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GRANULOMATOUS PROSTATITIS INDUCED BY CAPSULE-DEFICIENT CRYPTOCOCCAL INFECTION

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ABSTRACT

A 59-year-old man with prostatism, in otherwise good health, was treated with transurethral prostatectomy and ketoconazole. At microscopic examination of the prostatic tissue he had acute and chronic prostatitis with granulomatous lesions, in the center of which capsular-deficient cryptococcal organisms were demonstrated. The patient was well without evidence of systemic or local infection at 22 months. The differential diagnosis of granulomatous prostatitis is discussed. (*J. Urol., 143: 365–366, 1990*)

Cryptococcus neoformans, a worldwide fungal organism with a characteristic microscopically detectable capsule, usually involves the respiratory system and potentially is fatal when it occurs in the central nervous system. It can involve the prostate without systemic infection.[1,2] However, capsule deficient C. neoformans is considerably rarer and when present it usually causes disease localized to the lungs[3–6] or in a disseminated form.[7] We describe the sole presence of capsule deficient C. neoformans confined to the prostate and presenting clinically as prostatitis in an immune competent patient.

CASE REPORT

A 59-year-old afebrile Hispanic man was admitted to our medical center with urinary retention 2 days in duration. He was otherwise in good health. Vital signs were pulse 88 per minute, respirations 70 per minute and blood pressure 130/90. The bladder was palpated a third of the distance from the pubis to the xiphoid. Rectal examination revealed a bilaterally symmetrical enlarged prostate gland with midline sulcus present. No meningeal signs were present.

Complete blood count was unremarkable: hemoglobin was 10.7 gm./dl., and urinalysis revealed 6 to 8 white blood cells per high power field, 1+ proteinuria and 3+ hematuria. Urine cultures for bacteria and fungi times 3 were negative. Chest x-ray was negative. An excretory urogram subsequently showed the presence of a pelvic mass, which computerized tomography (CT) confirmed to be an enlarged prostate. Transurethral resection was performed.

The prostatic tissue showed chronic granulomatous prostatitis with fungal stain positivity for capsule deficient C. neoformans. In addition, the serum determination for cryptococcal antigen by latex fixation methodology was positive at 1:32.

Clinically, the disease was localized to the prostate, since a search for multiple organ involvement, including cranial CT, and liver and renal scans, was negative. He was judged to be immune competent on the basis of normal lymphocytic studies, including B cell number, T helper suppressor numbers and ratios, serum immunoglobulins, and a normal intradermal response to tetanus toxoid and Proteus antigen skin tests.

Ketoconazole at 400 mg. daily was instituted for 1 week postoperatively. The patient remained stable and was discharged from the hospital after an uneventful course. He remained active, healthy and without urinary symptoms 22 months after this episode.

Pathological findings. The prostatic chips showed extensive acute and chronic prostatitis with foci of centrally necrotic granulomatous lesions consisting of histiocytes, giant cells and lymphocytes (fig. 1). In the center of the granulomas Grocott's methenamine silver stain revealed spherical thin-walled yeast-like organisms measuring 4.0 to 8.0 μm. in diameter with occasional single thin-necked budding (fig. 2, *A*). The usual red appearance of the capsule after mucicarmine stains was absent.

FIG. 1. Granulomatous involvement of prostate gland (center) with characteristic giant cells and lymphocytes in glandular lumen. Reduced from ×115.

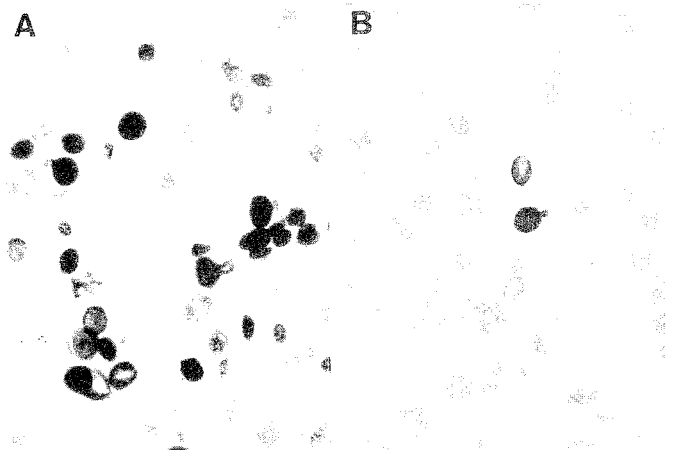

FIG. 2. Section of prostate shows scattered nonencapsulated cryptococci in granulomatous area. *A*, Grocott's methenamine silver. *B*, Fontana-Masson silver, reduced from ×1,287.

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The modified Fontana-Masson silver[8] stain revealed a dark brown to black color in the wall of the organism (fig. 2, *B*). For control, Pneumocystis carinii and Blastomyces dermatitidis were used and remained unstained. Taking into consideration the morphology of the organism, the tissue reaction, staining properties and serological positivity for cryptococcal antigen, cryptococcal prostatitis by capsule deficient C. neoformans was diagnosed.

COMMENTS

Whereas granulomatous prostatitis is a relatively frequent finding in prostatic tissue examined either at autopsy or as a surgical pathology specimen, 2 categories may be recognized: 1) idiopathic and 2) that of infectious etiology. In category 1 it has been postulated that prostatic secretions, spermatozoa, bacterial products or urine acting as foreign body agents may be responsible for the granulomatous response.[9-11] Category 2 includes infectious causes, such as actinomycosis, blastomyocosis, candidiasis, coccidioidomycosis, syphilis, tuberculosis and cryptococcosis,[12-16] which is a mycosis of worldwide distribution caused by C. neoformans. The source is presumed to be exogenous, since the organism is found in avian excreta and in the soil. The primary infection is believed to be in the lung but the organism has marked predilection for the brain and meninges. In some instances after a primary pulmonary infection spread may be limited to a few organs without central nervous system involvement. In these cases the disease usually takes a benign course. Rare cases of cryptococcal infections have been reported as involving the prostate without systemic infection. These cases have always occurred in a setting of a partly or fully immune compromised host.[1, 2]

Isolated cases of infection caused by the capsule-deficient form of cryptococcus have been described in the literature, including 4 cases of localized pulmonary infections[3-6] and 1 of disseminated disease.[7] We report a capsule deficient cryptococcal infection of the prostate in an otherwise healthy man.

In our patient a fungal culture of the prostatic tissue was negative. To classify further the Grocott's methenamine silver positive, mucicarmine negative fungus, we used the Fontana-Masson stain for melanin to identify the capsule deficient C. neoformans, which can be specific for the histological diagnosis of cryptococcal infection.[6, 17] This stain will detect pathogenic C. neoformans and C. laurentii, which is considered an occasional nonsystemic pathogen. B. dermatitides and Histoplasma capsulatum, which can be confused in tissue sections with C. neoformans, do not have melanin-like pigment in the capsules and, therefore, are negative for Fontana-Masson stain.

Our case illustrates 4 important clinical points: 1) a diagnosis of nonspecific granulomatous prostatitis should be made only after thorough investigation for possible etiological agents, 2) C. neoformans infections can occur in an immune competent individual, 3) C. neoformans can be localized to 1 organ without clinically apparent pulmonary lesions and 4) the diagnosis of capsule deficient C. neoformans depends on proper histological examination and thorough familiarity with special stain techniques.

REFERENCES

1. Hinchey, W. W. and Someren, A.: Cryptococcal prostatitis. Amer. J. Clin. Path., **75:** 257, 1981.
2. O'Connor, F. J., Foushee, J. H. S., Jr. and Cox, C. E.: Prostatic cryptococcosis: a case report. J. Urol., **94:** 160, 1965.
3. Farmer, S. G. and Komorowski, R. A.: Histologic response to capsule-deficient Cryptococcus neoformans. Arch. Path. Lab. Med., **96:** 383, 1973.
4. Gutierrez, F., Fu, Y. S. and Lurie, H.: Cryptococcosis histologically resembling histoplasmosis: a light and electron microscopic study. Arch. Path. Lab. Med., **99:** 347, 1975.
5. Harding, S. A., Scheld, W. M., Feldman, P. S. and Sande, M. A.: Pulmonary infection with capsule-deficient Cryptococcus neoformans. Virch. Arch. Path. Anat., **382:** 113, 1979.
6. Ro, J. Y., Lee, S. S. and Ayala, A.: Advantage of Fontana-Masson stain in capsule-deficient cryptococcal infection. Arch. Path. Lab. Med., **111:** 53, 1987.
7. Attal, H. C., Grover, S., Bansal, M. P., Chaubey, B. S. and Joglehar, V. K.: Capsule deficient Cryptococcus neoformans: an unusual clinical presentation. J. Ass. Phys. India, **31:** 49, 1983.
8. Kwon-Chung, K. J., Hill, W. B. and Bennett, J. E.: New, special stain for histopathological diagnosis of cryptococcosis. J. Clin. Microbiol., **13:** 383, 1981.
9. Symmers, W. St. C.: Non-specific granulomatous prostatitis. Brit. J. Urol., **22:** 6, 1950.
10. Tanner, F. H. and McDonald, J. R.: Granulomatous prostatitis: histologic study of group of granulomatous lesions collected from prostate glands. Arch. Path., **36:** 358, 1943.
11. Kelalis, P. P., Greene, L. F. and Harrison, E. G., Jr.: Granulomatous prostatitis: a mimic of carcinoma of the prostate. J.A.M.A., **191:** 287, 1965.
12. Brooks, M. H., Scheerer, P. P. and Linman, J. W.: Cryptococcal prostatitis. J.A.M.A., **192:** 639, 1965.
13. Salyer, W. R. and Salyer, D. C.: Involvement of the kidneys and prostate in cryptococcosis. J. Urol., **109:** 695, 1973.
14. Dreyfuss, M. L. and Sommer, R. I.: Granulomatous prostatitis due to Cryptococcus neoformans (Torula) with disseminated cryptococcosis and meningitis. N. Y. State J. Med., **61:** 1589, 1961.
15. Brock, D. L. and Greico, M. H.: Cryptococcal prostatitis in a patient with sarcoidosis: response to 5-fluorocytosine. J. Urol., **107:** 1017, 1972.
16. Tillotson, J. R. and Lerner, A. M.: Prostatism in an eighteen-year-old boy due to infection with Cryptococcus neoformans. New Engl. J. Med., **273:** 1150, 1965.
17. Ro, J. Y., Ayala, A. G. and Lee, S. S.: Infection by capsule-deficient cryptococci: in reply. Arch. Path., **111:** 688, 1987.