Case histories of infectious disease management in developing countries: Phnom Penh and Kabul

As doenças infecciosas nos países em desenvolvimento: Phnom Penh e Cabul

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ABSTRACT

Healthcare in developing countries is affected by severe poverty, political instability and diseases that may be of lesser importance in industrialized countries. The aim of this paper was to present two cases and histories of physicians working in hospitals in developing countries and to discuss the opportunities for clinical investigation and collaboration. Cases of patients in Phnom Penh, Cambodia, with histoplasmosis, cryptococcal meningitis, crusted scabies, cerebral lesions and human immunodeficiency virus and of patients in Kabul, Afghanistan, with liver cirrhosis, nephrotic syndrome and facial ulcer are discussed. Greater developmental support is required from industrialized nations, and mutually beneficial cooperation is possible since similar clinical problems exist on both sides (e.g. opportunistic cardiovascular infections). Examples for possible support of hospital medicine include physician interchange visits with defined objectives (e.g. infection control or echocardiography training) and collaboration with clinical investigations and projects developed locally (e.g. epidemiology of cardiovascular diseases or nosocomial bloodborne infections).


MATERIAL AND METHODS

The case histories and clinical observations for this report were collected at hospitals in Phnom Penh, Cambodia (Khmer Soviet Friendship Hospital), and Kabul, Afghanistan (Ali Abad Hospital) during discussions with healthcare workers and patients and after reviewing the medical records. Photographs
were obtained with a digital camera (Canon 530A). The study was approved by both hospitals (Khmer Soviet Friendship Hospital and Ali Abad Hospital). Verbal consent was obtained before taking clinical photographs.

RESULTS AND DISCUSSION

Phnom Penh. A 42-year-old male Khmer patient with acquired immunodeficiency syndrome (AIDS) that was being treated with lamivudine, stavudine and efavirenz was admitted with a generalized papular skin rash, weight loss and fever (Figure 1A, Figure 1B and Figure 1C). Blood cultures did not show any growth of fungi or mycobacteria, while fungal culturing of a skin biopsy was positive for *Histoplasma capsulatum*. A test for serum cryptococcal antigen was negative and lumbar puncture and the serum VDRL (venereal disease research laboratory) test were not performed. He was treated with intravenous amphotericin B for disseminated histoplasmosis. Other fungal infectious causes of generalized skin rash in HIV-infected patients in Cambodia include *Cryptococcus neoformans* and *Penicillium marneffei*.

A 43-year-old male Khmer patient with AIDS was admitted with headache. Cryptococcal meningitis was diagnosed based on positive serum and cerebrospinal fluid (CSF) cryptococcal antigen and CSF fungal culture (Figure 2A). He was treated with intravenous amphotericin B and, after an initially poor clinical response, flucytosine was added. Serum flucytosine testing because of the risk of high levels of bone marrow suppression was not available. This patient required repeated lumbar punctures to treat the elevated intracranial pressure that was causing the headache (Figure 2B). Controlling elevated CSF pressure by means of lumbar drainage improves the symptoms of and outcome from cryptococcal meningitis.

A number of patients were seen who required repeated lumbar punctures for elevated CSF pressure. For some patients, lumbar drains were placed (Figure 2C) by the physicians as a bedside procedure. Ventriculoperitoneal shunts were not used. On admission to hospital in Cambodia, most patients present with undiagnosed advanced HIV disease and are not taking HIV medication. Coinfection with tuberculosis or cryptococcal meningitis is common. When HIV treatment is started together with other treatments, e.g. for cryptococcal infection, patients frequently deteriorate with decreasing consciousness levels due to immune reconstitution syndrome (IRS). For this reason, clinicians avoid starting HIV therapy in hospital and clinical studies are in progress regarding the time to start antiretroviral treatment among patients with coinfections.

A 32-year-old male Khmer soldier with HIV infection and a history of treated tuberculous meningitis was admitted with hemiplegia (Figure 3A and Figure 3B). Examination of cerebrospinal fluid was negative for cryptococcal antigen and the VDRL serological test was negative. Brain imaging using computed tomography showed a single large cerebral lesion (Figure 3C). A number of patients with similar presentations were seen and treated empirically for toxoplasmosis with pyrimethamine and sulfadoxine. Investigations such as PCR (polymerase chain reaction) on CSF, serological tests for Epstein-Barr virus (EBV), cytomegalovirus (CMV) or JC virus and brain biopsy were not available.

Other possible causes of such lesions include tuberculoma, progressive multifocal leukoencephalopathy (PML), primary CNS (central nervous system) lymphoma and bacterial abscess. Only a few studies have been conducted in Southeast Asia on the
Cryptococcal meningitis management with repeated lumbar puncture and lumbar drain. This patient with AIDS and cryptococcal meningitis was treated with intravenous amphotericin B (Image A) and repeated lumbar puncture (Image B). Image B was taken during the lumbar puncture and shows the increased flow of cerebrospinal fluid secondary to increased cerebrospinal fluid pressure. After repeated lumbar punctures, a lumbar drain was inserted by the physician at the bedside (Image C).

FIGURE 3A-C
Intracerebral lesions in HIV-infected patients. This male Khmer AIDS patient and former soldier with hemiplegia (Image A and B) was treated empirically for toxoplasmosis with large intracerebral lesions (Image C). A number of patients were seen with a similar presentation. The available diagnostic investigations were limited and few studies on the causes of intracerebral lesions and their management have been conducted in Southeast Asia.

A male Khmer patient with HIV infection was admitted with a generalized rash that had lasted for months (Figure 4A and Figure 4B). There was no evidence of any adverse reaction to frequency of brain involvement with bacteria (e.g. Nocardia species), fungi (e.g. Candida species, Histoplasma capsulatum, Penicillium marneffei), protozoa (e.g. Entamoeba histolytica) or helminths (e.g. Gnathostoma spinigerum) and the management of such situations5.
his HIV medication, and serum VDRL was negative. Histological analysis on a cutaneous biopsy was inconclusive and he was treated with pyrethrin and ivermectin for Norwegian or crusted scabies. Different patients with skin rashes associated with antiretroviral therapy were seen, and these rashes were especially associated with nevirapine. This drug is the non-nucleoside reverse transcriptase inhibitor (NNRTI) most frequently used in Cambodia, and efavirenz is not available to most patients due to higher costs. Unlike efavirenz, nevirapine has to be given twice daily and it has greater potential for severe adverse reactions such as hepatotoxicity and rash. It typically causes an erythematous maculopapular rash. Figure 5 shows a female Khmer patient with HIV infection who developed a generalized skin rash attributed to treatment with nevirapine. The factors that may increase the frequency of side effects from highly active antiretroviral therapy (HAART) in developing countries include anemia, malnutrition, tuberculosis and advanced HIV disease. Kabul. A 42-year-old male Afghan patient was admitted with abdominal swelling that had lasted for years (Figure 6). Liver disease had been diagnosed in the past and, because of increasing abdominal swelling over recent years, he had decided to come to the hospital from an outlying province. Because of a positive serum HbsAg test, he was clinically diagnosed with liver cirrhosis with portal hypertension and ascites, probably due to chronic hepatitis B virus (HBV) infection. He was treated with fluid restriction, diuretic therapy and repeated paracentesis.

No published epidemiological data are available, but from discussions with clinicians, the most common causes of liver cirrhosis in Afghanistan are HBV and hepatitis C virus (HCV).
infection. Alcohol is unlikely to be a common cause due to limited availability. The prevalence of serum positive for hepatitis B surface antigen was 8.3% among Afghan refugees living in Pakistan and 4.1% among Afghan refugees living in the United States3. It is not known how many infections are transmitted through sexual intercourse, unsafe injection practice or other procedures, but it is likely that HBV is frequently acquired perinatally or during early childhood in Afghanistan. An effective vaccine against HBV is available but not offered as part of any public health program due to limited availability of funding.

The above patient is representative of a large number of patients in Afghanistan with complications from chronic hepatitis, including liver cirrhosis and hepatocellular carcinoma. It is likely that HBV vaccination for children and risk groups would be as effective as found previously elsewhere e.g. in Taiwan or the United States15. A 21-year-old male Afghan patient was admitted with mild leg-swelling and a history of renal disease five years earlier. Based on normal serum creatinine concentration and proteinuria, nephrotic syndrome was diagnosed and diuretics and steroids were started (Figure 7). Nephrotic syndrome may include membranous glomerulopathy, minimal change disease and focal and segmental glomerulosclerosis, and treatment with corticosteroids may lead to improvement12. Treatment with steroids shows no consistent improvement of membranous glomerulopathy, which is associated with certain infections that are prevalent in Afghanistan: HBV, HCV, syphilis, Plasmodium malariae, leprosy, tuberculosis, streptococcal infection, abscess and filariasis.

FIGURE 7
Afghan patient with nephrotic syndrome treated with corticosteroids. This 21-year-old male Afghan patient was diagnosed with nephrotic syndrome based on normal serum creatinine concentration and proteinuria. He was treated with oral prednisolone and diuretics for suspected nephrotic syndrome with steroid-responsive glomerular disease.

The use of steroids, for example for nephrotic syndrome in Afghanistan and other developing countries, is limited by higher prevalence of infections such as those due to Mycobacterium tuberculosis, Strongyloides stercoralis, and Leishmania major, which may be latent or undiagnosed and become symptomatic during steroid treatment.

A 29-year-old Afghan male patient with a facial ulcer and enlarged cervical lymph nodes for one year was seen in Kabul (Figure 9A and Figure 9B). The wound had healed intermittently in the past and had been treated topically with different steroid creams. The possible causes of the facial ulcer included cutaneous leishmaniasis, mycobacterial infection and fungal infection (e.g. sporotrichosis)1.
clinicians in Kabul and Phnom Penh were more likely to rely on a single test result to confirm or rule out a diagnosis (e.g. chest X-ray for heart failure or sputum microscopy for tuberculosis). Long-term management with drugs such as statins or angiotensin-converting enzyme (ACE) inhibitors for cardiovascular disease were less frequently used in Phnom Penh and Kabul. This may be due to the higher drug costs and because the benefit from treatment is not immediately apparent to patient and doctor.

Furthermore, not all evidence-based guidelines from North America or Europe may be applicable to developing countries, given that different patient populations are addressed. For example, different outcomes were observed with the use of dexamethasone for bacterial meningitis among adults in Europe, Malawi and Vietnam.

The trend in clinical decision-making in industrialized nations is to diagnose or rule out an increasing number of causes of medical disorders (e.g. pulmonary embolism in patients with pneumonia or myocardial infarction in patients with cardiac failure). On the other hand, in the resource-poor setting of both Cambodia and Afghanistan, clinicians were more likely to discontinue a diagnostic work-up after one possible cause was identified. For example, iron-deficiency anemia was explained in terms of poor nutritional intake or hookworm infection and not further investigated for additional causes such as duodenal ulcer or other gastrointestinal disorders.

In conclusion, increased support for healthcare development in developing countries is required from industrialized nations, and mutually beneficial cooperation is possible since similar clinical problems exist on both sides (e.g. HIV or HBV). Examples for possible support of hospital medicine are physician interchange visits with defined objectives (e.g. HIV inpatient care, echocardiography training, gastro-intestinal endoscopy or hospital infection control) and research collaborations (e.g. epidemiology of cardiovascular disease, hospital-acquired bloodborne infections, long-term benefits of aspirin, statins and ACE-inhibitors) that continue locally developed projects.

REFERENCES


