Rift Valley fever hepatitis complicated by disseminated intravascular coagulation and hepatorenal syndrome

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Bunyaviridae named after a town in Africa are known to cause disease in both animals and humans. The illness on a large part mild in humans can cause a lethal hemorrhagic syndrome sometimes complicated by hepatorenal syndrome (HRS). The viral infection once confined to the African continent now poses a threat to farmers and travelers in the Southern region of Kingdom of Saudi Arabia (KSA). We describe a typical case of Rift Valley fever (RVF) virus in a farmer of Gizan who died with the severe form of the illness, his presentation, diagnosis and the management problems of a disease associated with a public fear of unknown infection in our society.

A 70-year-old male from Gizan, KSA presented to the accident and emergency department of Riyadh Medical Complex, Riyadh, in September 2000 with fever, loose motions and frequent vomiting for the last 3 days from his arrival in Riyadh via plane. The fever was not associated with rigors and increased at night, the motions were passed painless amounted to a frequency of 4-5 times a day and were watery and not accompanied by bleeding. Vomiting occurred only with food intake and was accompanied with nausea. Upon systemic enquiry he reported occasional episodes of wheezing in cold weather from childhood but had no other complaint. His past medical and surgical history were unremarkable. He had no known allergies and currently was on no medication. The physical examination revealed a febrile, thin build, elderly male, in no distress, with a temperature of 37.5°C, with a blood pressure of 110/70 mm Hg, a regular pulse of 84 beats per minute and a respiratory rate of 18 breaths per minute. He had no lymphadenopathy, no jaundice and had no signs of chronic liver disease. There was no skin rash or lower limb edema. Examination of the chest revealed expiratory wheezes in both lung fields and on examination of the central nervous system, fundal examination was normal and only a mild tremor of his outstretched hands but no flapping was observed. The cardiovascular and abdominal examination were unremarkable. Urinalysis was normal. Laboratory tests showed a white cell count of 2.6 x10^9 per cubic millimeter with a differential of 73% neutrophils, 0.4% eosinophils, 1.3% basophils, 5.1% monocytes and 20.2% lymphocytes and a hemoglobin of 10 g/dl, hematocrit of 30.7, mean cell volume (MCV) of 75.1, mean corpuscular hemoglobin (MCH) of 26.2 and a platelet count of 42. The erythrocyte sedimentation rate was 45 mm on the first hour and the serum electrolytes were showing urea of 5.2 mmol/l, creatinine 79 µmol/l, sodium 143 mmol/l, chloride 110 mmol/l, a potassium level of 3.2 mmol/l indicating hypokalemia and a random glucose level of 6.8 mmol/l. Liver function tests revealed an aspartate aminotransferase (AST) of 11106 u/l, alanine aminotransferase (ALT) of 4321 u/l, alkaline phosphatase (ALP) of 79 u/l, total bilirubin of 21 µmol/l, total protein of 62 g/l and an albumin of 31 g/l. Amylase level was 59 u/l. Cardiac enzymes showed a lactate dehydrogenase (LDH) of 10480 u/l and a creatine phosphokinase (CPK) of 288 u/l with normal creatine kinase isoenzyme containing M and B subunit fraction. His coagulation profile revealed a prothrombin time of 38.3 seconds, partial thromboplastin time of 65.4 seconds with an international normalized ratio of 2.78. Three thick and thin films for malaria parasite were reported as negative. Stool analysis revealed many pus cells, no occult blood and no ova or parasites detected. Sputum, urine, stool, aerobic and anaerobic blood cultures were reported as negative. Serology for Brucella abortus and melitensis was negative, a Widal test was negative, indirect hemagglutination antibody for Echinococcus weakly positive.

Screen for hepatitis A, B, C and HIV 1 and 2 were negative. Electrocardiogram revealed a normal sinus rhythm with inferolateral T wave inversion. Chest radiograph showed a right hilar calcified lymph node and a trachea deviated to the right, plain x-ray of the abdomen showed a calcified lesion in the liver region (Figure 1). Ultrasound of the abdomen showed a calcified cyst most likely hydatid in the left liver lobe. Computed tomography of the abdomen confirmed the finding as well as normal liver and spleen size.

As the patient fulfilled the diagnostic criteria for a possible RVF infection he was admitted in an isolation ward with barrier nursing, which had been prepared following an alert by the Ministry of Health as regard to possible cases of RVF reaching the capital city of Riyadh, despite the quarantine measures commenced by government agencies. The
ward staff was given twice daily N, N-diethyl-3-methylbenzamid (DEET) containing mosquito repellent and the ward was sprayed twice daily with a commercial insecticide. He was given gentamycin 80 mgs intravenously stat dose, ceftriaxone 2 gms intravenously once daily and metronidazole 500 mgs intravenously 3 times a day in addition to intravenous fluids in the form of dextrose 5% per saline 0.9% at 100 ml per hour, vitamin K orally in a dose of 10 mg daily and lactulose 10 ml orally 3 times a day. In the evening of the day of admission he was reexamined and found to be fully oriented, ambulant, with no evidence of bleeding from any orifice, yet his complete blood count revealed thrombocytopenia of 15 and he was transfused 6 units of platelets then took his dinner and had an uneventful night. On the second day of admission, he remained afebrile fully oriented with a mild tremor in the outstretched hands, a few expiratory wheezes and loose motions now associated with some mucus. The AST had risen to 14547, ALT 5275, ALP remained normal with 91, total bilirubin 27, LDH 10480. Prothrombin time of 36.8 seconds and a partial thromboplastin time of 78.6 seconds with a INR 2.6, fibrinogen level 1.37g/l (normal range: 2-4 g/l) and D-Dimer level >400 (normal range: <250). Fresh frozen plasma (FFP) 3 units were administered and a bone marrow aspiration and biopsy performed and sent for microscopy and culture. Serology and culture for RVF virus was arranged. On the morning of the third day of hospitalization the patient developed a coarse flapping tremor but remained conscious, alert, oriented and ambulant. No lymphadenopathy or rashes were noted. He had developed a hemorrhagic lesion at the left side of his tongue but was not bleeding actively. Mild dependent edema was noted. Abdominal examination revealed tenderness in the right upper quadrant. The complete blood count revealed pancytopenia with a white blood count of 1.6, neutrophils of 73%, a hemoglobin of 9.4, MCV of 75, MCH of 23 and a platelet of 25. Bone marrow aspiration was reported as a dry tap. Creatinine had risen to 173 µmol/l. The arterial blood gases showed a metabolic acidosis with a pH of 7.273, PCO: 33.8 and HCO3: 15.2. A nephrology consult was made in anticipation of a developing HRS. In the afternoon of the third day of hospitalization the patient became anuric and creatinine had risen to 561. Furosemide 60 mg intravenously and sodium bicarbonate 8.4% 50 ml intravenously each one dose were given a strict input output chart commenced with fluids restricted to 2 liters per day.

At that point he was clinically compensated. He had a cardiorespiratory arrest in the early morning of his fourth hospital day just prior to transfer to the intensive care unit. The relatives declined post-mortem liver biopsy.

In the absence of a post-mortem examination the exact cause of death could not be ascertained. Rift Valley fever antigen and IgM antibody were subsequently reported as positive, ribavirin had been ordered but could not be acquired prior to his death. The virus known as RVF virus belongs to the Phlebovirus genus, one of the 5 genera in the family of Bunyaviridae. It causes several pathogenic syndromes in human beings including an acute febrile illness, hemorrhagic fever, hemorrhagic fever with hepatitis and infection of the nervous system and ocular disease. The mortality rate for hemorrhagic fever with hepatitis reaches 36%, however, overall mortality rate is less than 1%. The virus is contracted by direct handling of infected animals and consumption of their products, mosquito bites and inhalation of infectious aerosols and hence poses an occupational hazard for farm workers and related professions, laboratory and medical staff and a health risk for travelers to endemic areas. After introduction into the body the virus moves to the draining lymph nodes, where it replicates; and from there it spreads throughout the body to the critical organs such as the spleen, liver and brain. It gains entry into the cell via endocytosis and uses the host’s replicative machinery to transcribe its RNA which is eventually translated in the cytoplasmic ribosomes, the assembled virions are then accumulated in the Golgi apparatus and exocytosis disseminates them further. Though infecting many different organs, the liver is one of its prime targets and there lays its propensity for causing death via inducing a hemorrhagic fever and the lethal acute form of the HRS. The liver upon light microscopy reveals mid zonal hyaline changes leading to necrosis and bodies resembling the Councilman bodies of yellow fever. Our patient, who was a farmer, fulfilled the US centers for disease control case definition of RVF most likely contracted the illness from his animals and had a severe affection to the liver. In
this case, the remarkable clinical signs was the complete absence of severe hepatic encephalopathy right up to the time of the patient’s sudden demise. Nausea and vomiting occurred in a great proportion of patients 91.5% in the recent outbreak in Gizan the southern region of KSA and loose motions in 43%.2 Our patient’s liver failure progressed at a rapid pace. The management problems, which we faced, compromised an inciting viral infection leading to hepatitis, was the development of disseminated intravascular coagulation (DIC) with the parallel development of HRS. Options to combat the inciting viral invader are limited to convalescent serum or the rare antiviral medication ribavirin.1 This broad spectrum antiviral drug is a triazole nucleoside first synthesized in 1970 resembling the structure of guanosine.3 Existing in the cell primarily in the triphosphate form it has 3 proposed mechanisms of antiviral action including potent inhibition of inosine 5’-monophosphate dehydrogenase activity, inhibition of guanosine triphosphate-dependent capping of the 5’ end of viral messenger ribonucleic acid (mRNA’s) and direct inhibition of RNA polymerase complex all resulting in inhibition of viral replication.3 In rodents and monkeys infected with RVF virus, ribavirin therapy resulted in reduced mortality with the only important side effect in humans being a manageable reversible anemia, no resistance to ribavirin was demonstrated.3 Although dispensed through the center for disease control in Atlanta, Georgia, USA we did not have enough time to procure it. Disseminated intravascular coagulation was the second problem faced in our patient. Even though etiologies vary they share on one common factor, which is the consumption of coagulant factors. These were replenished by FFP in our patient who did not exhibit severe external or internal bleeding tendency. Chuansumrit et al4 in Thailand used an interesting new approach for 2 cases of Dengue hemorrhagic fever. Recombinant factor VIIa (rFVIIa) was given for liver failure in conjunction with DIC and control of bleeding was achieved. However, the patients had more severe manifestations of hemorrhage and prolonged shock. Other novel approaches include the administration of antithrombin III concentrate and activated protein C concentrate as the final common pathway of activation of DIC is mediated by cytokines which depress the inhibitory mechanism of both antithrombin III and protein C. Controlled trials of these new strategies are awaited. The general consensus however, that is the cornerstone of DIC management is vigorous treatment of the underlying disorder, which in this case could not be dealt with in a timely fashion. Type 1 HRS occurred as a terminal event in our patient and could not be remedied. Hepatorenal syndrome is a specific form of renal failure in severe liver disease. It is a functional event causing decreased renal perfusion and especially in the renal cortex.3 The diagnosis is based on exclusion of other conditions causing renal insufficiency.3 Two types were distinguished: 1) Type 1 with a rapid and progressive increase of serum creatinine, which is observed within days and without orthotopic liver transplantation carries a poor prognosis with a mortality rate of 95% within a few weeks. 2) Type 2 is characterized by a moderate and stable reduction in kidney function.3 Orthotopic liver transplantation (OLT) is the only effective and permanent treatment for patients with HRS.5 However, recently 2 other options have received attention, first was the transjugular intrahepatic portosystemic stent-shunt (TIPS) that provides long term renal function and probably survival benefits in the majority of non-transplantable cirrhotics with HRS. It works by reducing the acidity of the renin-angiotensin and sympathetic nervous systems in cirrhotic patients with type 1 HRS. Second was long term administration (1-3 weeks) of analogs of vasopressin (omnipressin and terlipressin) or other vasoconstrictors together with plasma volume expansion with albumin, which reportedly were associated with a dramatic improvement in circulatory function and normalization of serum creatinine concentration in patients with severe HRS.3 In our patient with combined liver and renal failure, both standard hemodialysis and the newer continuous renal replacement therapies have been found to help maintaining fluid, electrolyte and acid base balance.3 Extra corporeal purification techniques would have been useful in our patient if available prior to his renal failure as they remove hepatic toxins and help in the replacement of clotting factors in liver failure without kidney dysfunction. According to our knowledge, our patient was one of the few infected people who were able to come to Riyadh despite the announcement of the discovery of the RVF epidemic in Southern region of Saudi Arabia and the subsequent quarantine measures implemented by the government through the Ministry of Health.2 This case demonstrates that with proper isolation and standard body fluid precautions a RVF patient can be cared for with minimal risk to hospital personnel. Although it is a mild illness with many subclinical cases the hepatic form of the disease occurred in 88% in those with severe illness.2 Inasmuch as the culprit is the RVF virus, ribavirin should be at the ready to study its clinical efficacy should a second epidemic occur to prevent the dire consequences of this illness in our population.

Received 29th October 2003. Accepted for publication in final form 20th December 2003.

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Breast cancer during pregnancy and lactation

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Pregnancy associated cancer is a cancer that is diagnosed during pregnancy or within a year after. Although its incidence is relatively rare, it is the most common malignancy encountered in pregnant women. It is seen in approximately 0.03% of pregnancies and only 1-2% of overall breast cancers is diagnosed during pregnancy or lactation. In recent years, gestational breast cancer seems to be occurring with increasing incidence, but clinicians often tend to attribute breast symptoms and signs to the physiological breast changes of pregnancy or lactation. The matter is further complicated by breast engorgement as pregnancy advances hiding any breast solid lumps. It is not surprising therefore that the breast cancer during pregnancy or lactation has the reputation of ‘bad prognosis’ mainly due to late presentation and delayed diagnosis which is very common.

We report 3 cases of gestational breast cancer that were encountered by the authors over a year period (1998) and discuss the diagnostic dilemma and modern management options.

The first case was a 38-year-old Saudi female who was 8 month pregnant presented with 3 month history of left breast lump and intermittent bloody nipple discharge. She started menarche at the age of 13 years and denied any past history of benign breast diseases or oral contraceptive pill. There was no family history of malignant breast disease. Clinical examination revealed an irregular hard lump (3x3 cm) in the subareolar area of the left breast with no palpable axillary or supraclavicular lymph nodes. Fine needle aspiration cytology (FNAC) showed infiltrating ductal carcinoma. She underwent left simple mastectomy and axillary clearance together with cesarian section (CS) and tubal ligation at the same time. Histology revealed grade II infiltrating ductal carcinoma with 2 of the 11 level I nodes were positive for malignancy. She later underwent adjuvant chemoradiation and remained well with no evidence of locoregional recurrence 34 months later (Table 1).

The second case was a 40-year-old Saudi female who has been lactating for 10 months presented with a left breast lump of one week duration. There was no history of breast pain or nipple discharge and denied any past history of benign breast disease. There was no family history of breast cancer. Clinically, there was a 2x3 cm irregular left breast mass, in the upper outer quadrant with no palpable axillary lymphadenopathy. Mammography revealed suspicious opacity in the left breast but bone scan and ultrasonography showed no bone or liver metastases. Fine needle aspiration cytology showed suspicious of malignancy. She underwent a wide excision and left axillary clearance. Histopathology showed grade II medullary carcinoma and 2 out of 20 axillary lymph nodes were malignant. She later underwent systemic chemotherapy and radiation to left breast and declared disease free 30 months later (Table 1).

The third case was a 32-year-old Saudi female who has been lactating for 5 months presented with a month history of a right breast lump. There was no history of nipple discharge or past history of any benign breast diseases. There was no family history of breast carcinoma. Clinically, there was an irregular right breast mass (5x3 cm) in the upper inner quadrant with palpable right axillary lymph nodes. She underwent right simple mastectomy and axillary clearance. Histology showed grade II infiltrating ductal carcinoma with 15/18 lymph nodes were positive. Postoperative adjuvant therapy was given but was lost to follow up 6 months after surgery (Table 1).

Contrary to the general belief, pregnancy does not appear to have an adverse effect on the disease process nor there is a solid evidence to implicate pregnancy or lactation as etiological factors. The reputation of ‘bad prognosis’ associated with pregnancy associated breast cancer is greatly attributed to late presentation and delayed diagnosis which is very common. Therefore, it is not surprising to encounter axillary lymph node involvement in 70-80% of operable breast lesions diagnosed during pregnancy, mainly due to delayed postpartum pregnancy.
cases 2 and 3 were postpartum and were only lactating. Termination of pregnancy is considered in females presenting early in pregnancy with advanced or metastatic cancer necessitating chemotherapy and radiation. However, there is no conclusive evidence that termination improves the prognosis or alters the natural history of the disease process.

Nevertheless, termination does permit standard aggressive therapy in advanced disease. If all the therapeutic options are explored with caution, the prognosis and survival for women with pregnancy associated breast cancer are similar to that of women of the same age and same stage of the disease treated similarly.

Received 9th September 2003. Accepted for publication in final form 7th December 2003.

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References


Table 1 - Details of presentation, operation, axillary nodal status and outcome of the 3 cases.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (year)</th>
<th>Status</th>
<th>Presentation</th>
<th>Operation</th>
<th>Node status</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>Pregnant</td>
<td>Breast lump, bloody nipple discharge</td>
<td>Mastectomy and axillary dissection</td>
<td>Positive (2/11)</td>
<td>Alive 35 months</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>Lactating</td>
<td>Breast lump</td>
<td>Lumpectomy and axillary dissection</td>
<td>Positive (2/20)</td>
<td>Alive 30 months</td>
</tr>
<tr>
<td>3</td>
<td>31</td>
<td>Lactating</td>
<td>Breast lump</td>
<td>Mastectomy and axillary dissection</td>
<td>Positive (15/18)</td>
<td>Lost to follow-up</td>
</tr>
</tbody>
</table>

diagnosis. All our 3 patients had metastatic axillary lymph nodes. The status of axillary lymph nodes is considered one of the best prognostic factors in breast cancer. It is clear that case 3 has worse prognosis than case one or 2. Unfortunately, case 3 was lost to follow up and was presumed dead. Generally speaking, treatment should follow the same line and principles applied for non-pregnant females, with the modifications required by pregnancy. Modified radical mastectomy is the best offered surgical therapy for stage I, II and selected cases of stage III. This is certainly the case for breast cancers diagnosed during the first and second trimesters, as adjuvant therapies need to be withheld until after delivery. However, recent evidence suggests that breast conservation surgery in the form of lumpectomy and axillary node dissection can be offered if feasible in the third trimester and radiotherapy is delayed until after delivery. Case 2 was offered breast conservation surgery without adverse consequences. However, in pregnancy risks and benefits of breast conservation should be thoroughly discussed with patient as it has its own problems and drawbacks. Chest wall radiation for cancers detected in the second or third trimester is delayed until after delivery to avoid fetal growth retardation and still births. The risk of abortion and fetal malformations is highest during embryogenesis in the first trimester and varies with the choice of chemotherapeutic agents. Recent evidence suggests that the risk of fetal malformations associated with administration of chemotherapeutic agents after the first trimester is not greater than the background control. The decision on postoperative adjuvant chemoradiation therapy in all the cases was made easy by the fact that CS was performed at the time of mastectomy in case one who gave birth to a healthy baby and that cases 2 and 3 were postpartum and were only lactating. Termination of pregnancy is considered in females presenting early in pregnancy with advanced or metastatic cancer necessitating chemotherapy and radiation. However, there is no conclusive evidence that termination improves the prognosis or alters the natural history of the disease process. Nevertheless, termination does permit standard aggressive therapy in advanced disease.

If all the therapeutic options are explored with caution, the prognosis and survival for women with pregnancy associated breast cancer are similar to that of women of the same age and same stage of the disease treated similarly.
Transport management of the critically ill. Outcome of study with recommendations

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Transfer of critically ill patients is a frequent occurrence at the hospitals with limited facilities. Such patients require inter-hospital transfer for specialized services (diagnostic or therapeutic). Those patients are at high risk for complications during transfer. Our establishment is a secondary care hospital situated on the main highway between Riyadh, Kingdom of Saudi Arabia (KSA) and Southern region (Khamis Mushayt and Abha) of KSA. The distance by road in each direction is approximately 700 kilometers for Riyadh and 400 kilometers for Khamis Mushayt and 400 kilometers for Abha. All hospitals along that route do not have neurosurgical service, diagnostic cardiac laboratory, open heart surgery or burn and plastic units. This retrospective study was conducted to audit the hospital process of inter-hospital transfer, to highlight the depth of the problem experienced by referring hospitals in remote areas and present findings to health care policy makers for consideration for future expansion of health services in the region. The records of critically ill patients admitted to the intensive care unit (ICU) from August 1998 until the end of July 2003 were reviewed. The hospital has an operational protocol for the transport of the critically ill patient drawn up from well established international guidelines with modifications to suit local conditions.

When a diagnostic or therapeutic facility is unavailable within our locality, contact with the referral hospital starts usually by faxing a medical report. Our hospital has a fleet of ambulances composed of 2 mobile ICU and 3 ordinary ambulances. A transport team composed of an anesthetist, a paramedic and an experienced nurse usually accompany the patient depending on the severity of the condition. To avoid possible delays or complications during transport, a checklist containing essential steps prior to transfer was followed. All patients accepted in the hospitals in Riyadh, KSA were transferred by medivac, while those transferred to Southern region were transported either by medivac or ambulance depending on their medical condition. It takes 5-6 hours for the ambulance to reach the hospitals in the Asir region, KSA (Khamis and Abha). The ambulance crew was provided with mobile phone.

There were 1495 patients admitted to the ICU during the period of the study. 55 of them were transferred to other centers. They constituted 3.7% of the total admissions. The male to female ratio was 1.1:1 (29 males and 26 females), with an average age of 50.6 years (range 4 months-92 years). One-third of them (18 patients) were mechanically ventilated during the transport. Table I shows detail of patients transferred. Two patients died during transport (3.6% of total transferred) aged 55 and 6-year-old. A third patient showed rapid oxygen desaturation due to the presence of dissipated blood clot inside the tracheal tube, the latter was replaced. Five times the ambulance cool air-condition was not functioning. Twice the ambulance was involved in collision with other traffic. There were no human injuries but one ICU ambulance was taken off service. One of the main and persistent problem we encountered in the majority of the cases was the situation of no response to our initial request for transfer. There is a multitude problems facing the safe and efficient inter-hospital transport of the critically ill patient.

These include the transport means, the transport team and equipment needed to keep the critically ill patient stable during transport. Aeromedical transport was found to be superior to ground transport. The helicopter has an important role to play in the inter-hospital transport, but there is no benefit if the distance by road is less than 30 minutes or beyond 300 kilometers or when helicopter flight time exceeds one hour. Here, the fixed-wing aircraft can overcome the delays inherent in transferring patients between hospitals and airports. In our situation, a helicopter is the most suitable mean of transport. It can be used in transporting critically ill patients to the airport where the medivac lands, thus avoiding the traffic problems, which the ambulance encounter during the one hour journey to the airport. In addition, it can be used in transporting acutely ill patients and trauma victims from the scene of the incident to the hospital (primary transport). Our hospital has already a landing space for 2 helicopters. Meticulous resuscitation and stabilization of the patient before transport is the key in avoiding complications during the journey. Our transport team is well trained and experienced in transporting critically ill patients. In fact, we run a one day course related to this subject, which is recognized by the Saudi Council for Health Specialties. There is evidence that the use of dedicated transport teams improves the outcome of critically ill patients transferred between hospitals. Nevertheless, adverse events during inter-hospital transport of the critically ill still happening. They may be equipment related or due to physiologic deteriorations connected to critical illness. However, death during transport is a rare event. In our study, 2 gravely ill patients, one adult and one child, died during transport. With the ever increasing population in
Table 1 - Details of 55 patients transferred to specialized hospitals.

<table>
<thead>
<tr>
<th>Transfer by specialty</th>
<th>n</th>
<th>Ventilated</th>
<th>Method of transport</th>
<th>Referral center in the Kingdom of Saudi Arabia</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Medivac</td>
<td>Ambulance</td>
<td>Riyadh, Khamis Mushayt</td>
</tr>
<tr>
<td>Neurosurgical</td>
<td>13</td>
<td>13</td>
<td>9</td>
<td>4</td>
<td>Riyadh, Khamis Mushayt</td>
</tr>
<tr>
<td>Cardiology</td>
<td>25</td>
<td>4</td>
<td>13</td>
<td>12</td>
<td>Riyadh, Khamis Mushayt</td>
</tr>
<tr>
<td>Renal</td>
<td>4</td>
<td>none</td>
<td>-</td>
<td>4</td>
<td>Wadi MOH*, Khamis Mushayt</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>Riyadh, Abha ACH</td>
</tr>
<tr>
<td>Hepatic</td>
<td>1</td>
<td>no</td>
<td>1</td>
<td>-</td>
<td>Riyadh</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>3</td>
<td>none</td>
<td>1</td>
<td>2</td>
<td>Riyadh, Wadi MOH*</td>
</tr>
<tr>
<td>Medical</td>
<td>2</td>
<td>none</td>
<td>1</td>
<td>1</td>
<td>Khamis Mushayt</td>
</tr>
<tr>
<td>Orthopedic</td>
<td>1</td>
<td>no</td>
<td>-</td>
<td>1</td>
<td>Wadi MOH*</td>
</tr>
<tr>
<td>Ear, Nose, Throat</td>
<td>1</td>
<td>no</td>
<td>1</td>
<td>-</td>
<td>Riyadh</td>
</tr>
<tr>
<td>Gunshot wounds</td>
<td>2</td>
<td>no</td>
<td>2</td>
<td>-</td>
<td>Riyadh</td>
</tr>
</tbody>
</table>

*patients referred include renal for hemodialysis and non-eligible civilians. MOH - Ministry of Health

the region, together with the creation of new major projects and with the tremendous rise in the amount of road traffic especially at the start and end of public holidays, the suggestion of having a trauma center on the highway between Riyadh and Southern region of KSA has become a necessity. A cardiac center is another requisition. Two dedicated helicopters must be readily available. The establishment of such centers will make inter-hospital transfer of patients a rarity. Collecting patients from the place of the accidents is the primary role of the helicopter. In the majority of cases, we experienced delays in responding to our first contact with all referral hospitals. To speed up the process of responding to referral requests, we suggest that referral hospitals appoint a named consultant available 24 hours a day to receive requests for transfer, to arrange with the concerned service the acceptance or non-acceptance of the case, and to reply to the referring hospital without delay.

In conclusion, our hospital has an adequate facilities for the transport of the critically ill patients. Our aim is to provide essential service to the critically ill patients. But lack of early response from referral hospitals hinders the quality of management and poses real threat in terms of mortality and morbidity. The need for specialized services in the area, particularly neurosurgical and cardiac, is timely due. Providing these centers with 2 helicopters will speed up the process of patients’ transfer especially from site of incidents and avoid hazards of road traffic and severity of regional climate.

Received 31st August 2003. Accepted for publication in final form 15th December 2003.

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References

Is surgical management of cataract and glaucoma patients in Yemen changing?

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Age related cataract is the leading cause of blindness in Yemen and all over the world. Cataract surgery techniques, however, have been improving over the years. In Yemen, eye doctors used to treat cataract patients using intracapsular techniques. Not until early 1990 when extracapsular technique was introduced. Intraocular lens implantation was also introduced at the same period but it was used in very few eye centers. Nowadays, small incision phacoemulsification technique with foldable intraocular lens implantation is the standard procedure for cataract surgery all over the world and some eye centers in Yemen. This technique was introduced only recently.

Glaucoma affects 0.5-1% of the population above the age of 40 years and is a common cause of blindness. Cairns in 1968 described trabeculectomy and subsequently it remains the most commonly performed glaucoma filtration procedure. There has been a debate regarding the timing of trabeculectomy in glaucoma patients. Advocates of primary surgery report success rates of approximately 90% and an additional benefit of this approach may be the avoidance of visual field loss whilst attempting to control glaucoma medically. However, in most cases surgery is considered only where maximal medical treatment has failed to halt disease progression. Over the last decade there have been significant developments in the medical treatment of glaucoma and it has been suggested that patient management strategies are likely to change with medical therapy being increasingly preferred in lieu of surgical intervention. Amongst patients who have received long term medical treatment prior to surgery, the success rates of trabeculectomies tend to be lower, ranging from 45-93%.

Developments in the diagnosis and monitoring of glaucoma may also affect the relative use of medical and surgical management. In Yemen, we recently observed that trabeculectomy cases performed are very low compared to the number of glaucoma patients among the population and that trabeculectomy rates have fallen. We therefore conducted this study to determine whether our observation was an issue or not. The total number of cataract and glaucoma operations performed in the Eye Department in Al-Thawra Hospital, Sana’a, Yemen for each year from 1995-2000 were obtained from the Department of Statistics, Sana’a, Yemen. Cataract operations were divided into those with and without intraocular lens implantation. Glaucoma surgery cases were also analyzed for each year.

Table 1 shows the number of cataract and glaucoma filtration surgery (trabeculectomy) performed from 1995-2000 and the comparison between number of glaucoma surgeries performed in the United Kingdom and Yemen for the whole population. Cataract surgery techniques are improving in Yemen and the visual outcomes and rehabilitation are also getting better. The number of cataract cases having intraocular lens implantation is surgical management of cataract and glaucoma patients in Yemen changing?

<table>
<thead>
<tr>
<th>Year</th>
<th>Total cataract surgery</th>
<th>Cataract surgery with IOL</th>
<th>Cataract surgery without IOL</th>
<th>N of glaucoma surgery</th>
<th>Glaucoma surgery in Yemen *</th>
<th>Glaucoma surgery in United Kingdom **</th>
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</thead>
<tbody>
<tr>
<td>1995</td>
<td>509</td>
<td>473</td>
<td>36</td>
<td>63</td>
<td>945</td>
<td>18,112</td>
</tr>
<tr>
<td>1996</td>
<td>346</td>
<td>312</td>
<td>34</td>
<td>42</td>
<td>630</td>
<td>18,928</td>
</tr>
<tr>
<td>1997</td>
<td>364</td>
<td>334</td>
<td>30</td>
<td>33</td>
<td>225</td>
<td>17,595</td>
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<tr>
<td>1998</td>
<td>386</td>
<td>314</td>
<td>72</td>
<td>29</td>
<td>435</td>
<td>14,507</td>
</tr>
<tr>
<td>1999</td>
<td>469</td>
<td>393</td>
<td>76</td>
<td>16</td>
<td>165</td>
<td>11,882</td>
</tr>
<tr>
<td>2000</td>
<td>380</td>
<td>266</td>
<td>114</td>
<td>22</td>
<td>195</td>
<td>9,181</td>
</tr>
</tbody>
</table>

*Yemen population 19 million and figures are predicted, **United Kingdom population 60 million, IOL - intraocular lens
Is surgical management of cataract and glaucoma patients in Yemen changing?

Is methotrexate safe in the treatment of psoriatic patients?

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Psoriasis is a common genetically determined, chronic, relapsing and remitting, inflammatory skin disease, with great physical and social impact. Accelerated epidermal cell replication, with abnormal pattern of keratinocyte differentiation and the presence of dermal and epidermal inflammatory cell infiltration have been considered to be the main pathological events in psoriasis. Topical applications of tar, steroids or calcipotriol are therapies of choice for patients with mild to moderate severity of psoriasis. However, in patients with severe psoriasis, systemic therapy is an established alternative, such as photochemotherapy (PUVA), retinoids, cyclosporine and methotrexate (MTX). Methotrexate is considered as a cytotoxic agent. It is an antimetabolite that mediate its antimitototic effects through inhibition of DNA synthesis by blocking dihydrofolate reductase and thymidylate synthetase enzymes. It also has anti-inflammatory effects through inhibition of leukocyte chemotaxis. These 2 principle actions explain its clinical effect in controlling psoriasis. Methotrexate is an effective treatment for severe psoriasis. It is particularly useful in controlling erythrodermic and generalized pustular psoriasis (GPP) form, where it may be a life saving drug. The most serious toxic effect of the drug is hepatotoxicity. The tendency to a liver damage may be related to multiple risk factors, such as advanced age, diabetes, alcohol intake, obesity and impaired renal function. Reported signs of MTX toxicity also include, bone marrow suppression with leukopenia and thrombocytopenia, gastrointestinal ulceration, pneumonitis, oligospermia and nephrotoxicity. Due to these reported toxic effects, many dermatologists limit its uses, although it is available and inexpensive as compared to other systemic drugs for psoriasis. Therefore, the present study was arranged to investigate further, the effects of long term, low dose MTX therapy, in the management of severe psoriasis in Iraqi patients.

One hundred and thirty-two patients with severe psoriasis consisting of 22 patients with erythrodermic form, 29 patients with GPP and 81 patients with widespread plaque psoriasis were selected from the Department of Dermatology and Venereology, Baghdad Teaching Hospital, Baghdad, Iraq to receive MTX therapy during the period October 1998 to September 2000. They were 79 females and 53 males with female to male ratio of 1:49. Their ages ranged from 18-66 years (mean 42.3 ± SD 10.2 years). All patients were informed of the memorandum issued by the Ministry of Health for the routine use of intraocular lenses in cataract surgery help in putting this technique as the standard for every cataract surgery. Unfortunately, the number of glaucoma filtration surgery (trabeculectomy) is very small and is falling over the years compared to the predicted affected patients with glaucoma. There are number of explanations for this low surgical intervention: 1. Most glaucoma patients in our community were presented late with advanced pale cupped discs and at this stage there are few that can be offered. 2. Many eye surgeons throughout Yemen avoid doing glaucoma filtration surgery (trabeculectomy) for lack of training. 3. The fear of complications of trabeculectomy especially in advanced cases, made experienced eye doctors to avoid surgical intervention. 4. The introduction of new generations of anti-glaucoma therapy with better hypotensive effect.

We need to tackle these problems by educating our patients and introducing screening programs within the Yemeni community: hence those glaucoma patients can be presented earlier and get treated safely. We also need to train more doctors to perform trabeculectomy filtration surgery and to know how to manage the complications of this procedure. This will decrease the number of blind people due to a reasonably treatable disease.

References

to avoid the drugs that may interact with MTX or may cause bone marrow suppression, nephrotoxicity or hepatotoxicity and instructed carefully to use contraceptive precautions during and after a minimum of 3 months of cessation of therapy. Pregnant women and nursing mothers, diabetic, alcoholic or patients with laboratory evidence of bone marrow, hepatic or renal impairment were not included. The starting dose of MTX for each patient in the study was 15-25 mg/week as a single intramuscular injection or triple oral doses (with 12 hours intervals), until adequate response was achieved, then, the doses were reduced gradually to 10 mg/week. Clinical response was assessed at week 1, 2, 4, 8 and then once monthly. Remission was considered as satisfactory when there is improvement (clearance) in more than 50% of the lesional surface area, with reduction in the severity of erythema, scale and elevation for individual psoriatic plaques, on a score from 0 to 4 as follows: 0 for absent, 1 for mild, 2 for moderate, 3 for severe and 4 for extremely severe. The side effects faced during the treatment intervals were also recorded. Serial laboratory evaluations for each patient in the study were performed, including complete blood count, liver function test and serum albumin were performed every 2-3 months of therapy. Liver enzymes were assessed 7 days after the last dose of MTX, to avoid the transient elevation that may occur during first few days of MTX intake. Renal function tests were performed every 2-3 months of therapy. Other investigations included chest x-ray, seminal fluid analysis, sperm counts, motility and morphology were analyzed every 2 months of therapy for 24 patients. Ultrasound (US) scanning of the liver were performed prior to therapy for 60 patients and repeated after 6 months of therapy. Liver biopsies were obtained from all patients with abnormal liver US scanning. The body weight of the patients ranged from 50-105 kg (mean 78.3 ± SD 14.7 kg). The duration of the disease ranged from 8 months to 32 years (mean 15.2 ± 8.4 years). Total duration of MTX therapy varied from 16-72 weeks (mean 41.1 ± SD 14.3 weeks) and total cumulative dose ranged from 240-960 mg (mean 604 ± SD 172.8 mg). Remission was achieved in 59 (44.6%) after 2 weeks of therapy, 83 (62.8%) after 4 weeks of therapy and 104 (78.8%) patients after 8 weeks of therapy. Similar responses as achieved after 8 weeks of therapy were observed after further therapy. A number of side effects were noticed in our study. The main cutaneous side effect was the intense itching on 55 (41.5%), loss of appetite in 40 (30.3%) and nausea in 40 (30.3%) patients. Headache and malaise were noticed in 19 (14.3%) patients, while menstrual disturbances, mainly, oligomenorrhea were observed in 14 patients (which constitute 17.7% of female patients). Serial laboratory evaluations for our patients showed a decrease in hemoglobin level in 4 (3%) patients, the lowest hemoglobin level recorded in one patient was 10 g/dl after 5 months of therapy. Ten patients (7.6%) had slight decrease in white blood cell counts and absolute neutrophil counts after 5-6 months of therapy. Liver enzymes, mainly, serum glutamate pyruvate transaminase and serum alkaline phosphatase were elevated in 8 (6%) patients after 16 weeks of therapy, but returned to normal level after discontinuation of therapy. Repeated seminal fluid analysis showed a slight reduction in the sperm counts in 8.3% (2 out of 24) patients. Abnormal result of US scanning of the liver (enlarged liver with fatty changes) were detected in 5% of the patients (3 out of 60 patients). Fortunately, their liver biopsies resulted in mild histological changes (septal inflammatory infiltrate with mild fatty changes). This study showed that MTX is an effective therapy for controlling severe psoriasis, as remission was achieved in 78.8% of patients. Transient subjective discomforts, such as nausea, vomiting, headache, itching, loss of appetite and dizziness were experienced in some of our patients (5-40%). These results are similar to other reported literature, that are transient and reversible with cessation of therapy. Ultrasound scanning is a safe and quick method for the detection of liver diseases. Previous literature suggest that patients with normal US scan prior or during MTX therapy, could be spared from liver biopsies, as referrals to other published literature, resulted in low incidence of liver damage and associated with few laboratory abnormalities. This could be due to proper selection of patients and absence of risk factors, mainly alcohol intake.

It can be concluded that, MTX is an effective drug for severe psoriasis and is relatively safe therapy if patients are carefully selected and regular monitoring for side effects is performed regularly during therapy.

Received 23rd October 2003. Accepted for publication in final form 28th December 2003.

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References