- 2 Grundmann E, Schlake W. Histological classification of gastric cancer from initial to advanced stages. *Path Res Pract* 1982;173:260-74.
- 3 Sugihara H, Hattori T, Fukuda M, Fujita S. Cell proliferation and differentiation in intramucosal and advanced signet ring cell carcinomas of the human stomach. *Virchows Arch (Pathol Anat)* 1987;411:17-27.
- 4 Dingemans KP. What's new in the ultrastructure of tumor invasion in vivo? *Path Res Pract* 1988;183:792-808.
- 5 Ghandur-Mnaymneh L, Paz J, Roldan E, Cassidy J. Dysplasia of nonmetaplastic gastric mucosa. A proposal for its classification and its possible relationship to diffuse-type gastric carcinoma. *Am J Surg Pathol* 1988;12:96-114.

Rapid diagnosis of *Candida* mediastinitis by coagglutination

A rare case of mediastinitis and septicaemia caused by *Candida albicans* in a patient who had undergone cardiac surgery was diagnosed sooner by a *Candida* coagglutination test than by culture findings. The *Candida* agglutination test had been successfully used by us for the detection of antigenaemia in 10 patients with systemic candidiasis, where the coagglutination titres varied from 2 to 54.¹

In the case reported here, a 28 year old man who had had aortic and mitral valve replacement developed mediastinitis caused by *Candida albicans* infection. The *Candida* coagglutination test was extended for the detection of *Candida* antigen on the first sample of mediastinal fluid received on day 17 after surgery in the laboratory; simultaneously, culture was carried out. Both tests were carried out on the second sample of mediastinal aspirate after an interval of 48 hours.

Candida albicans antiserum used in the test had been raised in rabbits² against whole cell antigen of *C. albicans* serotype A (kindly provided by Dr AA Padhye, Centers for Disease Control, Atlanta) and this serum yielded indirect haemagglutination (IHA) titre of 1280.¹ Cowan I *Staphylococcus aureus* was grown in Todd hewitt broth at 37°C, formalin added, and washed as described previously by Christensen *et al.*³ and coloured as described by Koshi *et al.*⁴ The reagents were prepared by mixing 1.0 ml of 10% Cowan I staphylococcal cells and 0.1 ml of *C. albicans* antiserum and incubated at room temperature for 30 minutes. A 2% suspension was satisfactory for the test.²

For the *Candida* coagglutination test the mediastinal fluid was centrifuged at 2500 rpm for 15 minutes. Supernatant (400 µl) was mixed with 20 µl of 2 M sodium hydroxide and heated at 100°C for 30 minutes to remove non-specific reactions, centrifuged at 2500 rpm for 10 minutes, and subjected to the coagglutination test as described previously.¹ Fluid treated with heat and alkali (20 µl) was mixed with 40 µl of 2% *Candida* coagglutination reagent, as well as coagglutination reagent using Cowan I cells coated with normal rabbit serum (NRS) separately in a ceramic ring VDRL slide and rotated for three minutes.¹ The reactions were graded as 4+, 3+, 2+, 1+ and negative based on the formation and size of the clumps and clearing. The coagglutination reaction was considered to be satisfactory when the fluid did not cross react with staphylococcal cells coated with NRS.

To confirm the specificity of the coagglutination reaction a blocking test was carried out by mixing 50 µl of alkali heat treated mediastinal fluid with 50 µl of *C. albicans* antiserum, incubated at 56°C for 10 minutes and then again subjected for the coagglutination test. Patient serum was also treated and tested similarly for *Candida* antigen, prepared from *C. albicans* and 0.03 M phosphate buffered saline (pH 7.2), served as positive and negative controls, respectively.

The coagglutination detected mannan antigen and the test results were available one hour after receipt of the specimens. The titre was 64 in the first sample of mediastinal fluid, and a significant increase in titre to 256 was shown in the second sample. The serum also had a high coagglutination titre of 64, confirming a diagnosis of invasive candidiasis.

Budding yeast cells with pseudohyphae were detected in the Gram stained smear. Further confirmation of diagnosis was made by the isolation of *C. albicans* in scanty and heavy growth from the first and second samples of mediastinal fluid, respectively. Repeat blood cultures also yielded pure growth of *C. albicans*. No bacteria were isolated from the mediastinal fluid of blood.

The high antigen titre and increase in the *Candida* antigen titre in the mediastinal fluid and serum with severe candidiasis was probably indicative of a poor prognosis; the patient died four days after diagnosis. Prolonged treatment with broad spectrum antibiotics combined with belated aetiological diagnosis and consequent delay in starting antifungal treatment probably caused the fatality in this patient.

The *Candida* coagglutination test was a useful adjunct for the detection of *Candida* antigen in body fluids. The coagglutination test was as specific, evidenced by the absence of a cross reaction with sera obtained from a variety of patients with bacterial and fungal infection as well as rheumatoid factor positive sera.¹ The coagglutination test described here is recommended as a simple, cost effective, and specific test in the rapid detection of *Candida* antigen in serum or body fluids.

Since this letter was written the authors have been informed of the coagglutination test for the detection of *Candida* antigenaemia, first described by Anyiwo (1979).

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Intraepithelial malakoplakia

Most cases of malakoplakia, a chronic inflammatory condition first reported in 1902 by Michaelis and Gutmann, and in 1903 by von Hansemann, occur in the genitourinary tract, though gastrointestinal, respiratory, cutaneous, skeletal and even ocular disease have been recorded. Microscopically, the mucosal and cutaneous lesions are characteristically composed of large eosinophilic cells with abundant cytoplasm and small eccentric nuclei (von Hansemann cells) which are situated in the lamina propria or dermis and are either covered by intact epithelium or ulcerated. The presence of laminated, concentric, basophilic, intracytoplasmic and extracellular Michaelis Gutmann bodies is generally accepted as necessary for diagnosis. A comprehensive review in 1983 and the subsequent literature do not mention intraepithelial von Hansemann cells.¹

A 77 year old woman with a history of chronic urinary infections and a radiological appearance of xanthogranulomatous pyelonephritis, had, on cystoscopy, a mucosal appearance suggesting cystitis follicularis.

Histologically, the bladder mucosa showed diffuse infiltration of the stroma by sheets of von Hansemann-type macrophages, many containing characteristic basophilic cytoplasmic Michaelis Gutmann bodies. The overlying transitional cell epithelium, however, also contained von Hansemann macrophages, some containing Michaelis Gutmann bodies. Periodic acid Schiff and von Kossa stained these inclusions, with the periodic acid Schiff showing a targetoid appearance. Immunocytochemistry with MAC 387 clearly showed the intraepithelial macrophages, which gave a negative reaction with CAM 5.2.

That there is an intraepithelial component of malakoplakia has not previously been reported, it may well be that as the cells are macrophages they have a capacity for translocation, as do other inflammatory cells. Either transepithelial migration or ulceration may be responsible for the occasional reports of von Hansemann cells shed in urine.

The presence of large, pale, eosinophil intraepithelial cells associated with a history of chronic infection should raise the possibility of malakoplakia.

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1 McClure J. Malakoplakia. *J Pathol* 1983;140: 275-330.

Expression of epithelial membrane antigen by carcinoid tumours

Carcinoid tumours are normally identified by their distinct morphological appearance, affinity for silver stains, and, at an ultrastructural level, presence of dense core neurosecretory granules. In small, crushed biopsy specimens or fine needle aspirates recognition may not be so easy, and application of a panel of immunocytochemical reagents may assist diagnosis. Neuroendocrine tumours vary in reactivity with different markers of putative neuroendocrine derivation. Less well known is the occasional expression of epithelial membrane antigen.

- 1 Koshi G, Viswanathan A, Chandy M, Jairaj PS. Development of a coagglutination (COA) technique to detect candida antigenemia. 1. COA versus candida isolation. *Am J Clin Pathol* 1987;88:429-35.
- 2 Hasenclever HF, Mitchell WO. Antigenic relationships of *Torulopsis glabrata* and seven species of Genus *Candida*. *J Bacteriol* 79:677-81.
- 3 Christensen P, Kahlmeter G, Johnson S, Kronvall G. New method for serological grouping of streptococci with specific antibodies absorbed to protein A containing staphylococci. *Infect Immun* 1973;7:881-5.
- 4 Koshi G, Thangavelu CP, Brahmadathan KN. The reliability and rapidity of the coagglutination technique and its comparison with precipitin techniques in the grouping of streptococci. *Am J Clin Pathol* 1979;71:709-12.
- 5 Anyiwo CE. Coagglutination for detection of candida antigenemia. *Nigerian J Med Sci* 1979;2:97-102.