Disseminated *Candida* infection syndrome in heroin addicts—dominance of a single *Candida albicans* biotype

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Summary. Among 21 intravenous heroin abusers with cutaneous and ocular manifestations of disseminated *Candida* infection, a single *C. albicans* strain type (serotype A, biotype 15³/₇) was isolated from skin lesions in 14 cases. This suggests that central contamination of the heroin with *C. albicans* is less likely to be the source of infection than an endogenous source, and that one particular strain type is either better adapted than others to grow in the lemon juice used as a heroin solvent, or more likely than others to cause the specific pathology seen in these patients.

Introduction

There is now an extensive literature on a specific syndrome of disseminated *Candida* infections in heroin addicts. The infections are characterised by several features, of which chorioretinitis and follicular and nodular skin lesions are the most common, and associated in some instances with costochondral arthritis (Barthelemy *et al.*, 1981; Dally *et al.*, 1982; Mellinger *et al.*, 1982; Badillet *et al.*, 1983; Collignon and Sorrell, 1983; Dally *et al.*, 1983; Drouhet and Dupont, 1983; Hoy and Speed, 1983; Mackay, 1983; Tápies Barba *et al.*, 1983; Cuadra *et al.*, 1984; Dupont and Drouhet, 1985; Servant *et al.*, 1985). *C. albicans* has been isolated almost invariably from the cutaneous lesions, but rarely cultured from the blood or vitreous fluid. The sources of the fungus in these cases remain uncertain. Although some authors have suggested that *C. albicans* may contaminate brown (street) heroin (Mellinger *et al.*, 1982; Dally *et al.*, 1983), attempts to culture *C. albicans* from the heroin involved have been unsuccessful (Mellinger *et al.*, 1982; Dally *et al.*, 1983; Dupont and Drouhet, 1985; Servant *et al.*, 1985; Shankland *et al.*, 1986), and there is evidence that heroin inhibits the growth of *C. albicans* *in vitro* (Dupont and Drouhet, 1985; Servant *et al.*, 1985; Shankland *et al.*, 1986). The lemon juice used by addicts as a heroin solvent has frequently been postulated as a source (Hoy and Speed, 1983; Mackay, 1983; Newton-John *et al.*, 1984; Servant *et al.*, 1985; Shankland *et al.*, 1986), and Shankland *et al.* (1986) recovered *C. albicans*

from the juice in two plastic lemons submitted by addicts. Other postulated sources are use of unhygienic injection techniques (Barthelemy *et al.*, 1981; Badillet *et al.*, 1983) and the direct spread of *C. albicans* from the gut (Dupont and Drouhet, 1985).

So far, no attempt appears to have been made to establish which biotype or biotypes of *C. albicans* have been involved in the heroin-associated infections, yet if a single biotype was responsible for all the cases it would be strong evidence in support of a single central source of infection. We have therefore undertaken a survey of *C. albicans* biotypes from cutaneous lesions in 21 Spanish patients with heroin-associated *Candida* infections.

Patients and methods

Patients

The study group comprised 18 male and three female heroin abusers, aged 19–33, who had presented at clinics in Madrid or Valencia within the last 2 years. The patients had high fever (not noted in one case only) that within 2–7 days was followed by the development of skin changes. All the patients had nodular or follicular lesions, or both, affecting the scalp. Males frequently had a folliculitis of the beard area. In four cases there were nodular lesions in the pubic area, and one patient had follicular lesions on the neck, chest and arms. There were signs of *Candida* endophthalmitis in 7 of the 21 patients. Blood cultures for bacteria and fungi gave negative results in all 21 cases; however, all the patients yielded high numbers of *C. albicans* in cultures from the skin lesions.

C. albicans biotyping

The *C. albicans* isolates were biotyped according to the methods of Odds and Abbott (1980, 1983). The biotyping tests were repeated on three occasions to ensure consistency of results. From 16 of the patients a single isolate was tested; from the other five, isolates from at least two anatomical sites were tested.

A control group of 45 *C. albicans* isolates was obtained from the same Madrid clinic that was attended by 12 of the patients with the heroin-associated *Candida* infection. Clearly, these control isolates could not be obtained from lesions similar to those of the heroin addicts; 43 were from patients with *Candida* vulvovaginitis, one each from skin and nail lesions.

Results

Fourteen (67%) of the 21 patients with heroin-associated disease were infected with *C. albicans* biotype 15³/₇. The other seven were types 075, 135, 137, 175, 253, 557 and one indeterminate type. All the isolates were serotype A and all could use citrate as a carbon source. In the three cases where isolates were obtained from different anatomical sites, all the isolates were type 15³/₇. The prevalence of biotype 15³/₇, serotype A strains in the control isolates was 11.1% (5 out of 45). Thirteen (28.9%) of the control isolates were serotype B; these did not include any examples of biotype 15³/₇.

Discussion

These results indicate a greatly heightened prevalence of *C. albicans* biotype 15³/₇ in patients with heroin-associated *Candida* infection that may be accounted for in two ways. First, the source of the fungus could be the heroin itself or its acid solvent; second, type 15³/₇, serotype A, whatever its source, may have a higher predilection for causing infection than other biotypes of *C. albicans*. If the heroin were the source, it is difficult to understand why some of the isolates were not biotype 15³/₇. The idea of contamination of the lemon juice solvent, either for individuals injecting their heroin alone or for small groups sharing lemon

juice, is entirely compatible with our results and with the observations that *C. albicans* grows well in fresh lemon juice (Newton-John *et al.*, 1984) and can sometimes be recovered from lemon juice used by addicts (Shankland *et al.*, 1986). It is notable that all the isolates from the addicts gave positive results in the citrate biotyping test, indicating their ability to grow on citrate at a low pH value (Odds and Abbott, 1980).

C. albicans type 15³/₇ is closely related to a type (0₁5⁵/₇) previously found to be responsible for an outbreak of systemic *Candida* infection in a hospital intensive care unit and to possess an enhanced ability to adhere to epithelial cells (Burnie *et al.*, 1985). Its isolation in the majority of cases of the *Candida*-heroin addiction syndrome is, therefore, compatible with the possibility of endogenous infection of the addicts. *C. albicans* is a ubiquitous member of the normal human microflora, and it is evident from the control isolates in this study that type 15³/₇ is a common biotype amongst vaginal isolates. A previous survey showed that the frequencies of different *C. albicans* biotypes are similar regardless of their anatomical site of isolation, and that types 153 and 157 belong to the most numerous group of *C. albicans* biotypes (Odds *et al.*, 1983). The 11% prevalence of type 15³/₇ in vaginal isolates is, therefore, likely to indicate the normal prevalence of this type in other sites, including the gut—normally held to be the major human reservoir of *C. albicans*.

In the absence of prospectively gathered data concerning *Candida* colonisation of heroin addicts with and without the systemic *Candida* infection syndrome we conclude that candidaemia may be a common sequel to intravenous heroin usage, either directly or indirectly (via lemon juice) from a reservoir, presumably endogenous to the user(s) and that *C. albicans* serotype A, biotype 15³/₇ is more likely to be involved in invasive disease in addicts than are other strain types of the fungus.

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