MYCOBACTERIUM ULCERANS INFECTION IN KUMASI, GHANA : CASE REPORT AND CLINICAL REVIEW

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SUMMARY : A mycobacterium ulcerans infection, Buruli ulceration is one of the tropical diseases. Four cases of Buruli ulcers seen in Kumasi, Ghana during an Interplast International Surgical Activity are presented. The lesions begin as solitary, hard, painless, subcutaneous nodules that subsequently ulcerate and become undermined. The disease is encountered Australia, Nigeria, Zaire, Gabon, Benin, Uganda, Mexico, Malaysia and Ghana. The majority of the ulcers are found in children and young adults. The extremities are more commonly affected. Although the diagnosis is made by clinical observation, bacteriologic studies are necessary to confirm the diagnosis. Effective chemotherapeutic treatment is not available at present. When applicable, excision with wide margins and subsequent grafting is the best treatment modality.

Key Words : *Buruli Ulcer, Searl's Ulcer, Mycobacterium Ulcerans.*

INTRODUCTION

Old hospital records revealed that Albert Cook described a strange ulcer in 1887 in Buruli District of today's Uganda, near Lake Victoria (10). In 1948 Mc Callum and colleagues reported a cluster of ulcers which were difficult to treat in Australia. Eventually they succeeded to isolate an unknown acid-fast rod, subsequently named Mycobacterium ulcerans (13). In 1960s a group of British physicians in Uganda found many more cases in the Buruli District. Since then Buruli ulcer has been identified in many countries in Africa, South America, South-East Asia and the Central Pacific.

MYCOBACTERIUM ULCERANS

Mycobacterium ulcerans, an acid-fast bacillus grows in Löwenstein-Jensen medium preferably at 33°C and growth is inhibited at body temperature (3). This is quite uncommon in human pathogens and may be explain the affinity of the bacillus for subcutaneous tissue. M. ulcerans produces a heat-labile toxin which has both cytotoxic and immunosuppresive properties and the tissue destruction is attributed to this toxin (13). It is possible to stain extracellularly located M. ulcerans clusters with the Ziehl-Neelsen (ZN) and Fite-Faraco (FF) procedures (10). Electron microscopy studies of the bacillus reveal similar structural properties as other mycobacteria. The mycobacteria are mostly found in the high exudate layer which is rich in granulocytes in the ulcer floor rather than the edges of the ulcer (10, 13).

EPIDEMIOLOGY

The natural habitat of the bacterium is not known. Endemic areas are found near large water accumulations (i.e., rivers, swamps, lakes) and

cases from arid sites are quite few. However, extensive testing for Mycobacterium ulcerans in water are all negative (12, 14). Insect bites, thorn pricks, direct transmission from person to person or waterborne infection are all blamed with no objective evidence. Considerably high rate of infection is found in closely related patients. But this does not necessarily imply person to person transmission, as it can be explained by a shared exposure to the same environmental source of infection. Therefore, the mode of transmission is still unknown. The disease has been reported in different parts of the world mainly from West Africa (Table 1). Seasonal variation is described, with peak incidence in September and October especially in cases from Ghana (1). The rate of illness does not seem to differ between males and females and younger patients are more susceptible (2, 9). Extremities are the main sites of ulcers. Upper extremities are affected in younger patients whereas lower extremities are the major site of infection in adults (18). Rare cases of lesions on head, neck and trunk are also described especially in children under 13 years of age (15).

CLINICAL COURSE

Early disease stages are not well described. Clinically the infection begins with a subcutaneous nodule attached to the overlying skin. After a period of weeks cellulitis with marked edema and necrotizing panniculitis become apparent. As the disease progresses the subcutaneous necrosis impairs the blood supply to the overlying skin which results in ulceration (13). This ulcer is generally the first diagnostic clue. The base of the ulcer is covered by calcified necrotic tissue. The edges are widely undermined and this is the evidence of subcutaneous tissue necrosis extending far beyond visible ulceration. Surrounding skin is shiny, hyperpigmented and often scaling (3, 5). Different from other bacterial ulcerations both pain and local heat are generally absent. In its general course, ulcers may heal by scarring with crippling contractures or lead to death due to septicemia (11). Accordingly, clinical disease staging can be made (Table 2) and patients can have lesions of different stages simultaneously (12). Buruli scar is deeply sunken into the surrounding skin as a result of complete loss of subcutaneous tissue that does not regenerate and the edges of the scar are overlapped by the healthy skin. Although in practice, Buruli ulcer is a reliable clinical diagnosis as its scar is highly characteristic, it can be confirmed by finding acid-fast bacilli in smears of the exudate from typical lesions or by finding in biopsy specimens the zone of coagulation necrosis containing the bacteria. On the other hand, to detect the causative agent is not possible in each case and this does not rule out the diagnosis.

TREATMENT

Many treatment modalities have been tried with disappointing outcomes. Although Mycobacterium ulcerans is sensitive to antibiotics, in vitro treatment with antibiotics have shown no beneficial effects. Long term treatments with cotrimoxazol, clofazimine, rifampin and topical application of honey failed to show a major

Angola	Cameroon	Gabon	Malaysia	Nigeria	Uganda
Australia	Congo	Ghana	Mexico	Papua New Guinea	Zaire
Benin	Cote d'Ivoire	Liberia	Mozambique	Sierra Leone	

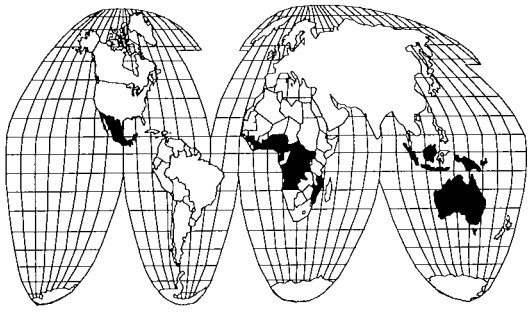

Table 1 : List of countries known to have mycobacterium ulcerans infection.

Stage I	Subcutaneous nodule
Stage II	Cellulitis
Stage III	Ulceration
Stage IV	Scar formation

Table 2 : Staging system of buruli ulcer.

progress in the course of the disease (4, 6, 8, 17). The use of topical antibiotics has not been attempted possibly due to the protection of the bacteria by surrounding necrosis. Heat treatments for long periods of time with application of hot-water-jackets have failed. Hyperbaric oxygen which accelerates healing in experimentally infected mice has also been tried with no promising results. The best form of therapy seems to be deep excision of the lesion with subsequent grafting. The skin graft take is generally poor with no logical explanation. Radical excision of ulcers is not possible in many cases owing to the size of a lesion or to proximity of tendons, nerves and important blood vessels. Even with small ulcers recurrences are quite common. It is mentioned that cases who had received Bacillus Calmetti-Guerin (BCG) vaccination had a shorter duration of the ulcer. A study revealed that some degree of protection was offered with an initial tuberculin reaction of 4mm (or greater) and proposed the use of BCG as a short term preventive measure (1, 16). However, the results of BCG vaccination are controversial and its usage as a preventive measure is highly debatable. There is still no gold standard for the treatment of Buruli ulcer and research is desperately needed to find an effective treatment for this crippling disease.

CASE REPORTS

During the International Interplast Surgical Activity in Kumasi, Ghana; four cases of Buruli ulcer were seen by the Turkish team of surgeons and anaesthesiologist, in Aninwah Medical Center. Three of the patients had their lesions on their lower extremities with almost similar pattern and the remaining patient had an ulcer on his face. All patients were male and coming from Ashanti region. The first case was a young male patient with an ulcer on the left side of his face involving the left eye and the nasal dorsum. The eye was destroyed and there was no remaining vision with left eye (Fig. 1, 2). As the ulcer was too extensive and involved vital structures radical excision was not feasible. Therefore, long term treatment with

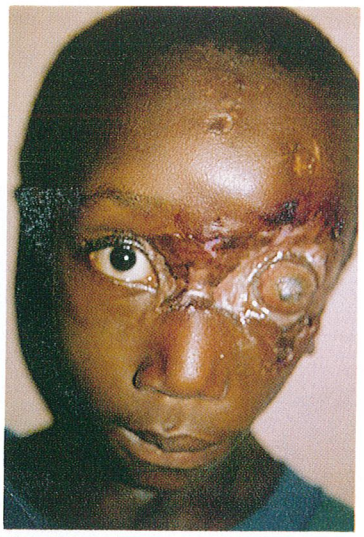

Fig - 1

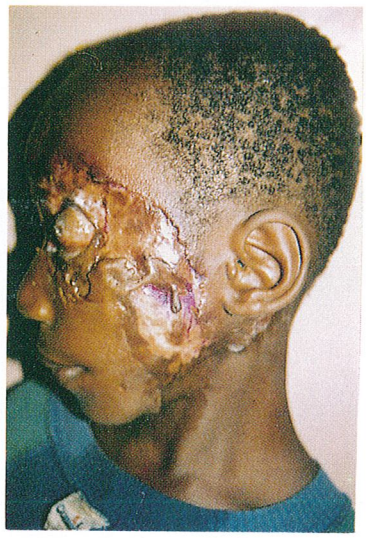

Fig - 2

antibiotics was planned. The second patient was an adult male with an extensive ulcer on his lower left extremity (Fig. 3, 4). The diagnosis of Buruli ulcer was made by the typical appearance of the ulcer. No further bacteriologic study was planned as the local physicians were quite experienced about the mycobacterium ulcerans and its clinical course. The treatment was started with serial debridements and a grafting procedure was scheduled for the patient. The surgical team was short of time, therefore the grofting procedure was handed over to local physicians. The other two patients were similar with the second one as for the ulcers and applied treatment protocol. According to the clinical staging system all ulcers were staged III and IV. To

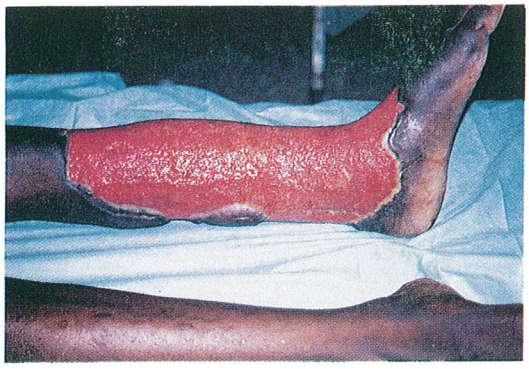

Fig - 3

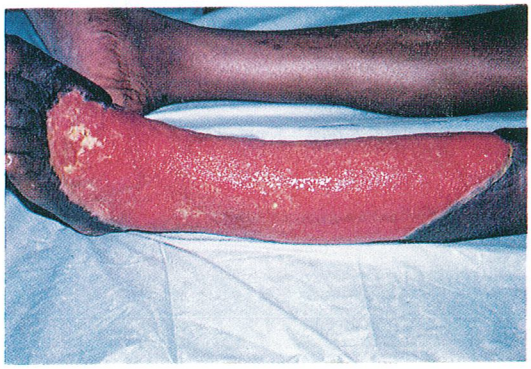

Fig - 4

our surprise there was no complaint due to pain.

DISCUSSION

Mycobacterium ulcerans infection known as Buruli ulcer is a serious health burden especially in endemic regions such as Uganda, Ghana, Nigeria and Ivory Coast (2). A number of epidemiological studies indicate a close relation between the Buruli ulcer and water courses, but no strict evidence has been found (7). There is almost no knowledge about its transmission mode and effective treatment. Neither of the treatments applied today is promising. Disappointing outcome of the treatment and devastating complications such as scarring, joint contracture, invasion of the vital structures such as an orbit are common (8). With the aid of high technology, people can travel around the world more easily and as a consequence hidden disease such as Buruli ulcers have a chance to spread widely as it has happened in AIDS. Therefore, urgent attention should be paid both for its epidemiology and mode of transmission. Research is desperately needed to find an effective treatment for this crippling disease.

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