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Weils' Syndrome and Concomitant Hepatitis B Infection

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ABSTRACT

Leptospirosis is a ubiquitous, spirochetal zoonosis which presents with a broad clinical spectrum. Weil's syndrome, characterised by jaundice, renal failure and bleeding manifestations is the most severe form. A high index of suspicion for the diagnosis is required to institute therapy promptly. We describe a case of serologically confirmed Weil's syndrome with concomitant hepatitis B infection.

Keywords: Weil's syndrome, hepatitis B

INTRODUCTION

A 30-year-old man from the Fujian province of China, was admitted to hospital with a four-day history of epigastric pain, fever, chills and a reduction in urine output. Examination on admission revealed deep jaundice only. Treatment with ceftriaxone and metronidazole was instituted.

The following day he became disorientated. An urgent gastroenterology opinion was sought. No further history was available. Examination revealed persisting deep jaundice, conjunctival suffusion, a left conjunctival haemorrhage and a flapping tremor. The blood profile was deranged (Table I). A provisional diagnosis of Weil's syndrome was made and intravenous penicillin 2 million units 6 hourly was commenced. He was transferred to the intensive care unit. Abdominal ultrasound revealed a normal liver and biliary system with gall bladder sludge.

Due to disorientation and aggression, he was sedated intermittently with haloperidol over 48 hours. Neck stiffness developed, cerebral CT scan was normal and electroencephalogram (EEG) examination done two days after cessation of haloperidol, while awake and during sleep, revealed diffuse slow wave activity. The penicillin dose was increased to 3 million units 4 hourly. Lumbar puncture was not performed because of coagulopathy.

By the sixth day he was conscious and responsive. He passed melaena stool. Upper gastrointestinal endoscopy showed minor diffuse gastric mucosal oozing and traces of altered blood in the stomach. There was neither active bleeding, nor was there further melaena. His haemoglobin level remained steady.

Occupational history revealed that he worked in an abbatoir without wearing protective clothing. In addition, hepatitis B serology was abnormal (hepatitis B: surface antigen, core IgM and e antigen positive). Hepatitis B virus DNA was also positive. He denied risk factors for hepatitis B acquisition.

Leptospira were not isolated from the blood using Fletcher's medium (rabbit's serum and semi-solid agar) during the first few days of illness. The initial serology for *leptospira* antibodies was normal, titre $< 1/50$. Convalescent serology eleven days later was positive – titre 1/1600. Urine culture for *leptospira* was negative in the convalescent period, three weeks after presentation.

DISCUSSION

Leptospirosis is a rare cause for hospitalisation in Singapore, representing 0.0029% of all hospital admissions between 1992 and 1996 (Ministry of Health, Singapore). The sero-prevalence may vary between 16% and 72%[1,2], with regional variation demonstrated within the same country[2].

Human infection occurs via contact with infected soil or water[3]. Multiple serotypes of *leptospira* exist and may infect animals, including pigs[4]. Our patient's occupation and lack of protective clothing, may have predisposed him to infection. The prevalence of leptospirosis is higher in males and increases with age. A higher prevalence in agricultural and manual labourers compared to non-manual outdoor workers is also reported[5].

The primary lesion is believed to be a cell membrane defect involving small blood vessel endothelium which results in haemorrhage, ischaemia and secondary degenerative changes. The renal lesion is characterised by interstitial nephritis and secondary tubular changes while the liver lesion consists of hepatocyte degeneration, disorganisation of liver architecture with swollen kuppfer cells containing *leptospiral* debris. The organism's glycoprotein may be responsible for injury at an ultrastructural level[6].

Deep jaundice, renal failure, petechial, conjunctival haemorrhage, marked hyperbilirubinaemia, minimal cholestatic and modest transaminase activity, were the most useful clues in the diagnosis of a disorder that may prove difficult even in referral centres[7]. Thrombocytopaenia, without evidence of disseminated intra-vascular coagulation, may occur in leptospirosis[8]. Hyperamylasaemia, without evidence of pancreatitis is most likely due to renal failure in the acute period.

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Table I – Investigations

	4.4.97 admission	8.4.97	14.4.97	20.6.97 outpatient
Hb g/dL (14 – 18.0)	11.1	10.0	10.6	15.9
Plt X 10^9/L (140 – 400)	30	70		
Cr mmol/L (44 – 144)	651	95	85	
Ur mmol/L (2.8 – 7.7)	45.9	28.2	5.0	
Bil μmol/L (3 – 24)	430	427	115	14
ALP μmol/L (32 – 103)	218	128	128	96
ALT μmol/L (7 – 36)	246	98	49	48
AST μmol/L (15 – 33)	22	37	38	29
GGT U/L (9 – 41)	127	120	177	56
DDimer μg/mL (< 0.5)	> 2			
PT sec (12)	14	14		
APTT sec (< 25)	43	32		
Amylase U/L (< 100)	997	61		
EEG (awake & asleep)		slow waves		

Abbreviations: Hb haemoglobin; PLT platelets; Cr creatinine; Ur urea; Bil bilirubin; ALP alkaline phosphatase; ALT alanine amino-transferase; AST aspartate amino-transferase; GGT gamma glutamyl transpeptidase; PT prothrombin time; APTT activated partial thromboplastin time; EEG electroencephalogram

Meningism, mental obtundation and EEG findings of diffuse slow wave activity, suggest encephalitis. Leptospirosis, has been implicated in 10% of previously unexplained cases of meningitis and encephalitis[8]. Although the serum urea was elevated on admission, the rapid resolution of renal failure and uraemia with persisting altered conscious state would have made this an unlikely cause for the altered mental state. Gastrointestinal bleeding was of small volume and transient, due to diffuse mucosal oozing of blood.

A high index of suspicion for Weil's syndrome resulted in the prompt use of high dose penicillin. Despite, equivocal evidence from controlled studies in man[9,10], conventional teaching generally supports the use of penicillin or doxycycline[8,11].

The diagnosis of leptospirosis was confirmed by serology. Culture of the organism from blood, in the early period of the illness and urine in the convalescent phase, was negative despite the use of specialised media. The failure to make a microbiological diagnosis, during the optimal periods for isolation of leptospires, in a patient with severe infection highlights a significant problem that may occur.

Our patient had hepatitis B infection with active viral replication. It is unknown whether this represented reactivation of a carrier state or recent acute infection. The clinical and biochemical features were atypical of overt hepatitis B infection and the rapid improvement, after antibiotic therapy supports leptospirosis as the predominant illness rather than hepatitis B. It is likely that dual infection in our patient represents a chance occurrence between a rare (leptospirosis) and a common (hepatitis B) infectious agent, as they have differing vectors and modes of acquisition. It is apparent from this case that clinicians need to be aware that on occasion rarer causes of jaundice may co-exist with commoner causes.

As far as we are aware, concomitant hepatitis B infection, whether reactivation or acute infection and leptospirosis have not been previously reported. Despite the combined hepatic involvement by these two illnesses and the severe systemic manifestations of leptospirosis, a disorder with a mortality rate of up to 16%[12], our patient made a full recovery from leptospirosis.

Our patient with Weil's syndrome and concomitant hepatitis B infection, with active viral replication, is the first reported case as far as we are aware. A positive microbiologic diagnosis of Weil's syndrome may not be possible but a presumptive bedside diagnosis with serological confirmation may be made if a high index of suspicion is maintained.

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