16 CASES OF ACUTE RENAL FAILURE DUE TO LEPTOSPIROSIS

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SUMMARY

A study was carried out on 16 cases of leptospirosis with acute renal failure (ARF) detected in adult patients admitted into the Medical and Nephrology wards of the General Hospital, Kuala Lumpur, over a four-year period from 1980 to 1983. Most of the cases were male, Malays and older adults. The predominant infecting serovars were L. celledoni *(of the serogroup* L. javanica *and* L. pomona *(of the* L. pomona *serogroup). All the cases survived, including those who required peritoneal dialysis.*

The sensitised erythrocyte lysis (SEL) antibody prevalence rate of the chronic renal failure cases (10.4%) was found to be similar to that of the healthy population in West Malaysia (12.7%), confirming the observation by other workers that leptospirosis is not an important cause of chronic renal failure.

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INTRODUCTION

Serological surveys and clinical studies have indicated that leptospirosis was highly endemic in West Malaysia.[1-4] About 30 different serovars of leptospires have been isolated and all the known serogroups were represented in the agglutinins found in positive sera. This possibly accounts for the wide clinical spectrum of leptospirosis in Malaysia which varies from mild to severe, depending on the infecting serovar.

Severe cases of leptospirosis may succumb to acute renal failure (ARF) or to hepatic failure. This study aims at determining the importance of leptospirosis in Malaysia as a cause of ARF. The influence of age, sex and racial distribution of these cases, and the role of peritoneal dialysis in the prognosis of the patient is also discussed.

MATERIALS AND METHODS

Acute renal failure[5,6] is defined as a sudden decrement in glomerular filtration rate associated with an increase of serum creatinine to a level of 200μmol/l and above. It develops over days or weeks and is usually reversible. Oliguria may or may not be present.

The adult cases with ARF admitted to the General Hospital, Kuala Lumpur, during the four-year period of study from 1980 to 1983 could be categorised under the following groups, viz., surgical, obstetrical and medical.

The surgical cases included those of acute cholecystitis, subacute bowel obstruction, necrotising enterocolitis, gastro-intestinal bleeding, appendicular abscess and breast abscess with septicaemia.

The obstetrical cases were those suffering from post-partum haemorrhage, septic abortion and pre-eclamptic toxaemia.

The medical cases included: subgroup 1-those with acute glomerulonephritis, acute tubular necrosis associated with blood loss, drug-induced ARF and ARF associated with severe infection; subgroup 2-patients with acute systemic manifestations of fever, malaise, liver pathology, lymphadenopathy, conjunctival injection and myalgia.

Paired sera were collected from 14 selected cases of medical subgroup 1, and 36 cases of subgroup 2. The latter were investigated as and when they were detected on admission. Their sera were examined for significant rise in titres of leptospiral agglutinins.

The microscopic agglutination (MA) test was used, employing live Patoc 1 strain (*L. biflexa* species) as antigen. The live culture was originally obtained from the WHO Leptospirosis Reference Laboratory in London, UK, in 1957 and has since been propagated in the Virology laboratory at the Institute for Medical Research, Kuala Lumpur. In addition, the prevalence of past infection with leptospirosis was determined on single serum specimens of 48 medical and surgical cases with chronic renal failure using the sensitised erythrocyte lysis (SEL) test.[7] The antigen used was prepared also from the Patoc 1 strain. The SEL test had been evaluated and found to be more suitable for serological studies than the MA test.[1]

The presumptive infecting serovars were determined from the positive sera by the MA test using live antigens of 14 serovars belonging to the *L. interrogans* species. The prototypes were obtained from the WHO Leptospirosis Reference Laboratory, London, UK.

Isolation of leptospires was attempted in blood specimens taken on the fifth day of illness or earlier. A volume of 0.5 ml of the specimen was inoculated intra-peritoneally into a weanling hamster. One week later blood from the heart of the hamster was inoculated into two tubes of Korthof's[8] and one tube of Fletcher's[4] medium and the cultures were examined for six weeks.

RESULTS

Of the 36 ARF cases in medical subgroup 2, 16 (44.4%) were diagnosed as recent cases of leptospirosis serologically in all the cases, and by culture in one case. None of the 14 cases in medical subgroup 1 was positive.

There seems to be a preponderance of positive cases in the older age-group 41–55-years-old, but as the numbers are small these rates may not be conclusive. However, it appears that males (93.8%) predominated over female cases and the Malays (75.0%) over the other two races, Indians (18.8%) and Chinese (6.2%).

The clinical features were moderately severe (Table I). All had an acute onset of fever. Gastrointestinal symptoms (anorexia, nausea and vomiting) were highly prevalent (87.5%). Conjunctival injection (68.8%), jaundice (62.5%) and headache (62.5%) occurred in more than half the number of cases. Myalgia and hepatomegaly were found in 50% of the cases and muscle tenderness and haemorrhagic symptoms (subconjunctival haemorrhage and bleeding diatheses) in 31.3%. Signs of meningeal irritation were present in one case.

In all the cases, the blood urea level (mean 49.1 mmol/l) and serum creatinine level (mean 623.7 μmol/l) on admission were raised (the criteria for the chronic of the study subjects were based on these). The leucocyte count was slightly increased but the relative counts of neutrophils and lymphocytes appeared normal. Five (55.6%) out of the nine cases had proteinuria.

The presumptive infecting serovars of the 16 cases of leptospirosis with ARF were determined.

TABLE I

CLINICAL FEATURES AND LABORATORY FINDINGS IN 16 CASES OF LEPTOSPIROSIS WITH ACUTE RENAL FAILURE

Clinical features	No. of cases
Fever	16
Gastric symptoms	14
Conjunctival injection	11
Jaundice	10
Headache	10
Myalgia	8
Hepatomegaly	8
Muscle tenderness	5
Haemorrhagic symptoms	5
Lymphadenopathy	2
Meningeal symptoms	1

Laboratory findings*	Range	Mean
Blood urea (mmol/l)	9.6 – 110	49.1
Serum creatinine (μmol/l)	200 – 1,230	623.7
Leucocyte Count (cells/mm^3)	5,200 – 26,800	12,381.0
Neutrophils (%)	50 – 95	75.7
Lymphocytes (%)	2 – 44	12.7

*On admission.

Most of the patients were found to have been infected by serovars *L. celledoni* (of the serogroup *L. javanica*) and *L. pomona* (of the *L. pomona* serogroup). One positive culture was obtained and was identified as belonging to *L. sejroe* serogroup.

The number of deaths from ARF during the four-year study was 27 of which **none** was due to leptospirosis. The prognosis of leptospirosis complicated by severe renal failure was good where peritoneal dialysis was instituted as soon as possible on admission and repeated, if necessary, until the blood urea level falls to 30 mmol/l or lower. This, and possible other favourable factors (e.g. low dose and virulence of the infecting strain, high resistance of the patient, proper nursing care, etc.,) could have accounted for the 100% recovery rate in the ten patients who were thus treated. The average period of dialysis required was three days and the average length of stay in the hospital ward, two weeks. The indications for peritoneal dialysis were based on clinical grounds when a progressive uraemia was observed. Renal biopsy was performed in only case and histology showed an interstitial nephritis.

DISCUSSION

Renal involvement is the most serious complication in leptospirosis and the commonest cause of death. Oliguria or anuria may occur during the second week of illness but may come on as early as the fourth day. Most patients with renal failure also have significant hepatic involvement.

Patients suffering from leptospirosis may show all or only a few of the clinical features produced by the serovar involved. Some serovars tend to cause severe, often fatal illness *(icterohaemorrhagiae)*, others cause a moderately severe illness *(australis, autumnalis, bataviae, pyrogenes)*; while still others cause a mild 'benign' form of illness *(ballum, canicola, celledoni, grippotyphosa, hebdomadis, hyos, pomona sejroe).*[10] However, the pathogenicity of strains varies with geographical distribution. Thus, the oriental strains of *bataviae* tend to cause more severe, often fatal illness in Europe than the European strains there; *grippotyphosa* infections are severe in Central Africa and Israel but are usually mild in Europe; and *sejroe* infections tend to be more severe in Italy than in Denmark.[10] These differences in pathogenicity cannot be explained by any differences in agglutinogenic characters and remain a mystery.

In Malaysia, all the known serogroups are represented by the strains prevalent in the country. The two most highly prevalent serovars in West Malaysia since 1978 have consistently been *L. celledoni* (of the serogroup *L. janavica*) and *L. pomona.* These were also the two most commonly observed causes of leptospirosis with ARF. It is interesting to note that these serovars are usually recognised as causing 'benign' illness in general, but in these 16 cases, the more severe end of the clinical spectrum was observed. Apparently, factors other than just the infecting serovar have some influence on the course of the disease.

Although the number of cases of leptospirosis studied here was small, the epidemiological pattern was strikingly similar to that consistently reported annually[11] with a predominance of Malay male adults.

The prevalence rate of leptospiral antibodies in the chronic renal failure cases detected by the sensitised erythrocyte lysis (SEL) test was 10.4%. This was almost similar to that obtained in a serological (SEL) survey on 4,646 healthy persons in West Malaysia which was 12.7%.[12] This agrees with the observation that leptospirosis does not usually lead to chronic renal failure as the renal pathologic changes in leptospirosis are reversible, evidenced by the return of normal functions and by the absence of histologic abnormalities in biopsy specimens obtained during convalescence.[13]

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