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Medical Memoranda

Urinary Tract Infection with *Torulopsis glabrata* Treated by Alkalinization of Urine

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It has been known for many years that *Torulopsis glabrata* can be isolated from the urinary tracts of human beings (Lodder and Kreger-van Rij, 1952). It seems to be fairly common nowadays, since routine cultures in 100 women with infections of the urinary tract demonstrated *T. glabrata* in six cases (Guze and Haley, 1958). *T. glabrata* is an anascosporegenous yeast not forming pseudomycelia, which ferments and assimilates glucose but not galactose, sucrose, maltose, and lactose. However, little is known about the clinical and non-taxonomic microbiological characteristics of this yeast. Its pathogenicity has been doubted or considered limited, but more recently fatal infections have been described—for example, Minkowitz *et al.* (1963); Edebo *et al.* (in press).

During the course of a septicaemic infection blood cultures from the patient were inoculated on to blood and haematin agar and also into anaerobic blood culture flasks. Only weak growth of *T. glabrata* resulted; the colonies were so small and the broth so clear that the diagnosis was almost missed. However, close to a disk impregnated with terramycin the growth was more abundant (Edebo *et al.*, in press).

EXPERIMENTAL OBSERVATIONS

It was found possible to obtain larger yeast colonies on blood agar by the addition of a small amount of hydrochloric acid or acetic acid on to the inoculum streak. Where the drops fell, the colonies reached the same size as those grown on Sabouraud agar (pH=5.6).

The influence of pH on the growth *in vitro* of *T. glabrata* was further investigated in Sabouraud dextrose broth with different amounts of citric acid or sodium citrate added. Volumes of 50 ml. of broth with pH values ranging from 3.5 to 8.8 were added to each of a number of 250-ml. Erlenmeyer flasks provided with side tubes fitting a Coleman junior spectrophotometer. The flasks were inoculated to a concentration of 2.5×10^5 cells/ml. with each of four different isolations of *T. glabrata* from the patient described here, and with two isolations from a patient described earlier (Edebo *et al.*, in press). As a comparison one flask each of *Candida albicans* and *Torulopsis dattila* were inoculated to the same concentration of cells. After 16 hours at 37° C. the absorbance at 650 nm. and the pH were measured (Fig. 1).

The growth of *T. glabrata* at pH values above 6.4 was very scanty. However, when inoculated into flasks with moderately high pH (probably as a result of fermentation) the yeast succeeded in lowering the pH of the medium—for example, from 7.5 to 6.3, where full growth was observed. In one flask, where the initial pH was 8.8, the pH was reduced to 7.1 without conspicuous growth.

These experiments indicated that *T. glabrata* would grow well only in acid media—a property common to many non-

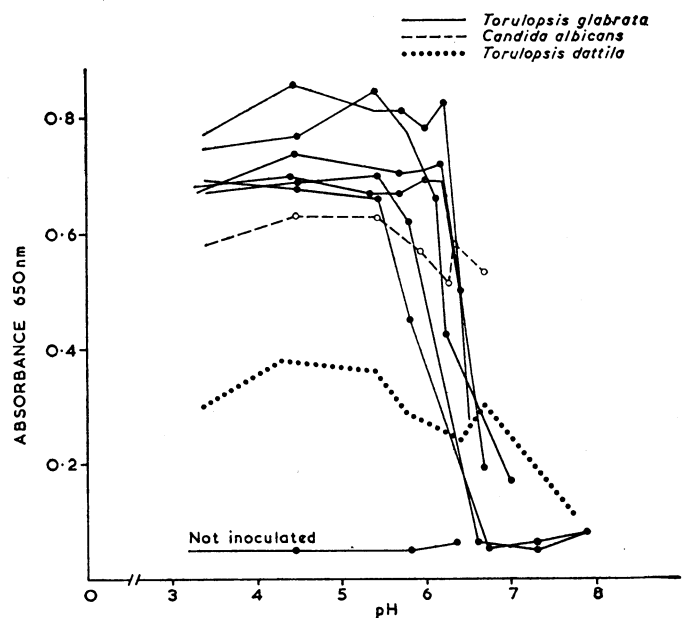


FIG. 1.—Different isolations of *Torulopsis glabrata*, *Candida albicans*, and *Torulopsis dattila* inoculated into Sabouraud broth with various pH. The growth and pH was recorded after 16 hours at 37° C. Since no growth of *T. dattila* could be observed then, those flasks were incubated for another 24 hours before reading off.

pathogenic yeasts (Morris, 1958). This feature suggested that unfavourable conditions for growth of the yeast could be obtained in the urinary tract by rendering the urine alkaline. *Candida albicans* grew well in all tubes, lowering the pH from 8.8 to 6.7. Similar results have been obtained with *C. albicans* on Czapek's medium (Johnson *et al.*, 1954).

CASE REPORT

A 78-year-old widow (526/1963) had a brother who had died of pulmonary tuberculosis, and a father and elder sister who had suffered from diabetes mellitus. Her previous medical history

included a gastric ulcer, proved radiologically in 1947, and diabetes, diagnosed in 1950. This latter was treated by diet alone until 1952, when she was transferred to insulin after a diabetic coma. Subsequent control was good.

After an acute attack of gastro-enteritis in the autumn of 1963 she suffered a left hemiplegia with partial recovery; this was complicated by a basal pneumonia, which resolved quickly with tetracycline. She was then transferred to Södertull Hospital for continued rehabilitation and responded well to ordinary physiotherapy.

Later the patient clinically developed a pyelocystitis with fever, chills, malaise, and bladder symptoms. Her urine turned milky-white and opaque, and cultures showed abundant growth of *Torulopsis glabrata*. At cystoscopy the mucous membrane of the bladder was intensively red, swollen, and covered with slime and pus; a biopsy from the bladder mucosa showed massive infiltration of the yeast, but repeated cultivation from pharynx, sputa, stools, and blood were negative. The concentration of yeast cells in the urine was followed by counting in a Buerker chamber; serum from the patient agglutinated the homologous strain at a dilution 1:80. The patient was given a 30% solution of sodium citrate which resulted in a change in the urinary pH from 4-5 to 6-8. The yeast disappeared completely in less than 14 days, and the disorder regressed concurrently (Fig. 2).

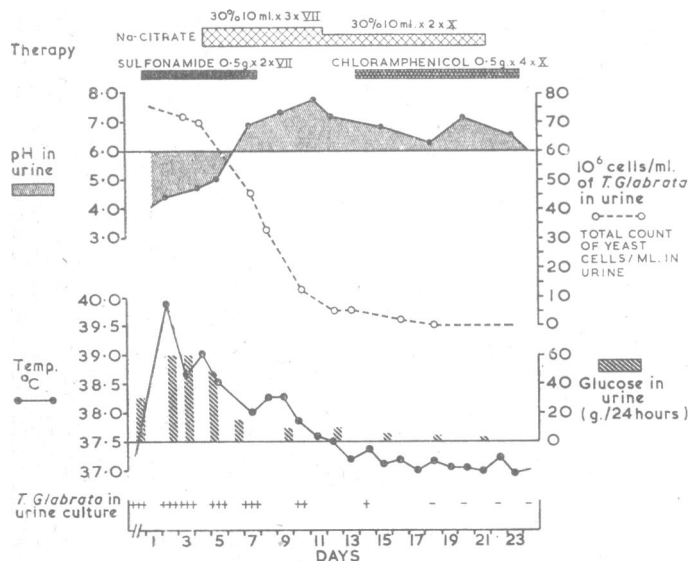


FIG. 2.—The clinical course, laboratory findings, and treatment of the patient describe.

Repeated urine cultures after this showed no growth of *T. glabrata*, but coliform bacilli and enterococci, which were finally cleared by chloramphenicol. Radiographs of the lungs and urinary tract were unremarkable. A cystoscopic examination was carried out just over three weeks after the start of the infection and revealed a practically normal condition. Apart from a temporary rise in blood urea and disturbance of her diabetic control during the acute phase of her illness, laboratory findings were normal. The infection did not relapse. A moderate iron-deficiency anaemia developed, but the patient was later placed in a home for aged people in good health.

DISCUSSION

Elderly women with diabetes in particular tend to suffer from this type of infection (Guze and Haley, 1958; Spetz, in press),

and the causative yeasts are often difficult to eradicate in the absence of effective and innocuous therapy.

It has been shown in this paper that *T. glabrata* grows only in acid media. If this yeast is inoculated into a moderately alkaline medium containing glucose it can, however, create conditions favourable for growth—probably by fermentation of the glucose. When the first urinary specimen from this patient arrived at the mycological laboratory and the rubber stopper was removed from the test tube the urine effervesced, presumably as a result of glucose fermentation by the yeast.

The fact that the patient was treated with tetracycline for a basal pneumonia shortly before the acute pyelocystitis occurred may have some relevance. It has been previously shown that the virulence of *Candida albicans* in mice is increased by the administration of aureomycin (Seligmann, 1952), and, further, it has been suggested that tetracycline might increase the virulence of *T. glabrata* by modifying the microflora, lowering host resistance, and changing the pH of the urine to the acid range (Pratt and Dufrenoy, 1953; Spetz, in press).

By giving the patient sodium citrate by mouth and by increasing the insulin dosage the urine was made alkaline (maximum pH=7.8) and practically free from glucose. Soon after this condition was attained the yeast cells disappeared from the urine, and they did not return when the treatment with sodium citrate was stopped. When the urine had been sterile for some days it was possible to reduce the insulin dosage, and, finally, after the patient had been transferred to a home for aged people, diabetic control was maintained satisfactorily by oral drugs.

It is difficult to establish whether the removal of glucose from the urine by diabetic control or the alkalization of the urine was more important for the successful cure of this patient, but since *T. glabrata* has also been isolated from the urinary tract of non-diabetic patients (Guze and Haley, 1958) the glucose does not seem to be necessary for the establishment of this yeast. *In vitro* experiments have shown that *T. glabrata* is able to acidify an alkaline glucose-containing medium, probably by fermentation of the sugar. It seems reasonable, therefore, to reduce both the glucose and hydrogen ion concentration of the urine in diabetic patients whose urinary tract is infected with this yeast.

L. EDEBO, M.D.
Å. SPETZ, M.D.

Institute of Bacteriology,
Uppsala and Södertull Hospital,
Gävle, Sweden.

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