KORLE-BU PAEDIATRIC SURGICAL EXPERIENCE OF BURULI ULCER

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SUMMARY

Buruli ulcer is a chronic skin ulcer caused by the organism Mycobacterium ulcerans. In the paediatric surgical practice at the Korle-Bu Teaching Hospital, 15 patients with confirmed Buruli ulcers aged from 3 to 10 years were seen and treated over the period 1989-1991. Diagnosis was by biopsy which was positive in all cases in which it was done. Surgery by wide excision was the mainstay of treatment. Skin grafting was done in 3 cases. Length of hospital stay was in excess of 2 months. There were no deaths in the group presented, however, residual deformity occurred in all cases. The experience of these cases is presented here with a review of the literature.

INTRODUCTION

Buruli ulcer is a chronic infection of the subcutaneous fat leading to the formation of a chronic indolent ulcer. The causative organism is Mycobacterium ulcerans, an atypical Mycobacterium which is a free living saprophyte, growing best at a temperature of 32-33°C and very difficult to grow in the laboratory.

The mode of transmission of the infection is not precisely known. However, all the reported cases have one thing in common: the disease usually occurs in isolated clusters in riverine areas and swamps in tropical and subtropical regions of the world.

Mycobacterium ulcerans causes its pathological effects by the production of a toxin which causes coagulation necrosis of the dermis, panniculus and deep fascia with destruction of nerves and blood vessels. In active lesions there are few inflammatory cells probably due to the local immunosuppression produced by the toxin.

As optimum temperature for growth in humans is 35°C, the infection is usually confined to tissues superficial to the deep fascia and in the periphery where body temperatures are cooler. Various drugs including Clofazimine, Co-trimoxazole and Rifampicin have been reported effective in the management of the disease.

The disease is gradually becoming well known in Ghana. In our paediatric surgical practice at Korle-Bu Teaching Hospital, 15 patients with Buruli ulcers have been seen and treated over the period 1989-1991. The experience with ten of these cases is presented.
MATERIALS AND METHODS

Records of paediatric in-patients with the diagnosis of Buruli ulcer from January 1989 to December 1991 were analysed. The total number of Buruli ulcer cases seen over the period was 15, however, only 10 folders could be traced.

On admission, a full history was taken including a social history, geographic travel and the socio-economic status of the patients. A full physical examination was done noting the presence or absence of anaemia, septicaemia, lymphadenopathy, sites and size of the lesion, and the presence of other disabilities.

A full haematological screen, bacteriological swabs of all sites of the lesion for microscopy and culture were taken. Biopsies were taken from the edges and base of the lesion for histology.

The lesions were thoroughly debrided to remove all abnormal looking and necrotic tissue, and were then dressed with Povidone-iodine dressings on a daily or alternate day basis. Antibiotics were given according to sensitivity results in addition to the routine antituberculous drugs: Rifampicin, Isoniazid and initially Streptomycin in various combinations. Skin grafting was done where indicated, when the wound was granulating healthily and all signs of infection were absent. Physiotherapy was also commenced as soon as practicable to prevent contractures.

RESULTS

There were 15 cases of Buruli ulcer seen in the Paediatric Surgical Unit between 1989-91. However, the full records were only available for 10 cases (See Table 1).

The mean age of the patients was 6.9 ±0.5 years (range 3 to 10 years). There were 6 females and 4 males. Nine patients had lesions of the limbs, with the upper limb being involved in 8. One patient presented with her ulcer on the lumbar region. This patient was the only who presented early with an indurated lesion on the lumbar area of his trunk. All the other 9 cases presented late with ulcers in various stages of development. The ulcers varied in size from 3cm in diameter in two cases to very extensive ulceration involving the whole of the left thigh and leg in one case (case no. 3).

Table 1: Case Reports of Buruli Ulcer in Paediatric Patients at Korle-Bu Teaching Hospital, 1989-91

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (Yrs)</th>
<th>Sex (M/F)</th>
<th>Duration in Hospital</th>
<th>Location of Ulcer</th>
<th>Histology</th>
<th>Microbiology (AFB Seen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>F</td>
<td>2/12</td>
<td>Lumber Region</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>F</td>
<td>4/12</td>
<td>Rt Upper Limb</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>F</td>
<td>16/12</td>
<td>Lt Leg &amp; Thigh</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>M</td>
<td>4/12</td>
<td>Rt Arm</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>F</td>
<td>8/12</td>
<td>Lt Forearm &amp; Hand</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>F</td>
<td>8/12</td>
<td>Lt Forearm &amp; Hand</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td>M</td>
<td>4/12</td>
<td>Lt Forearm &amp; Hand</td>
<td>Nil</td>
<td>Negative</td>
</tr>
<tr>
<td>8</td>
<td>6.5</td>
<td>M</td>
<td>3/12</td>
<td>Lt Forearm &amp; Hand</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>M</td>
<td>2/12</td>
<td>Lt Forearm &amp; Hand</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>F</td>
<td>5/12</td>
<td>Lt Forearm &amp; Hand</td>
<td>Positive</td>
<td>Negative</td>
</tr>
</tbody>
</table>

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The length of the history given by our patients varied from 2 weeks to 6 months. The shorter period was given by the patient whose initial presentation was of a tender swelling which was initially diagnosed as pyomyositis.

Four patients presented very ill and with fever with temperatures between 38°C and 39°C as a result of secondary infection. The other patients looked quite healthy and well on admission. One patient presented in a rather advanced stage of the disease with a long history of an extensive ulcer of the volar aspect of the left forearm and contracture of the right elbow and wrist joint (Figure 1).

Generally on admission, the ulcers were very dirty, had undermined edges and a floor covered with necrotic tissue and varying degrees of induration of the base of the ulcer. Four out of 8 (50%) smears from wound swabs taken from the ulcer bases were positive for AFB. In contrast, all seven biopsies that were sent for histology were reported positive for AFB’s. In three patients, who presented with characteristic ulcer, no records could be found of any biopsy result. The diagnosis of Buruli ulcer was therefore made on both clinical and histological grounds in 7 patients and on clinical grounds alone in 3 patients.

Culture of wound swabs isolated Staphylococcus epidermidis as the commonest super-added bacterial infection (9 out of 10 cases); other organisms were Staphylococcus aureus (2 cases), Pseudomonas aeruginosa (2 cases), Coliform (1 case), and Proteus (1 case).

Wide excision of the ulcer was performed in all patients. However, the extent of the lesion necessitated skin grafting within 4 weeks of excision in 3 patients (Table 2). In addition to wound excision patients were given Rifampicin, Isoniazid, Streptomycin which were the available anti-tuberculous drugs at the time. It was found that therapy with Rifampicin and Isoniazid, in addition to surgery, produced satisfactory healing (Table 2). The minimum hospital stay was 2 months and the longest was 16 months; mean hospital stay was 5.6 months. All the patients with lesions on the limbs in our experience suffered cosmetic and functional disfigurement, with varying degrees of shortening and contracture.

In 7 out of the 10 cases there was documented evidence of a visible BCG vaccination scar. Five of the patients were from an area where there was a river source but five patients were from urban Accra and had lived there all their lives.

**Figure 1: Extensive Ulceration of Left Forearm**
Table 2: Treatment and Outcome

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Surgery Performed</th>
<th>Chemotherapy</th>
<th>Duration of Treatment</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Wide Excision</td>
<td>S + INAH then R + INAH</td>
<td>5 months</td>
<td>Healed</td>
</tr>
<tr>
<td>2</td>
<td>Wide Excision</td>
<td>S + INAH</td>
<td>9 months</td>
<td>Healed</td>
</tr>
<tr>
<td>3</td>
<td>Wide Excision + Skin Graft</td>
<td>S + INAH then R + Septrin</td>
<td>19 months</td>
<td>Healed</td>
</tr>
<tr>
<td>4</td>
<td>Wide Excision + Skin Graft</td>
<td>R + INAH + Septrin</td>
<td>9 months</td>
<td>Healed</td>
</tr>
<tr>
<td>5</td>
<td>Wide Excision + Skin Graft</td>
<td>S + INAH then R + INAH</td>
<td>11 months</td>
<td>Healed</td>
</tr>
<tr>
<td>6</td>
<td>Wide Excision</td>
<td>R + INAH</td>
<td>12 months</td>
<td>Healed</td>
</tr>
<tr>
<td>7</td>
<td>Wide Excision</td>
<td>R + INAH</td>
<td>7 months</td>
<td>Healed</td>
</tr>
<tr>
<td>8</td>
<td>Wide Excision</td>
<td>R + INAH</td>
<td>7 months</td>
<td>Healed</td>
</tr>
<tr>
<td>9</td>
<td>Wide Excision</td>
<td>R + INAH</td>
<td>6 months</td>
<td>Healed</td>
</tr>
<tr>
<td>10</td>
<td>Wide Excision</td>
<td>R + INAH</td>
<td>9 months</td>
<td>Healed</td>
</tr>
</tbody>
</table>

*R = Rifampicin  INAH = Isoniazid  S = Streptomycin  Septrin = Co-trimoxazole*

**DISCUSSION**

The exact incidence of Buruli ulcer in Ghana is not known, but certain known foci exist in the Ga-rural districts around Accra, and Agroyesum area and the Afram valley in the Ashanti region. Five of our patients were from the same village near Amasaman in the Ga-rural district and presented within 2 weeks of each other. This village is on a tributary of the river Densu. Bayley, in 1971, reported on a single paediatric case seen in Korie Bu. She also reported three other probable cases who were all living along tributaries of river Densu. It would therefore seem that there has been a focus of infection along tributaries of river Densu for at least twenty years.

The peak incidence of our cases was in the age group 5-10 years which was similar to that reported in the literature. Our cases were 10 years and below, with the youngest being 2 years old (Table 1). It must be noted that since our unit only deals with paediatric cases (< 12 years) our age range is highly biased.

In general the patients were well nourished and in good health, this is generally true for most cases in the literature except the few with septicemia secondary to bacterial infection of the ulcers. All our cases were from a low socio-economic group. However, we believed that this was incidental as the disease is known to affect all socio-economic groups and all races.

One of our patients (Case 1) had the ulcer on the lumbar area. The distribution of the lesions on the body has been reported to be related also to the sex and age of the patients. In this series 9 out of the 10 patients had the lesion on the upper limbs. There were three times as many lesions on the right upper limb as on the left. The significance of this is not known. It may, however, be related to the handedness of the patients, as the majority in any population are right handed and are more prone to injury on that hand. However, it is to be noted that the two who had left sided upper limb lesions were female. The only patient who had a lower limb lesion initially presented as pyomyositis which in our experience is an important differential diagnosis of infected Buruli ulcer. It was not clear whether in her
case the organism had been introduced by traditional scarification.

Our experience contrasts with the findings of the Ugandan group where in about half of their cases, the lesions occurred on the leg and only a third on the arms. This may be because of the smaller numbers involved in our series and/or the differences in the age distribution of our series and those reported from Uganda. The Ugandan experience is that in children less than five years old the lesion may occur almost anywhere except on the scalp, palms or soles of the feet. As the children get older, the head and trunk are less affected and the limb lesions become more frequent. Above the age of 10 years, the lesions are more frequent on the lower limbs than the upper limbs in males but equally distributed in females.

Although the infection is usually confined to the superficial tissues, it is our experience that uncontrolled infection can extend beyond the deep fascia to bone as occurred in two of our cases. Bone and muscle were rarely involved in the Ugandan experience. In our series, the onset of secondary infection usually signalled spread to muscle although bone was not invariably involved. Fat necrosis, calcification and undermining of the skin can occur to produce an indolent ulcer. There may be a tendency to spontaneous healing and, occasionally, healing may occur at one end whilst active disease progresses at another, as was our experience in the case which presented with contracture. It has been reported in some instances that bridges of surviving skin can cross an ulcer but this was not our experience.

Our finding that smears of material taken from the ulcer base with a wound swab were positive for acid-fast bacilli (AFB) in only 50% of cases were similar to those previously reported in the literature. A negative smear result does not therefore exclude the diagnosis. Wound swabs are, however, useful in indicating superadded infection and should always be performed.

In our experience, as in others, histopathology always confirmed the diagnosis with the characteristic appearance in the subcutaneous tissues of spreading necrosis with mild inflammatory reaction but surrounded by chronic inflammation sometimes with giant cell granulomas. Caseous necrosis was never seen. A striking feature is the lack of a local inflammatory reaction in the early necrotic state of the disease. Large clusters of acid-fast Mycobacterium ulcerans were usually found in the necrotic tissue at the base of the ulcer towards the edge of the lesion under the skin margin. The location of the mycobacteria in the necrotic tissue makes it imperative that a biopsy of the ulcer should include necrotic tissue at the base and/or under the skin margins. If this is not done, as most surgeons are most likely to take a biopsy from the skin margins, the diagnosis may be missed.

X-ray of the affected area may show specks of calcification beneath the ulcers. Other investigations do not aid in diagnosis.

Our patients were treated by wide excision of the lesion to remove all necrotic tissue. Indeed, at the moment, this is the most effective treatment of the disease. This encourages and speeds up healing and reduces, if not removes, the mycobacteria load. The literature suggests that if the lesion is small and without ulceration the defect can be primarily sutured after excision of all abnormal tissues. This is now our preferred practice in cases that present early. Furthermore, our experience indicates that wide excision is needed because of the undermining nature of the ulcer as the over lying skin may look healthy, despite extensive underlying tissue destruction. Indeed, the ulcers are usually more extensive than the preoperative assessment suggests and a probe may extend several centimetres beyond the apparent ulcer margin.
Skin grafting is an essential adjunct when the wound is clean and the disease has been controlled by chemotherapeutic agents as determined by healing and healthy granulation at the periphery of the ulcer and lessening of surrounding induration. This is usually possible four or more weeks after the excision. The three patients who needed skin grafting had extensive lesions which would not have healed without the graft. In the other 10 patients, the wounds healed without grafting after the initial infection was controlled.

Reports of experience with chemotherapy are scanty and not encouraging. Drug sensitivity testing of the organism has not been extensively reported, especially with modern drugs. However, the mainstay of chemotherapeutic treatment is the anti-tuberculous agents. The organism has been shown to be partially resistant to Isoniazid, PAS and to Streptomycin. Various combinations of Rifampicin, Ethambutol, and Clofazimine (Lamprone) have been used in various centres. However, no one drug combination has been determined as it has been for tuberculosis. In Accra, we have found that Rifampicin and Isoniazid with or without Streptomycin were effective (Table 2). Based on our experience as reported, our drug treatment now comprises of Rifampicin and a fixed combination of Isoniazid and Thiacetazone (the "Blue tablet") which are the anti-tuberculous drugs in use in our hospital at the time of study.

As most wounds in Accra have multiple infecting organisms, specific antimicrobial agents, indicated by microbiological sensitivity tests were added to the anti-tuberculous agents. The duration of treatment has not been determined. Our practice is to continue anti-tuberculous treatment until three months after complete wound healing. Follow up to check on recurrence is important. There has not been any recurrence in our cases during the period of review.

Other treatment modalities have been tried. Workers in Nigeria have found heat treatment using short wave diathermy to be an effective adjunct to management in early cases. We are yet to try out this mode of treatment as most of our patients presented late.

Since the mode of transmission and spread of the disease is not known, its prevention and eradication is besieged with difficulties. The Ugandan Buruli Group were able to conclude that BCG immunisation offered some small and temporary protection to groups at risk, but our experience has not borne this out as seven of our patients had had BCG vaccination. Recent work has confirmed that BCG immunisation has some protective effect but that this is temporal and lasts only for less than 6 months.

CONCLUSION

Buruli ulcer is a disease with minimal mortality rate but a very high morbidity rate. The average length of stay in hospital was 5.5 months with a range of 2 to 16 months in this series. The disfigurement produced may not be fully amenable to surgery due to the extreme destruction of the subcutaneous tissues and the close proximity of vital blood vessels and nerves. Early recognition and treatment is needed to prevent the severe disfigurement and disability that may occur.

In view of the economic constraints on our continent, this disease poses enormous strain on our health resources and a high index of suspicion needs to be maintained by all health professionals in order that new cases are diagnosed early and management commenced as soon as possible. Doubtless further cases will be discovered in the future from riverine areas in the country. The evidence for protection afforded by BCG immunisation of the affected population ought to be looked at more closely in our environment should an epidemic occur. Consider-
able research needs to be carried out in Ghana to provide answers to all questions that this disease poses.

REFERENCES


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