expiratory reserve volume, and chest wall compliance are often reduced by obesity, and a change from sitting to the supine position may further reduce them.⁶⁻⁷ Nevertheless, the fall in oxygen saturation—which occurs predominantly during rapid eye movement sleep—is significantly greater in those women with abnormal prolactin secretion (non-responders). This group of women cannot be distinguished from responders by weight, body mass index, age, or physical characteristics. We and others⁸⁻⁹ have suggested that the alterations of prolactin secretion in obesity may result from a disorder of hypothalamic function rather than as an effect of prolactin itself on fat metabolism. Our present findings are further evidence for a disturbance of central nervous function in such women.

Prolactin secretion fluctuates during sleep: the highest plasma concentrations are seen during non-rapid eye movement sleep, whereas the lowest concentrations are associated with rapid eye movement sleep.¹⁰ Respiratory drive is also altered by the stage of sleep and may be reduced during rapid eye movement sleep with a concomitant small decrease in oxygen saturation.¹¹ There is evidence that prolactin secretion is predominantly under the inhibitory control of hypothalamic dopaminergic mechanisms,¹² but there are also stimulatory serotonergic mechanisms.¹³ Furthermore, dopaminergic pathways appear to be important for rapid eye movement sleep and serotonergic pathways for non-rapid eye movement sleep.¹⁴ We may only speculate that these two central nervous mediators are also implicated in the control of respiration.

We conclude that a decrease in oxygen saturation (but not apnoeic episodes) occurs in premenopausal obese women during sleep. Those women with abnormal prolactin secretion show a significantly greater fall in oxygen saturation. This is evidence for central as well as mechanical factors in the genesis of the nocturnal hypoxia and supports the hypothesis for a central disturbance in obesity.

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Disseminated candidiasis: evidence of a distinctive syndrome in heroin abusers

PETER J COLLIGNON, TANIA C SORRELL

Abstract

Seven young men developed similar manifestations of disseminated candidiasis after a single episode of intravenous heroin abuse. Sequential development of lesions of the eye, skin, and bone or costal cartilage was noted within 10 days after injection. Skin lesions were confined to the scalp and other hair bearing areas. *Candida albicans* was cultured readily from affected skin and

costal cartilage. Histological examination of scalp biopsy specimens showed infiltration of hair follicles with chronic inflammatory cells and *C albicans*. Pseudo-hyphae of *C albicans* were also identified in and around hair shafts. The skin, skeletal, and small eye lesions resolved on systemic treatment with 1 g amphotericin B plus flucytosine. Pars plana vitrectomy plus local instillation of amphotericin B cured progressive chorioretinitis.

These features may represent a distinctive syndrome of disseminated candidiasis in heroin abusers. Systemic antifungal treatment is curative in most cases.

Introduction

After intravenous heroin abuse seven young men presented with disseminated candidiasis affecting several organs. Characteristic skin and eye lesions, and frequent inflammation of

Infectious Disease Medicine, Westmead Hospital, Westmead, New South Wales 2145, Australia

PETER J COLLIGNON, MB, BS, senior registrar

TANIA C SORRELL, MD, FRACP, head (also senior lecturer in medicine, University of Sydney)

Correspondence to: Dr T C Sorrell, Department of Medicine, Westmead Hospital, Westmead, NSW 2145, Australia.

cartilage or bone, are features that have been noted only rarely in previous reports.^{1 2}

Case reports

Nine young men injected themselves with the same heroin on the night of 26 August 1982. Two of the men boiled the heroin preparation before injection; they remained well. Characteristic multiple pustular scalp lesions and subcutaneous nodules associated with hair follicles developed in the seven other patients three to seven days later; pustules were also noted in the beard area in four (fig 1) and in the pubic and axillary hair bearing areas in three. Six had enlarged occipital nodes. *Candida albicans* was cultured from multiple skin lesions in all cases.

Indirect haemagglutination antibody titres against *C. albicans* ranged from 1/1280 to 1/10 240. Four patients noted transient jaundice three to seven days after injection; all seven patients had raised liver enzyme activities at presentation, but serum bilirubin concentrations remained normal. Repeated cultures of blood and urine yielded negative results.

Localised pain and tenderness in bone or over costal cartilage was noted seven to 10 days after injection by five patients. Inflammation of the vertebral column, ribs, or acetabular region was confirmed by technetium bone scans in four, and *C. albicans* was cultured from costal cartilage in the fifth patient. The eye was affected in all cases: two patients had episcleritis and five chorioretinitis, with symptoms beginning three to seven days after injection. Two of the seven patients underwent pars plana vitrectomy and local instillation of amphotericin B (5 µg) after progression of chorioretinal lesions despite systemic treatment.

Treatment with amphotericin B and flucytosine was started in six patients. Five patients received 1 g amphotericin B, and their skin, musculoskeletal, and small eye lesions resolved. One patient, who discharged himself after receiving 300 mg amphotericin B, returned five weeks later with persisting costochondral infection. The seventh patient had only mild folliculitis, and eye examination showed occasional cells in the vitreous humour. These lesions resolved spontaneously.

Discussion

Our patients had a distinctive syndrome of hepatitis followed by eye lesions, skin lesions, osteomyelitis, and costochondritis due to *C. albicans*. The symptoms became evident within 10 days after intravenous injection of heroin. This syndrome has not been reported previously, although in a recent report on antifungal treatment, reference was made to 34 heroin abusers with disseminated candidiasis of the skin (32 cases), eyes (21), bone or joints (seven), and costal cartilage (one).³

FIG 1—Characteristic pustules in beard areas of neck. The skin surrounding the pustules is erythematous.

FIG 2—Scalp biopsy specimen of characteristic skin lesions. Pseudohyphae of *C. albicans* are seen invading the hair shaft at the orifice of an inflamed hair follicle. Organisms are stained black. Periodic acid-Schiff preparation $\times 103$.

The occurrence of macronodular lesions in the scalp associated with regional lymphadenopathy, and folliculitis, may be a unique feature of disseminated candidiasis in heroin abusers. Invasion of hair follicles and hair shafts by pseudohyphae of *C. albicans* was noted in scalp biopsy specimens in our cases (fig 2) and by Drouhet *et al.*³ Macronodular skin lesions, not affecting hair bearing areas, have been noted only in severely immunocompromised patients.⁴

Osteomyelitis is a well documented manifestation of disseminated candidiasis⁴; haematogenous candida costochondritis, however, has been reported rarely.² Costochondritis was diagnosed in four of our patients.

Optimal regimens of antifungal treatment in disseminated candidiasis have not been defined. Small metastatic lesions may resolve spontaneously, as in one of our cases. Courses of up to 2 g amphotericin B have been recommended for deep seated infection.⁴ Cure was achieved with 1 g amphotericin B plus flucytosine in five of our cases. Extension of chorioretinal lesions into the vitreous occurred during systemic treatment in two patients. Therapeutic vitrectomy plus intravitreal instillation of amphotericin B was curative in both. The therapeutic value of intravitreal amphotericin B remains controversial owing to potential retinal toxicity.⁵

Further studies are required to determine the role of amphotericin B and less toxic drugs such as ketoconazole in the management of this syndrome. Ketoconazole has failed to be effective in candida endophthalmitis and chondroarticular infection,³ which suggests that amphotericin B will remain the agent of choice.

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