	ND	All survived
Chuah, 1987 [13]	1	M/31	Transient ventricular bigeminy	ND	Survived

Progress


400
300
200
100
Haematocrit (HCT)
Platelets (PLT)
White Blood Cell (WBC)
129
122
137
138
119
119
34.4
33.4
44.7
39.4
40.3
37.3
3.8
4.1
11.4
9.4
9.6
6.8
18/01/2015 08:01
17/01/2015 07:06
17/01/2015 09:54
18/01/2015 00:08
18/01/2015 13:46

Case 2

- 22Y male from China, in Singapore for 2 years, construction in Marina Bay
- No past medical history
- Presented 3 days fever
  - No headache, myalgia, rash or bleeding
  - No respiratory, urinary or gastrointestinal symptoms
- No past dengue or sick contact
- Referred from emergency to outpatient clinic
  - Reviewed day 1, admitted day 2

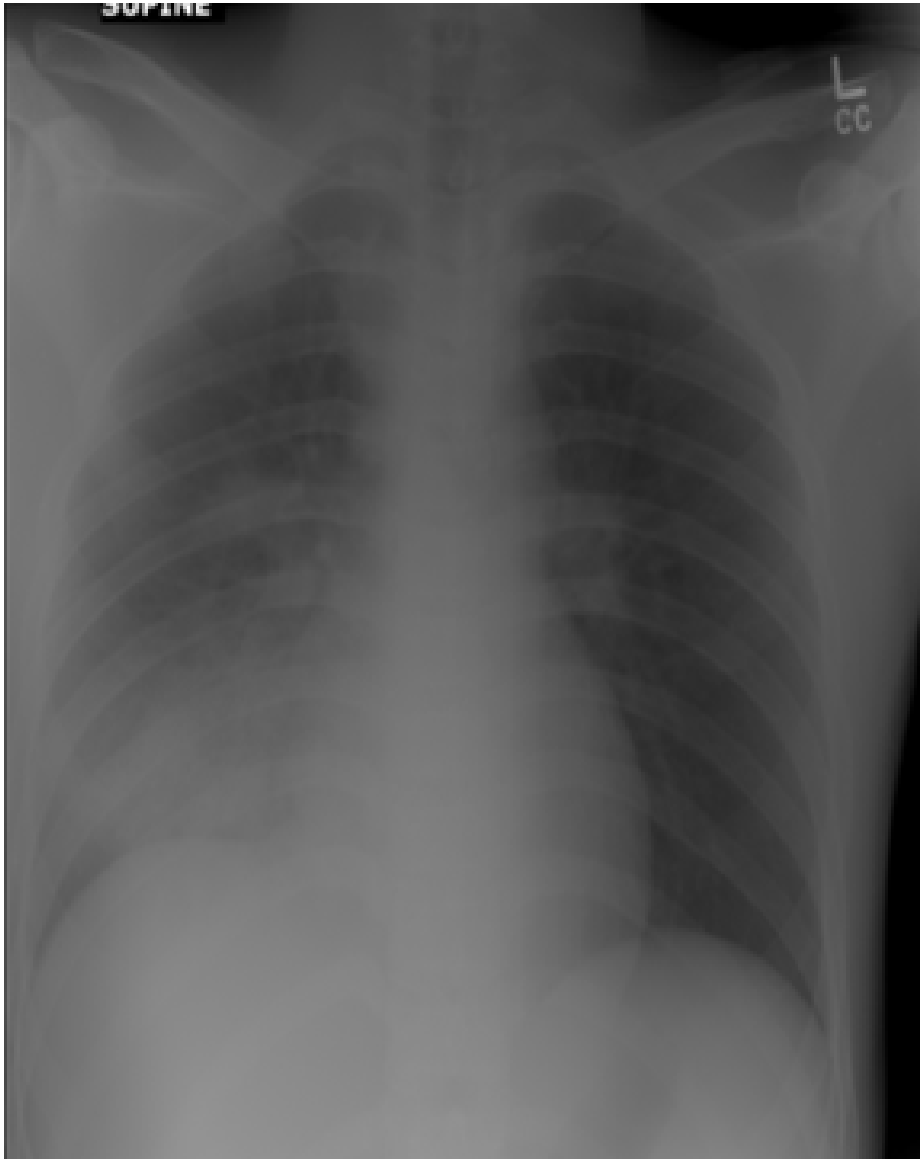
Examination and investigations

- 36.9°C, 95/min, 116/75mmHg
- Oximetry 100% room air
- Dual heart sounds, lungs clear to auscultation, abdomen soft and non-tender, no rash
- TW/HCT/PLT 1.7/41/124 → 1.3/47/38
  - % lymphocytes 23.1 → 47.7
- Creatinine 103, ALT 87, AST 195, urea 3.1, protein 59, APTT 59
- Dengue IgM +ve, IgG –ve

Progress

- Diagnosed as dengue fever
- Admitted at mid-day, BP 70/30mmHg at 11PM
- Vomited 3, diarrhoea 1, no bleeding
- Lungs clear, abdomen soft and non-tender
- After 3 litres fluid resuscitation over 4 hours, BP 80/60mmHg
  - Dengue shock syndrome, aspiration pneumonia
  - IV ceftriaxone and metronidazole
  - Transferred to high dependency within 2 hours, BP 88/76mmHg, RUQ tenderness, bibasal crackles, high flow oxygen

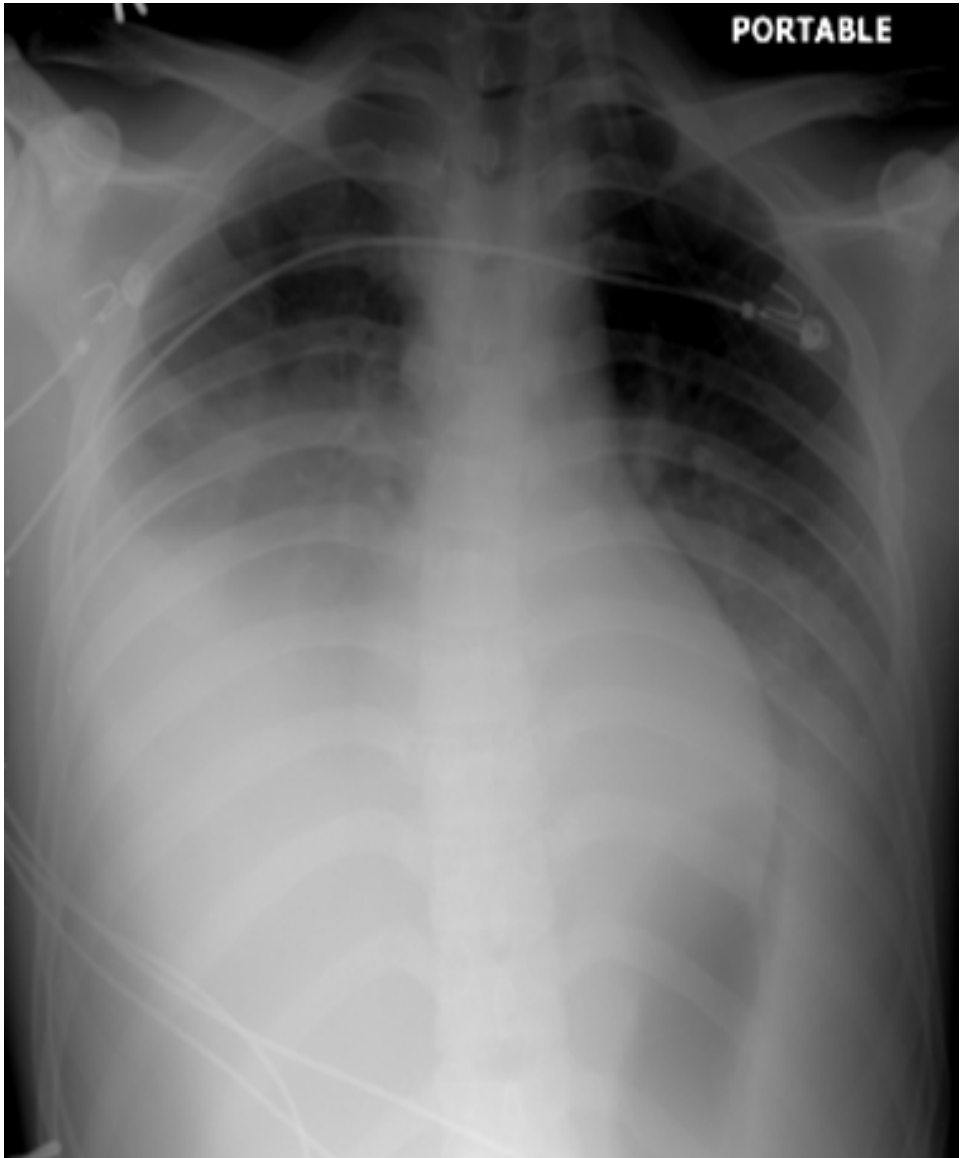
First chest X-ray



Progress

- Interim diagnosis: DSS, severe CAP
  - Ceftriaxone → ceftazidime (concern of melioidosis)
  - Clarithromycin → levofloxacin
- Blood culture on day 2 hospitalisation → gram negative rod day 3
- Worsening respiratory status → ultrasound guided pleural drain right chest → desaturation leading to intubation day 4

Interval chest X-ray

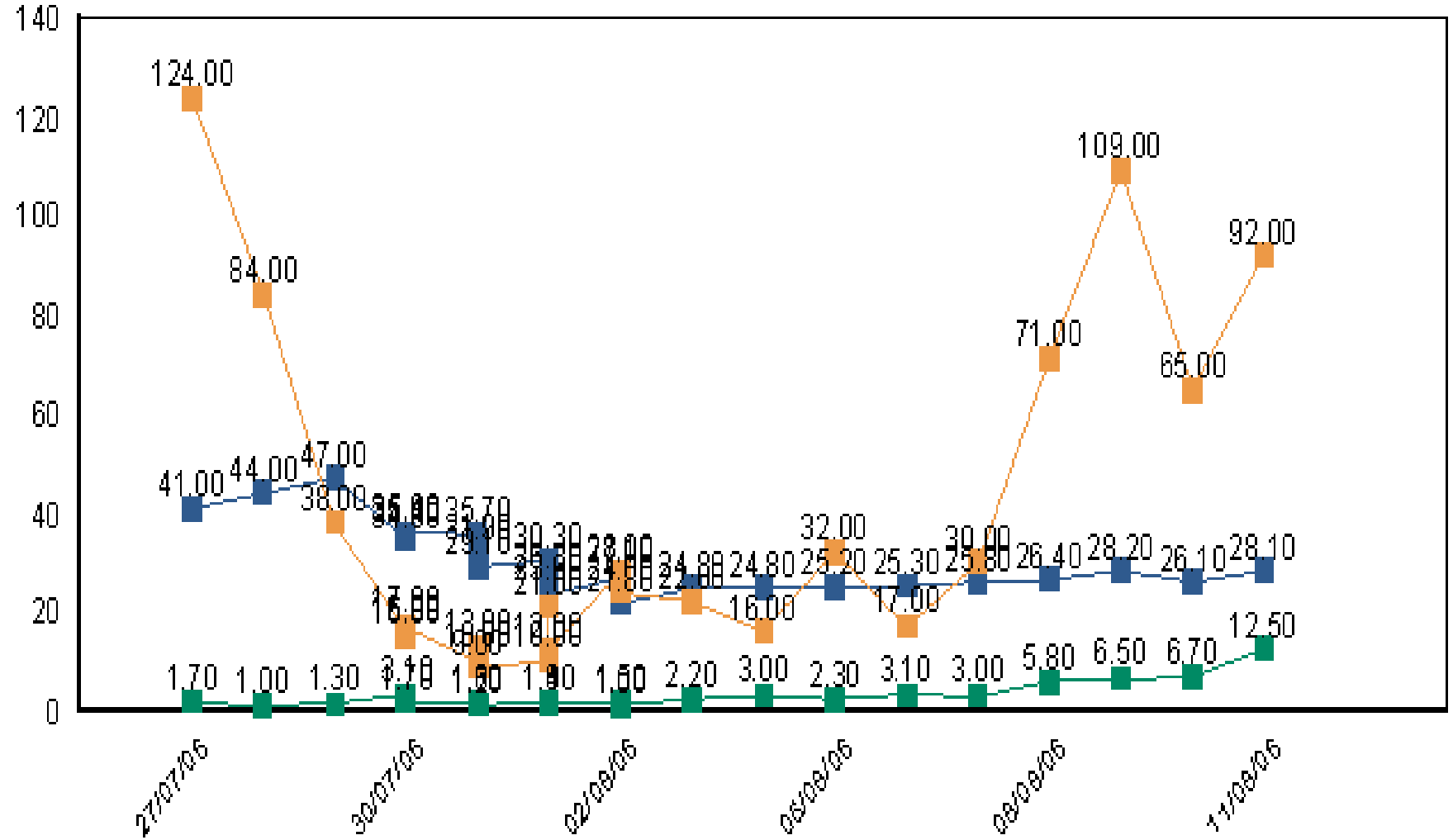


US abdomen day 4

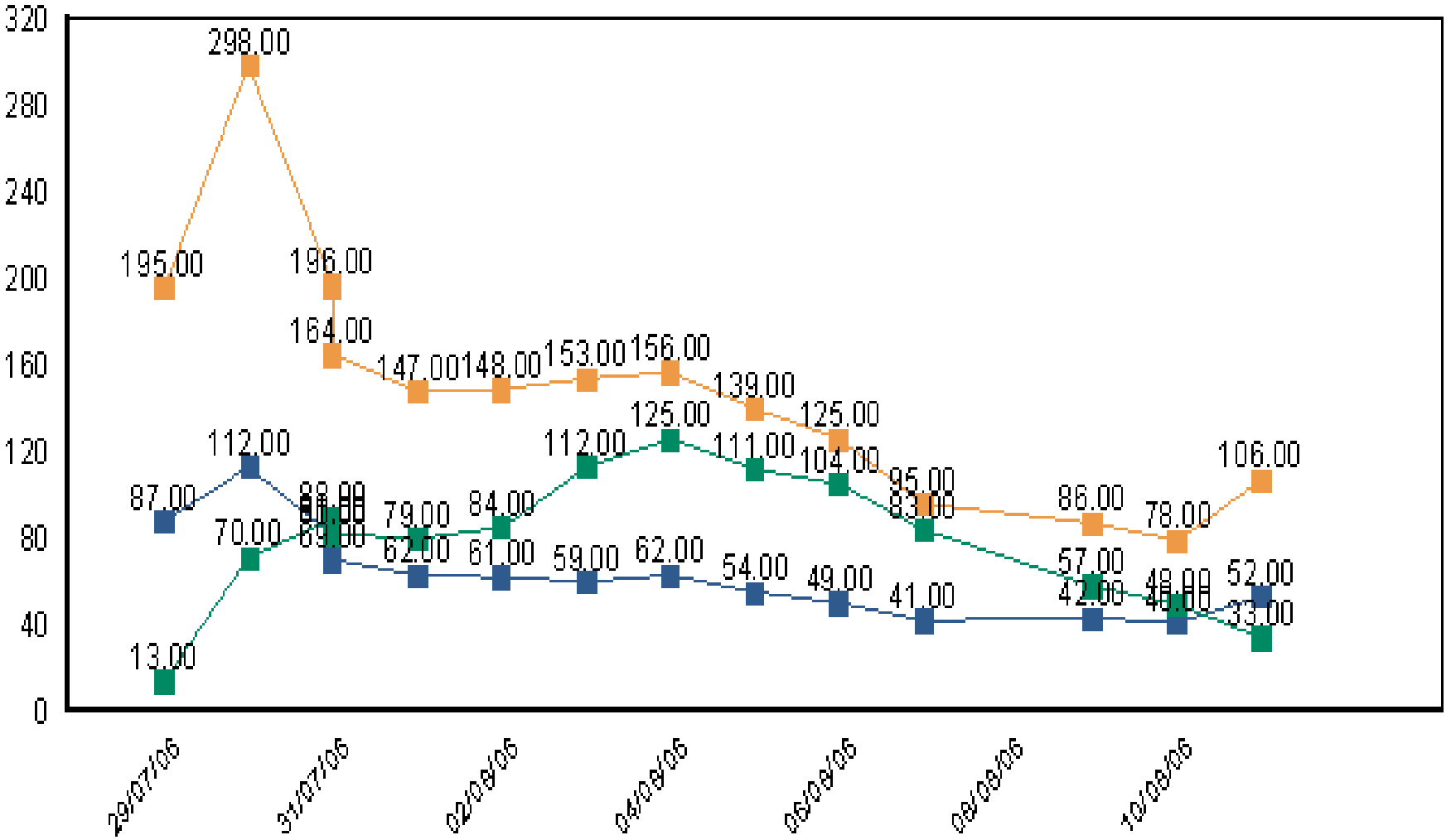
- Right pleural effusion
- No focal hepatic lesion
- Splenomegaly
- Given scan findings in gallbladder and presence of Gram negative sepsis, acalculous cholecystitis to be considered

Progress

- Blood culture 2 of 4: *Pseudomonas aeruginosa* S ceftazidime, gentamicin, ciprofloxacin
- Recurrent fever from day 5 to day 12 hospitalisation
  - Pleural fluid day 4: ESBL *Citrobacter koseri*, *Pseudomonas aeruginosa*
  - Endotracheal aspirate day 8: ESBL *E coli*, *Pseudomonas aeruginosa*
- Tension pneumothorax → chest tube
  - Bronchopulmonary fistula → subcutaneous emphysema
- Acute respiratory distress syndrome
- Demise day 14 hospitalisation



Yellow=platelet
Green=leukocyte
Blue=haematocrit



Blue=ALT
Yellow=AST
Green=bilirubin

Treatment received

- 32 units platelets and 4 units pooled platelets
- 3 units fresh frozen plasma
- 1 unit packed red blood cells, 1 unit whole blood

- Ceftriaxone 1 day → ceftazidime 5 days → imipenem 8 days
- Clarithromycin 2 days → levofloxacin 3 days

- Dopamine days 4-6, days 8-14
- Noradrenaline

Was it dengue?

- Dengue serology repeated day 6 hospital: IgM +ve, IgG –ve
- Dengue PCR on dengue serology day 1 hospital: positive

Final diagnoses

- Primary dengue
- Dengue shock syndrome
- Pseudomonas aeruginosa bacteraemia and community acquired pneumonia
- Ventilator associated pneumonia
- Acute respiratory distress syndrome

Dengue co-infection

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Case	Sex	Age (yr)	Severity	Coinfections				Distinctive Clinical Clues
				Organism	Organ	Diagnosis	Diagnosed by	
1	F	½	DSS	*Burkholderia pseudomallei*	Chest	Melioidosis	Culture (pleural fluid)	Persistence of fever and dyspnea
2	M	4	DSS	*Burkholderia pseudomallei*	Systemic	Melioidosis, disseminated	Culture (blood, pleural fluid, CSF, ascitic fluid)	Persistence of fever, ARDS
3	F	7	DSS	Varicella zoster	Skin	Chickenpox	Clinical	Vesicles
4	M	14	DF	*Salmonella*	Systemic	Salmonellosis	Culture (blood)	Prolonged fever (10 days), diarrhea
5	F	½	DHF	*Shigella*	GI	Shigellosis	Culture (stool)	Drowsiness, convulsion, positive Brudzinski Diarrhea, leukocytosis with left shift
6	F	1	DF	*Salmonella* *Escherichia coli*	GI GU	Diarrhea Vaginitis	Culture (stool) Culture (vaginal discharge)	Diarrhea, convulsion
7	F	6	DSS	*Salmonella*	Systemic	Salmonellosis	Culture (blood)	Leukocytosis
8	F	9	DF	Herpes simplex	Mucous membrane	Herpes labialis	Clinical	Vesicles
9	F	11	DHF	*Escherichia coli*	GU	UTI	Culture (urine)	
10	M	12	DF	*Mycobacterium tuberculosis*	Chest	Tuberculosis, pulmonary	AFB stain (sputum)	Prolonged fever and cough (10 days), weight loss
11	M	1	DHF	*Streptococcus pneumoniae*	Systemic	Pneumococcal bacteremia	Culture (blood)	Persistence of fever, leukocytosis
12	M	½	DHF	*Shigella*	GI	Shigellosis	Culture (stool)	Diarrhea
13	M	6	DSS	*Mycoplasma pneumoniae*	Chest	*Mycoplasma* pneumonia	Serology (CA, CF)	Prolonged fever and cough (3 wk)
14	F	½	DSS	*Escherichia coli*	GU	UTI	Culture (urine)	

DF, dengue fever; DHF, dengue hemorrhagic fever; DSS, dengue shock syndrome; GI, gastrointestinal system; GU, genitourinary system; UTI, urinary tract infection; CSF, cerebrospinal fluid; AFB, acid-fast bacilli; CA, cold agglutinin test; CF, complement-fixation test; ARDS, adult respiratory distress syndrome.

Pancharoen PIDJ 1998; 17: 81 Serologically and virologically proved

Am. J. Trop. Med. Hyg., 72(2), 2005, pp. 221–226

CLINICAL CHARACTERISTICS AND RISK FACTORS FOR CONCURRENT BACTEREMIA IN ADULTS WITH DENGUE HEMORRHAGIC FEVER

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Tan Tock Seng Hospital | IIDE Institute of Infectious Diseases and Epidemiology

PCR, acute ELISA IgM, 4 fold
Increase HI antibody

TABLE 2

Signs/symptoms and mortality rate in patients with dual infection and those with DHF/DSS alone (controls)*

Symptom/sign	Controls n = 93 (%)	Dual infection n = 7 (%)	*P*
Fever	93 (100)	7 (100)	–
Petechiae	73 (78.4)	5 (71.4)	0.647
Bone pain	67 (72)	5 (71.4)	1.0
Abdominal pain	64 (68.8)	4 (57.1)	0.677
Myalgia	60 (64.5)	4 (57.1)	0.700
Headache	57 (61.2)	3 (42.8)	0.433
Gum bleeding	32 (34.4)	5 (71.4)	0.098
Nausea	26 (27.9)	3 (42.8)	0.410
Skin rash	22 (23.6)	2 (28.5)	0.672
Cough	20 (21.5)	3 (42.8)	0.197
Gastrointestinal bleeding	19 (20.4)	4 (57.1)	0.047
Retro-orbital pain	13 (13.9)	3 (42.8)	0.079
Hemoptysis	4 (4.3)	1 (14.2)	0.310
Diarrhea	3 (3.2)	1 (14.2)	0.255
Altered consciousness	1 (1.1)	1 (14.2)	0.012
Facial swelling	0 (0)	1 (14.2)	0.070
Unusual dengue manifestations†	5 (5.3)	3 (42.8)	0.010
Mortality	1 (1.1)	2 (28.5)	0.012

* An individual patient might have more than one symptom and/or sign. DHF/DSS = dengue hemorrhagic fever/dengue shock syndrome.

† Unusual dengue manifestations were defined as absence of ≥ 3 of the 5 leading manifestations other than fever (e.g., petechiae, bone pain, abdominal pain, myalgia, and headache) found in 93 controls and/or presence of altered consciousness.

TABLE 1

Characteristics of patients with dual infection and those with DHF/DSS alone (controls)*

Variable	Dual infection group (n = 7)	Control group (n = 93)	*P*
Sex (M/F ratio)	4/3	50/43	1.000
Median age, years (range)	70.0 (47–75)	52.0 (22–88)	0.007
Underlying disease			
Hypertension (%)	4 (57.1)	22 (23.6)	0.073
Diabetes mellitus (%)	2 (28.5)	6 (6.4)	0.096
Malignancy (%)	1 (14.2)	2 (2.1)	0.197
Adrenal insufficiency (%)	1 (14.2)	3 (3.2)	0.255
Duration of fever, days, median (range)	8.0 (2–14)	4.0 (2–9)	0.004
DSS (%)	3 (42.8)	3 (3.2)	0.004

* DHF/DSS = dengue hemorrhagic fever/dengue shock syndrome.

TABLE 3

Laboratory findings in patients with dual infection and those with DHF/DSS alone (controls)*

Variable	Dual infection A/B (%)	Controls A/B (%)	*P*
Leukocytosis (WBCs > 12.0 × 10^9 cells/L)	1/7 (14.2)	4/93 (4.3)	0.310
Leukopenia (WBCs < 3.0 × 10^9 cells/L)	3/7 (42.8)	67/93 (72)	0.193
Thrombocytopenia (< 100 × 10^9 cells/L)	7/7 (100)	93/93 (100)	–
Prolongation of APTT†	5/5 (100)	68/69 (98.5)	1.0
Prolongation of PT‡	0/5 (0)	3/65 (4.6)	1.0
Elevated ALT (> 40 U/L)	6/7 (85.7)	66/76 (86.8)	1.0
(range)	(90–1,651)	(43–1,030)	
Acute renal failure	5/7 (71.4)	4/81 (4.9)	< 0.001
Peak of hematocrit (%)§			0.124
Mean ± SD	37.2 ± 8.57	40.5 ± 4.68	
Median (range)	36.6 (28.2–53.2)	40.1 (30.5–50.7)	

* DHF/DSS = dengue hemorrhagic fever/dengue shock syndrome; A = No. of patients; B = No. of patients with data available; WBCs = white blood cells; APTT = activated partial thromboplastin time; PT = prothrombin time; ALT = alanine aminotransferase.
† Prolongation of the APTT was defined as > 20% of the control.
‡ Prolongation of the PT was defined as > 3 seconds than the control.
§ All patients in both groups had data available.

TABLE 4
Details of seven patients with DHF/DSS and concurrent bacteremia*

Patient no.	Age (years), sex	Underlying disease	Initial laboratory data	Severity of DHF	Day of blood sampled for culture†	Clinical clue suggesting bacterial infection	Isolated bacterium	Bacterial infection source	Antibiotic treatment‡	Outcome
1	47, F	Uterus myoma	WBCs = 4.4×10^9/L PLT = 7.0×10^9/L PT = 10.8 sec APTT = 47.8 sec ALT = 30 U/L Hct = 36.6%	Grade II	Day 3	Prolonged fever (8 days)	*Rosemonas* species	Primary bacteremia	PIP plus GM, switched to AMC	Survived
2	70, M	Hypertension	WBCs = 2.8×10^9/L PLT = 3.0×10^9/L PT = 11.4 sec APTT = 47.8 sec Hct = 28.8% ALT = 1,651 U/L Cr = 2.1 mg/dL	Grade II	Day 2	Drowsiness	*Klebisella pneumoniae*	Bacterial meningitis	PIP plus AN, switched to CRO	Died
3	75, F	Hypertension, cervical cancer	WBCs = 8.7×10^9/L PLT = 43×10^9/L Hct = 39.9% ALT = 91 U/L	Grade II	Day 2	Prolonged fever (11 days)	*Klebsiella pneumoniae*	Primary bacteremia	CF plus GM	Survived
4	55, M	Alcoholism	WBC = 2.9×10^9/L PLT = 2.0×10^9/L Hct = 53.2% PT = 11.7 sec APTT = 73.4 sec ALT = 1,596 U/L Cr, 4.6 mg/dL	Grade III	Day 3	Prolonged fever (14 days)	*Klebsiella pneumoniae*	Primary bacteremia	CF plus GM	Survived
5	68, F	Diabetes mellitus, hypertension, adrenal insufficiency	WBCs = 10×10^9/L PLT = 13×10^9/L Hct = 33.5% PT = 10.4 sec APTT = 46.1 sec ALT = 134 U/L Cr = 2.2 mg/dL	Grade III	Day 2	Prolonged fever (10 days)	*Moraxella lacunata*	Primary bacteremia	CF plus GM, switched to Oxa	Survived
6	70, M	Diabetes mellitus, hypertension	WBCs = 2.5×10^9/L PLT = 9.0×10^9/L Hct = 40.7% PT = 11.8 sec APTT = 38.4 sec Cr = 2.9 mg/dL Glu = 788 mg/dL ALT = 90 U/L	Grade II	Day 1	Cheek swelling	*Klebisella ozaenae*	Facial cellulitis	CC plus GM, switched to CF	Survived
7	70, M	Parkinsonism	WBCs = 23×10^9/L PLT = 14×10^9/L Hct = 28.2% Cr = 2.3 mg/dL ALT = 154 U/L	Grade III	Day 1	Leukocytosis, drowsiness	*Enterococcus faecalis*	Primary bacteremia	PEN plus CRO	Died

* DHF = dengue hemorrhagic fever; DSS = dengue shock syndrome; WBCs = white blood cells; PLT = platelets; PT = prothrombin time; APTT = activated partial thromboplastin time; ALT = alanine aminotransferase; Hct = hematocrit; Cr = creatinine; Glu = glucose.
† Except for patient 4 whose antibiotics were prescribed on day 5, all patients received antibiotic therapy after blood was drawn for culture.
‡ PIP = piperacillin; GM = gentamicin; AMC = amoxicillin/clavulanate; AN = amikacin; CRO = ceftriaxone; CF = cefazolin; Oxa = oxacillin; CC = clindamycin; PEN = penicillin.

Beyond dengue
Impact of bacteraemia and nosocomial infection

- Lee JMII 2006
  - 5/8 deaths died at 5-32 hospital days from *K pneumoniae, M morganii, Ps aeruginosa*, and pneumonia (3)
- Ong IJID 2007
  - 3/7 deaths at 22-33 hospital days from septicaemia
- Rigau-Perez CID 2006
  - 3/23 deaths, one each of *Neisseria meningitidis* meningitis, *S aureus* and group C *Streptococcus* bacteraemia
- Lahiri TRSTMH 2008
  - 4/9 deaths had bloodstream infections: *E faecalis/E coli*, *A baumannii/Enterococcus*, MRSA, candidaemia → 3 at 7-10 hospital days
  - 2 concurrent infections at onset: *B pseudomallei* sputum, and *E faecalis/E coli* blood
- Wang AJTMH 2007
  - 4/11 acute respiratory failure had bacterial infections: disseminated *Klebsiella* infection, *A baumannii* urinary infection, *K pneumoniae* pneumonia, *K pneumoniae* bacteraemia
- Lee AJTMH 2009
  - 3/10 acute renal failure had bacterial infection: *K pneumoniae* bacteraemia 2, *E faecalis* 1

Early clinical and laboratory risk factors of intensive care unit requirement during 2004–2008 dengue epidemics in Singapore: a matched case–control study

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Background: Dengue infection can result in severe clinical manifestations requiring intensive care. Effective triage is critical for early clinical management to reduce morbidity and mortality. However, there is limited knowledge on early risk factors of intensive care unit (ICU) requirement. This study aims to identify early clinical and laboratory risk factors of ICU requirement at first presentation in hospital and 24 hours prior to ICU requirement.

Method: A retrospective 1:4 matched case–control study was performed with 27 dengue patients who required ICU, and 108 dengue patients who did not require ICU from year 2004–2008, matched by year of dengue presentation. Univariate and multivariate conditional logistic regression were performed. Optimal predictive models were generated with statistically significant risk factors identified using stepwise forward and backward elimination method.

Results: ICU dengue patients were significantly older (P=0.003) and had diabetes (P=0.031), compared with non-ICU dengue patients. There were seven deaths among ICU patients at median seven days post fever. At first presentation, the WHO 2009 classification of dengue severity was significantly associated (P<0.001) with ICU, but not the WHO 1997 classification. Early clinical risk factors at presentation associated with ICU requirement were hematocrit change ≥20% concurrent with platelet <50 K [95% confidence-interval (CI)=2.46-30.53], hypoproteinemia (95% CI=1.09-19.74), hypotension (95% CI=1.83-31.79) and severe organ involvement (95% CI=3.30-331). Early laboratory risk factors at presentation were neutrophil proportion (95% CI=1.04-1.17), serum urea (95% CI=1.02-1.56) and alanine aminotransferase level (95% CI=1.001-1.06). This predictive model has sensitivity and specificity up to 88%. Early laboratory risk factors at 24 hours prior to ICU were lymphocyte (95% CI=1.03-1.38) and monocyte proportions (95% CI=1.02-1.78), pulse rate (95% CI=1.002-1.14) and blood pressure (95% CI=0.92-0.996). This predictive model has sensitivity and specificity up to 88.9% and 78%, respectively.

Conclusions: This is the first matched case–control study, to our best knowledge, that identified early clinical and laboratory risk factors of ICU requirement during hospitalization. These factors suggested differential pathophysiological background of dengue patients as early as first presentation prior to ICU requirement, which may reflect the pathogenesis of dengue severity. These risk models may facilitate clinicians in triage of patients, after validating in larger independent studies.

Risk Factors for Fatality among Confirmed Adult Dengue Inpatients in Singapore: A Matched Case-Control Study

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Objectives: To identify demographic, clinical and laboratory risk factors for death due to dengue fever in adult patients in Singapore.

Methods: Multi-center retrospective study of hospitalized adult patients with confirmed dengue fever in Singapore between 1 January 2004 and 31 December 2008. Non-fatal controls were selected by matching age and year of infection with fatal cases. World Health Organization 1997, 2009 criteria were applied to define dengue hemorrhagic fever (DHF), warning signs and severe dengue. Statistical significance was assessed by conditional logistic regression modeling.

Results: Significantly more fatal cases than matched controls had pre-existing co-morbid conditions, and presented with abdominal pain/tenderness. Median pulse rates were significantly higher while myalgia was significantly less frequent in cases. . Fatal cases also had higher leucocyte counts, platelet counts, serum sodium, potassium, urea, creatine and bilirubin levels on admission compared to controls. There was no statistical significant difference between the prevalence of DHF and hematocrit level among cases and controls. Multivariate analysis showed myalgia and leucocyte count at presentation were independent predictors of fatality (adjusted odds ratios 0.09 and 2.94 respectively). None of the controls was admitted to intensive care unit (ICU) or given blood transfusion, while 71.4% and 28.6% of fatal cases received ICU admission and blood transfusion.

Conclusions: Absence of myalgia and leucocytosis on admission were independently associated with fatality in our matched case-control study. Fatalities were also commonly associated with co-morbidities and clinicians should be alarmed if dengue patients fulfilled severe dengue case definition on admission.

Summary

- Dengue in elderly
- Dengue encephalopathy
- Dengue myocarditis
- Dengue with concurrent bacteraemia
- Dengue in ICU
- Dengue death

Thank you for your attention

Questions?

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