Cells of similar morphology were identified in a patient with a biopsy taken and in the narrow and peripheral blood.

Chromosome analysis of phytohaemagglutinin stimulated peripheral blood lymphocytes was carried out as mitoses were not observed in unstimulated cultures. Of 48 G banded cells, one showed a 46,XY, normal male karyotype and 14 cells showed a complex karyotype of 43,Y, t(X;14) (q26,q11), -12, -13, -20, t(3;7;9) (p21;q11); 41q2; t(11;19)(q13;p13), del(6)(q13), + mar 1, + mar 2, + mar 3. The translocations (t(3;7;9) and t(11;19) appeared to be not completely reciprocal as the derivative chromosome 7 (der(7)) and der (11) were missing, or involved in the formation of the marker chromosomes. Marker 1 involved the q arm of the deleted chromosome 6 and marker 2 involved der (9) of the t(3;7;9). Marker 3 may have represented der (14) from the t(X;14). The remaining three cells also showed the above karyotype with del (17) (p11) (figure).

His clinical condition continued to deteriorate. He died three days after starting combination chemotherapy. At necropsy multiple thick walled abscesses were found along the pancreatic border (probably derived from pseudocysts) and in the small bowel mesentery and retroperitoneum. Lymphomatous deposits were present in the liver but not in the spleen or marrow (effect of chemotherapy)?

A computer search of the literature has shown that although pancreaticitis has been reported with a variety of solid tumours, such as carcinoma of the stomach, lung, and tonsil, it has rarely been found with lymphoma. Francis and Glazer reported direct pancreatic disease with Burkitt's lymphoma, but in other cases of tumour associated pancreatitis obstruction to the pancreatic duct was postulated. The second patient reported by Anderson et al had pseudocyst formation as reported here. The digital gangrene and uveitis remain unexplained; vasculitis was not found at necropsy.

The most common chromosome abnormality in non-Hodgkin's lymphoma is t (14;18), found in association with follicular lymphoma of follicle centre cell origin. This patient showed a translocation involving chromosome band 14q11. Croce et al postulated that all rearrangements affecting 14q11 in T-lineage malignancies involve the T cell receptor (TCR) chain locus, which is present within this chromosomal band. The del (6) described in our patient has previously been reported in non-Hodgkin's lymphoma.

We can find no cytogenetic data in earlier reports. The combination of clinical features with the cytogenetic findings and T cell origin of this lymphoma seems to be unique.


Intraepithelial stage of signet-ring cell carcinoma of the stomach

Histological observations on minute gastric carcinomas have indicated that "differentiated" (intestinal) type carcinomas seem to originate in metaplastic entestinal epithelium and that "undifferentiated" (diffuse) type carcinomas containing signet-ring cells (SRC) seem to originate in non-metaplastic gastric mucosa. Dysplastic and in situ changes in intestinal metaplasia associated with differentiated (intestinal) type carcinoma are well known. It is generally believed that SRC gastric carcinoma arises de novo at the glandular neck level and forms a layered structure in the lamina propria.

According to the multipath theory of neo-plasia, it is equally possible to have a sequential evolution of the SRC gastric carcinoma from an intermediate intra-epithelial stage. On the other hand, it has already been demonstrated that many metaplastic cells often spread through tissue strictly adhering to pre-existing basement membrane. Recently, Ghan-dur-Mnaymneh et al defined the criteria for dysplasia of non-metaplastic gastric epithelial tissue and postulated that it may have a possible association with diffuse type gastric carcinoma. The main feature of this dysplasia is the replacement of the differentiated cells lining the glands by undifferentiated cells with a varying degree of atypia, but in the absence of architectural glandular derangement.

We document an additional case of intraepithelial carcinoma associated with multifocal, minute, poorly differentiated adenocarcinoma with an SRC component, in a resected stomach specimen of a 60 year old man. The intraepithelial carcinoma cells ended abruptly at the junction with the adjacent periodic acid Schiff positive foveolar cells (figure). Fusion or severe distortion, or both, of the neighbouring tubules were not detected.

The component cells of the intraepithelial carcinoma were uniformly of a columnar shape with a thin brush border (figure). They showed enlarged, ovoid, vesicular, moderately pseudonatrified nuclei with prominent nucleoli (figure). The cytoplasm was generally not stained with periodic acid Schiff, alcin blue, or high iron diamine. Very occasionally these intraepithelial carcinoma cells exhibited small vacuoles, which appeared "optically empty" or contained a variable amount of neutral mucins, sialomucins, and sulphomucins. Atypical mitoses were frequently found. A histological continuity between intraepithelial carcinoma and poorly differentiated adenocarcinoma glands was observed in some figures (figure).

Both the poorly differentiated adenocarcinoma cells and isolated SRC showed a granular positivity for sialomucins as well as large cytoplasmic vacuoles, which appeared "optically empty" (figure).

In our case the presence of intraepithelial carcinoma may reflect the proliferative activity of a distinct population of atypical cells which are not fully transformed into malignant cells, being between adenoma and invasive cancer in nature. In fact, besides possessing the ability to migrate along the foveolar wall, the intraepithelial carcinoma cells show peculiar morphohistochemical features such as their columnar shape, brush border, and rare mucin granules. By contrast, invasive adenocarcinoma is represented in our case by tumour cells which are capable of forming gland-like structures (poorly differentiated adenocarcinoma) or which show a complete loss of the gland-forming ability (isolated SRC). Moreover, abundant mucus production seems to be a feature seen predominantly in invasive adenocarcinoma and only in a few cells of the intraepithelial carcinoma.

In conclusion, our data indicate the possibility of an intraepithelial stage with peculiar morphohistochemical features during the progression of SRC gastric carcinoma.

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Rapid diagnosis of Candida mediasinosis by coagglutination

A rare case of mediastinitis and sepsisemia 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 coagglutination test had been successfully used by us for the detection of Candida albicans 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.3,4 Jensen et al5 and control as described by Koshi et al.6 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 VDLR slide and rotated for three minutes. The reactions were graded as +, ++, ++++ and +++++ 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, 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 0.3 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 to the 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 antigenemia, first described by Anyiwo (1979).

Intraepithelial malakoplakia

Most cases of malakoplakia, a chronic inflammatory condition first reported in 1902 by Michiels 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 cyttoplasmic 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 clone 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 the cells are macrophages they have a capacity for translocation, as do other inflammatory cells. Either transmepithelial 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.