Mucocutaneous buruli ulcer disease (caused by infection

Literature, Russian Literature

MUCOCUTANEOUSMYCOBACTERIOSIS : A SURPRISING PRESENTATIONAbstractBuruliulcer disease (caused by infection with Mycobacterium ulcerans) is the thirdmost common mycobacterial disease in immunocompetent people. Mycobacteriumulcerans belongs to large group of environmental mycobacteria. Individual ofall ages are affected, but children 15 years of age or younger constitute about75% of all cases. Spectrum of clinical disease includes nodules, plaques, edema, characteristics skin ulcers, sometimes massive osteomyelitis. We hereby reporta case of a 38 year old man presenting with edematous and plaque like lesionsof the nose since one year followed by pus discharging sinuses in the axillaryregion and was investigated on the lines of hidradenitis suppurativa andtuberculosis.

Biopsy was taken from the axillary region; histopathology ofexcision biopsy revealed suppurative granulomatous inflammation but negativefor Acid-fast bacilli. Conclusive diagnosis was made only when smears from pusdischarge, scrapes were found to be highly positive for AFB, later confirmed byculture to be of mycobacterium ulcerans. IntroductionThecommon mucocutaneous mycobacterial infections presenting with ulceronodular lesionsare tuberculosis, leprae, mycobacterial ulcerans and others.

After tuberculosis and leprosy, Buruli ulcerdisease (caused by infection with Mycobacterium ulcerans) is the third mostcommon mycobacterial disease in immunocompetent people. 1 Mycobacteriumulcerans belongs to large group of environmental mycobacteria. It is an acid-fast bacillus (AFB) with anoptimal growth temperature of 320C on routine microbiological media. 2In

contrast to tuberculosis & leprosy, BU is related to environmentalfactors & thus considered non-communicable. M.

ulcerans infection survivesbest under low oxygen tensions, such as exists in mud in the bottom of swamps. Although the ultimate source of M. ulcerans remains obscure, the organism hasbeen found in aquatic insects such as water bugs, firefly larvae & beetlesin stagnant water of West Africa.

3 Individual of all ages are affected, but children 15 years of age or younger constitute about 75% of all cases. 4Today, BU is recognized as a spectrum of clinical disease that includes nodules, plaques, edemas, characteristics skin ulcers, sometimes massive osteomyelitis. 5There is evidence that the disease may bypass the nodular stages anddisseminate contiguously in the skin. Such lesions are usually advanced whendetected & require extensive excision & skin grafting, often leading tocosmetic disfigurement & disabling complication. 2Keywords – mucocutaneousmycobacteriosis, buruli ulcer, atypical mycobacteriaCASEREPORTWe hereby report a caseof a 38 year old man presenting with edematous and plaque like lesions of the nosesince one year for which the patient was diagnosed as a case of rhinophyma(Fig. 1). After another year, he developed pus discharging sinuses in theaxillary region and was investigated on the lines of hidradenitis suppurativaand tuberculosis. Biopsy was taken from the axillary region; histopathology ofexcision biopsy revealed suppurative granulomatous inflammation but negativefor Acid-fast bacilli (Fig 3).

The patient was further evaluated fortuberculosis but there was no evidence of any other lesion elsewhere (lungs, bones, lymph nodes) on clinico-imaging investigations. In the mean time, theswelling of nose had spread to the adjoining face with development of ulceratedlesions on the mucosal surface of the nose and developed ulcerative lesions ininguinal and genital region as well (Fig 2). In view of suppurative granulomasseen on the biopsy, antitubercular treatment was started. Induction ofanti-tubercular therapy resulted in hepatitis like syndrome with icterus, jaundice, raised serum transaminases within 3 weeks leading to discontinuationof therapy. Repeated pus and blood cultures (BACTEC) were found to be negativefor acid fast bacilli (AFB).

Mantouxtest was 11 mm after 72 hours. Review of earlier biopsies with further sectionsconfirmed the previous findings. Patient was then asked to prepare scrapesmears from the ulcerated nasal lesions. To our surprise, smears from pusdischarge, scrapes, Fine needle aspiration cytology (FNAC) smears from all thesites were heavily positive for AFB (1% H2SO4) with suppuration and collectionof epithelioid cells in FNAC smears (Fig.

4). Tubercular serology (ELISA)revealed IgG-664(control> 225-positive) and IgM-1. 0(control> 1. 0-positive).

In the mean time, Pus DNA-PCR turned out to be positive for Mycobacteriumtuberculosis complex. The culture for AFB came positive at 32? C. DISCUSSION In 1948, MacCallum inAustralia was the first to isolate the etiologic agent of BU in culture frompatients. MacCallum & colleagues

provisionally named this mycobacterium asBairnsdale bacillus, after the region where five of the six patients lived. Itwas subsequently renamed Mycobacterium ulcerans.

6Despitethe increased interest in BU, the disease remained largely ignored by many nationalpublic health programs for decades. In 1988 the World Health Organization (WHO)recognized BU as an emerging health problem, primarily due to its frequentdisabling & stigmatizing complications. 7Thedisease is endemic in rural wetlands of tropical countries of Africa's, theAmericas, and Asia & Australia but remains uncommon in non-Africancountries. 8 In India there has beenno reported case of buruli ulcer so far to the best of ourknowledge. Buruli ulceris rarely, ever, contagious. Humans become infected by traumatic introductionof M. ulcerans into skin from the overlying M-ulcerans –contaminated surface.

M. ulcerans has an optimal growth temperature at about 32oC, but it'sunique among mycobacteria because it produces a family of toxic macrolides, themycolactones, that are required for virulence. In thenatural history of the disease, it has been observed that following traumaticinoculation, active infection develops & causes the various manifestationsof buruli ulcer. After a few weeks or several months of active infection, progressivenecrosis of the dermis usually leads to degeneration of the epidermis &ultimate ulceration. A necrotic slough develops in the base of the ulcer &the surrounding skin is undermined, indurated, and hyperpigmented. Ulcers ofteninvolve massive areas of skin. 9, 10, 11The infection in most instances presents as a painless lump justunder the skin.

The infection is mostly on the limbs, most often on exposedareas, but not on the hands or feet. In children, all areas may be involved, including the face or abdomen. A more severe form of infection produces diffuseswelling of a limb, which, unlike the papule or nodule, can be painful andaccompanied by fever. Inthe present case studied, clinically, patient presented with rhinophyma and perianalulceronodular lesions and within a span of two and half years there wasdisseminated disease with plaques, nodules and ulceronodular lesions in theperianal region, axilla & thighs. Initially BUpresents as a nonulcerative lesion and can eventually evolve to ulcerativelesions. In both types of lesion, the histopathologic sections show prominentacellular areas of tissue necrosis with variable numbers of bacilli, usuallyextracellular. Areas of inflammatory infiltrates are also seen withintracellular M.

ulcerans infection. Connor & Lunn in 1966 developed ahistopathologic classification of the disease involving 3 stages –active, organizing(granulomatous) & healing. The active stage has the most striking anddiagnostics features, ie, contiguous coagulation necrosis of the lower dermis& subcutaneous fat with much acid fast bacilli. The organizing stage isseen in longstanding lesion, and is characterized by formation of granulomas. Healing is characterized with formation of granuloma. Our biopsy was mainly inactive stage. For laboratory diagnosis, four methodscurrently in use include 1) direct smear examination for AFB by ZN or auraminestain, 2) in vitro culture 3) IS2404 PCR and 4) histopathologic

examination. 5The most frequently available diagnostic technique is direct smear examination.

In endemic areas culture and histopathology are not easily available. PCR can only be performed in well-equippedlaboratories. In this case smears from pus discharge, scrapes, FNACs from allsites were heavily positive for AFB (1% H_2SO_4). FNAC smears showed suppuration& collection of epithelioid cells. Repeated pus and blood cultures werenegative initially but came positive under strict temperature of 32°C. and other culture requirements Similar toMycobacteriumtuberculosis, M. ulceransis a member of the slow-growing group of mycobacteria. However, M.

ulceransis considered extremelyslow-growing as cultures must be incubated for 6 to 8 weeks (or longer) underappropriate laboratory conditions prior to forming distinct colonies. M. ulcerans grows optimally onmycobacteriological media (e.

g., Löwenstein-Jensen medium, Middlebrook 7H10medium, etc.) under the same. Samples analyzed within 24 h are preferentiallykept at 4°C in a sterile vial without additive. For longer transportationtimes, tissue samples should be introduced into a transport medium: Middlebrook7H9 broth supplemented with polymyxin B, amphotericin B, nalidixic acid, trimethoprim, and azlocillin (Becton Dickinson, Sparks, MD); oleic acid, albumin, dextrose, and catalase (Difco Laboratories, Detroit, MI); and 0.

5%agar, also named semisolid transport medium (STM). This medium has beenrecommended for use, since specimens kept in it for up to 21 days were

stillculture positive. 11 Primary cultures from clinical specimens areusually positive within 6 to 12 weeks of incubation at 29 to 33°C, althoughmuch longer incubation times of up to 9 months have been observed. 12Excisedbiopsy from perianal region and axilla showed suppurative granulomatousinflammation. The common differential diagnosis of pre-ulcerative lesions(plaques & edematous lesion) is pyogenic cellulitis.

A short trial oftreatment with antimicrobial therapy may be considered until a diagnosis ofburuli ulcer is made. Treatment options for BU include antibiotics &surgical intervention. The choice of treatment usually based on the morphologyand extent of the lesions, as well as availability of antibiotics &surgical facilities. Physiotherapy is imperative for all BU patients.