南區頭痛讀書會
Case Sharing

Cheng-Yang Hsieh
Department of Neurology, Tainan Sin Lau Hospital
& Institute of Biopharmaceutical Sciences
National Cheng Kung University
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Case Presentation

- A 22-year-old woman
  - Presented in Aug, 2010
- Headache for 3-4 days
  - Bilateral frontal areas, persistent
  - Dull and tightness, non-pulsatile
  - Photophobia (-), phonophobia (-), nausea (-), vomiting (-), blurred vision (-)
- Associated with fever, off-and-on
- NE: neck supple (+), disc edema (-)
- Skin rash (+): salt on meat

Further work-up

- Lab data:
  - WBC: 5k
  - Platelet: 71K↓
  - GOT/GPT: 83/77 IU/L↑
- Refer to ID man for further evaluation
  - Dengue fever work-up: negative
  - Suspect non-specific viral infection
- Self-limited clinical course

Further inspiration

- Headache vs. dengue fever
  - Retro-ocular pain
  - Myalgia
  - Arthralgia
  - Bone pain (斷骨熱)
- Characteristics
- Diagnostic clues
- Pathophysiology & treatment

Introduction

- Dengue:
  - The most frequent human arbovirus infection
    - Nearly 50 million infections annually
  - Caused by a flavirus transmitted in urban areas by the female *Aedes aegypti*
    - Breeds in domestic collections of clean water
  - Four distinct virus subtype
    - Primary infection by one of them-> lifelong immunity
    - Secondary infection by one of the other serotypes may still occur

Introduction (cont.)

- Risk of a serious disease increases if secondary infection
  - Pre-existing neutralizing antibodies against a previous serotype may increase the number of infected monocytes
  - More cell-presented dengue viral antigens to T-lymphocytes
  - More intense activation of the immune system

Clinical presentation

- Classic dengue fever (DF)
  - High fever
  - Severe headache, retro-orbital pain
  - Myalgia, arthralgia
  - Skin rash
- Ranges from asymptomatic infection to severe hemorrhagic disease with shock
- Dengue hemorrhagic fever (DHF)
  - Hepatomegaly, hemoconcentration, severe thrombocytopenia, and shock

BRIEF REPORT

Headache features in patients with dengue virus infection

RB Domingues[1], GW Kuster[1], FL Onuki de Castro[1], VA Souza[2], JE Levi[2] & CS Pannuti[2]

[1]Escola de Medicina da Santa Casa de Misericórdia de Vitória (EMESCAM), Pathology, Vitória, ES, and [2]Laboratório de Virologia, Instituto de Medicina Tropical, Universidade de São Paulo, Infectious Diseases, São Paulo, SP, Brazil

Cephalalgia

Domingues RB, Kuster GW, Onuki de Castro FL, Souza VA, Levi JE & Pannuti CS. Headache features in patients with dengue virus infection. Cephalalgia 2006; 26:879–882. London. ISSN 0333-1024

- To describe:
  - The frequency and features of headache among patients with confirmed dengue virus infection
  - To compare the headache features in patients with dengue fever (DF) and dengue hemorrhagic fever (DHF)
- Setting: single hospital
- Time period: Oct, 2002~Feb, 2003

(cont.)

- Subjects: patients of dengue infection
- Diagnosis by at least one of the criteria:
  - IgM (+)
  - Fourfold rise in IgG titer
- Secondary infection
  - Higher affinity anti-dengue IgG antibodies
- Serum RT-PCR to identify subtype
- Headache characteristics

Results

- Confirmed diagnosis: n=83
  - IgM (+): n=30
  - Fourfold rise in IgG titer: n=14
  - Both: n=49
- Mean age: 42 ± 23.9 years
- Female: 61.7%
- Headache (+) in 97.6%
  - Mean duration of fever was 6 ± 2.6 days, while headache was 5 ± 2 days

Results (cont.)

- Other symptoms:
  - Myalgia: 98.8%
  - Malaise: 97.5%
  - Joint pain: (38.3%)
  - Diarrhea: (22.2%)
  - Abdominal pain: (24.7%)
  - Petechiae and purpura: (4.8%)
  - Rash: 20.7%
  - Gingival bleeding: 19.7%
  - GI bleeding: 12.3%
- Subtype:
  - Most: type 3, n=42
    - Type 1 in one, coinfected type 1 and 3 in one
- Primary infection (66.25%)
- Secondary infection (33.75%)
- Classic DF: n=65 (78.3%)
- DHF: n=18 (21.7%)

Headache characteristics

- Location:
  - Frontal: 65.4%
  - Retro-orbital: 49.4%
  - Diffuse (29.6)
  - Occipital (19.7%)
  - Neck (13.6%)
  - Temporal (8.6%)
- All were bilateral
- Throbbing: 59.3%
- Pressing/tightening: 40.7%
- Intensity:
  - Mild: 1.2%
  - Moderate: 19.5%
  - Severe: 27.1%
  - Extremely severe: 51.8%

Headache characteristics (cont.)

- Nausea and/or vomiting: 86.4%
- Photophobia: 55.5%
- Phonophobia: 62.9%
- Headache aggravated by:
  - Odours: 13.3%
  - Physical activity and Valsava manuver: 9.6%
- No aggravating factors: 54.2%

- All patients had complete remission of the dengue symptoms, including the headache
- Medication response
  - Dypirone: 16.9%
  - Acetaminophen: 39.8%
  - Analgesics ineffective: 43.3%

Headache characteristics (cont.)

- DF vs. DHF
  - Headache features: not significantly different
  - Headache intensities: more intense headache in classic DF than DHF

Why?

- Less intense headache in DHF?
- Postulate the pathogenesis of DF and DHF is different
  - Different in immunopathological mechanisms or neurotropism
  - In DHF, symptoms are related to liver failure and edema through the cerebral vasculature
  - In classic DF, less clear

9.1.2 歸因於淋巴球性腦膜炎之頭痛 Headache attributed to lymphocytic meningitis

診斷基準：

A. 頭痛至少具下列一項特徵，且符合基準C及D:

1. 急性發作
2. 重度頭痛
3. 伴隨後頸僵硬、發燒、噁心、畏光及/或怕吵

B. 腦脊髓液檢驗顯示淋巴球增生、蛋白質稍微增加和葡萄糖正常 (註1)

C. 頭痛發生和腦膜炎時間點上密切關連

D. 頭痛在感染治療成功或自然緩解後，三個月內緩解 (註2)

註記：

1.病毒、疏螺旋體屬 (borrelia)、李士德菌屬 (listeria)、黴菌、結核病或其他感染原可以經由適當的方法辨識

2.頭痛通常一星期內緩解

9.1.3 歸因於腦炎之頭痛 Headache attributed to encephalitis

診斷基準：

A. 頭痛至少具下列一項特徵，且符合基準C及D：

1.整個頭痛

2.強度增加至重度

3.伴隨噁心、畏光或怕吵

B. 有急性腦炎之神經學症狀和徵候，並經腦波、腦脊髓液檢驗、神經影像及/或其他實驗室檢查確定診斷 (註1)

C.腦炎期間發生頭痛

D. 頭痛在感染治療成功或自然緩解後，三個月內緩解

註記：

1. 聚合酵素連鎖反應檢驗（PCR）方法給予特定診斷

9.2.2 Headache attributed to systemic viral infection

9.2 歸因於全身性感染之頭痛 Headache attributed to systemic infection

登錄他處：

歸因於伴隨全身性感染之腦膜炎或腦炎的頭痛應該被登錄在 9.1 *歸因於顱內感染之頭痛*。

診斷基準：

A. 頭痛至少具下列一項特徵，且符合基準C及D：
   1.整個頭痛
   2.強度增強為中或重度
   3.伴隨發燒、全身乏力或其他全身性感染症狀
B. 證實有全身性感染
C. 頭痛發生在全身性感染時期
D. 頭痛在感染經有效治療後72小時內緩解

9.2.2 歸因於全身性病毒感染之頭痛 Headache attributed to systemic viral infection

診斷基準：

A. 頭痛符合9.2*歸因於全身性感染* 基準
B. 臨床及實驗室檢查 (血清學及/或PCR) 診斷為病毒感染

9.2.3 歸因於其他全身性感染之頭痛 Headache attributed to other systemic infection

診斷基準：

A. 頭痛符合9.2*歸因於全身性感染* 基準
B. 臨床及實驗室檢查 (血清學、顯微鏡檢、培養或由PCR) 診斷為非細菌或病毒感染

9.3 歸因於人類免疫缺乏病毒 (HIV)/後天性免

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Systematic Review

Clinical and laboratory features that distinguish dengue from other febrile illnesses in endemic populations

James A. Potts and Alan L. Rothman

Table 6 Studies with multivariable models presented as positive predictive values

Study	Predictors	Positive predictive value (%)
Sawasdivorn *et al.* (2001)	Fever + positive tourniquet test + leukopenia	73
McBride *et al.* (1998)	Rash + bleeding (gums, nose, vagina) + bone pain + taste alteration	73
Karande *et al.* (2005)	Arthralgia + thrombocytopenia	100

Table 5 Studies with multivariable predictor models presented as odds ratios

Study	Predictors	OR (95% CI)
Wilder-Smith *et al.* (2004)	Platelet count (10^9 platelets/l)	
	<140	456 (37, 5917)
	AST (IU/l)	
	>34	68 (6, 719)
	WBC (10^9 cells/l)	
	<5	47 (4, 518)
Phuong *et al.* (2004)	Petechiae	4.82 (2.71, 8.58)
	Hepatomegaly	
	>1 cm	2.93 (1.14, 7.53)
	Admission	
	After >3 days of illness	2.47 (1.38, 4.42)
	Haematocrit	1.13 (1.05, 1.22)
	Coryza	0.36 (0.16, 0.81)
	Sore throat	0.33 (0.14, 0.76)

Taiwan Epidemiology Bulletin

Dengue Fever Epidemic in Tainan, 2007

Chiao-Wen Lin[1], Chin-Xian Wang[1], Chein-Sheng Lin[1]
Mei-Ling Wu[1], Chin-Sheng Chi[1], Chiou-Yueh You[1]
Sheng-Tang Wei[1], Yi-Chun Wu[1], Chien-Chou Lin[2]

小心，dengue fever就在你身邊!!
病人可能因爲頭痛來看神經科!?

Reported: 2690 cases

Confirmed: 1821 cases

Negative cases: 269 cases

Uncertain: 501 cases

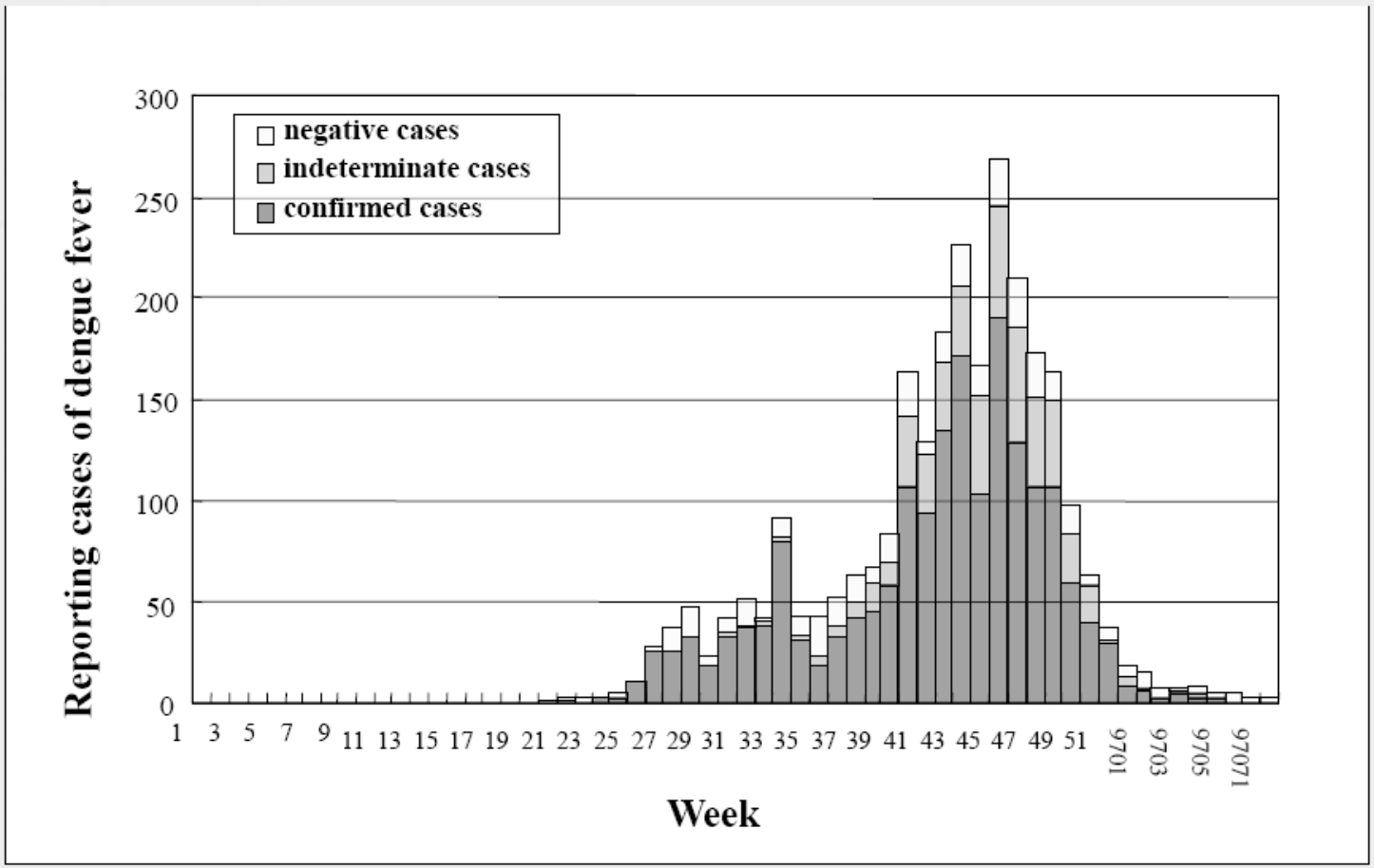

Figure 1. Weekly domestic dengue cases in Southern Taiwan, 2007