880–884

Correspondence

Defining epithelioid cell granulomas

A journal of evidence-based health care recently featured an editorial[1] emphasising interobserver disagreement between pathologists and ipso facto the unreliability of histopathology as the "gold standard diagnosis". Recent initiatives to clarify evidence-based histopathology and reduce interobserver disagreement are therefore welcomed. A recent case of clinical chronic ulcerative colitis in which sequential biopsies showed frequent pericryptal aggregates of epithelioid histiocytes caused us to consult both the guidelines for the initial biopsy diagnosis of chronic idiopathic inflammatory bowel disease (CIBD)[2] and a simultaneous publication by Lee *et al*[3] addressing the topic of the diagnosis and significance of intramucosal granulomas in CIBD. We were immediately struck by the disparity between the text definitions of epithelioid cell granulomas and the photomicrographs in both articles. Both defined these as discrete collections of at least five epithelioid cells with or without accompanying giant cells; however, in practice these are extremely difficult to count as cytoplasmic boundaries are invariably indistinct. Both articles emphasise the importance of distinguishing between epithelioid cell granulomas and pericryptal histiocytic aggregates (microgranulomas[2] and pericryptal granuloma[3]) composed of histiocytes lacking cytoplasmic features of activation. Both epithelioid cell granulomas[2 3] and microgranulomata[2 3] are illustrated. The numbers of epithelioid cells and giant cells counted by each of us independently in the paired photomicrographs are given in table 1.

Table 1 Independent counting of giant cells (GC) and epitheloid cells (EC) by two consultant pathologists

	Epithelioid granuloma		*Microgranuloma*	
Observer	*BSG inititative (fig 2b)*[2]	*Lee et al (fig 1)*[3]	*BSG inititative (fig 2c)*[2]	*Lee et al (fig 3)*[3]
1	GC 0	GC 8	GC 5	GC 0
	EC 44	EC 6	EC 5	EC 9
2	GC 0	GC 6	GC 1	GC 1
	EC 61	EC 55	EC 16	EC 42

This shows that both pathologists were unable to distinguish between activated and non-activated histiocytes, that at least five epithelioid histiocytes were counted in both epithelioid cell granuloma and microgranuloma, and that both articles illustrated epithelioid cell granulomas with granulomas much larger than the minimum definition given in the text description.

We suggest that rather than attempting to define epithelioid cell granulomas on the basis of numbers of histiocytes (presumably in a single en face section) they would be better defined in terms of size and relation to ruptured crypts. Hence on the basis of the photomicrograph given in the British Society of Gastroenterology guidelines an epithelioid cell granuloma would be defined as a discrete collection of epithelioid cells with or without accompanying giant cells measuring at least 0.2 mm in diameter (approximately two crypt diameters). If unrelated to crypt disruption these are considered to be a specific indicator of Crohn's disease.[2] If seen in association with cryptitis or crypt disruption a diagnosis of indeterminate colitis may be appropriate.[4] Smaller collections of histiocytes with or without accompanying giant cells (microgranulomas) should provoke a search for true epithelioid cell granuloma as defined above.[3]

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1 Moore A, McQuay H, Muir Gray JA. *Pathology as an art appreciation.* Oxford: Bandolier 1997;**4**:1–3.
2 Jenkins D, Balsitis M, Gallivan S. Dixon MF, Gilmour HM, Shepherd NA, *et al.* Guidelines for the initial biopsy diagnosis of idiopathic inflammatory bowel disease. The British Society of Gastroenterology initative. *J Clin Pathol* 1997;**50**:93–105.
3 Lee FD, Maguire C, Obeidat, Russell RI. Importance of cryptolytic lesions and pericryptal granulomas in inflammatory bowel disease. *J Clin Pathol* 1997;**50**:148–52.
4 Dundas SAC, Dutton J, Skipworth P. Reliability of rectal biopsy in distinguishing between chronic inflammatory bowel disease and acute self-limited colitis. *Histopathology.* [In press.]

Importance of cryptolytic lesions and pericryptal granulomas in inflammatory bowel disease

Professor Lee and colleagues[1] have addressed the significance of a granulomatous reaction to disrupted inflamed colorectal crypts in an important and meticulous study. This is a confusing area of colorectal pathology that has been neglected and Lee *et al*'s approach of separating true cryptolytic epithelioid cell granulomas from focal pericryptal chronic inflammation without epithelioid histiocytes (including "mucin granulomas") represents a major contribution to the biopsy diagnosis of inflammatory bowel disease.

While Lee *et al*'s findings indicate that segmental crypt disruption by proper epithelioid granulomatous inflammation is a much more specific marker of Crohn's disease than other forms of focal cryptitis, they demonstrate that there are nevertheless occasional instances when even this feature occurs in patients with probable ulcerative colitis, or indeed with no chronic inflammatory bowel disease at all, after full clinicopathological correlation. They also refer to published descriptions of pericryptal granulomas in infective colitis and diverticular colitis. We have had similar experiences of cryptolytic epithelioid granulomas in all of these situations as well as in pouchitis[2] and diversion colitis.[3] We have also observed the lesion, with an accompanying mild "colitis", misdiagnosed as Crohn's disease on an initial biopsy, when the ultimate diagnosis was secondary inflammatory changes immediately adjacent to a colonic adenocarcinoma.

We certainly agree with Lee *et al* that the finding of cryptolytic epithelioid granulomas should always raise the suspicion of Crohn's disease, sufficient to warrant further investigation, but we wish to reinforce caution that the diagnosis must not be made on this feature alone. We are particularly concerned about the implications of finding cryptolytic granulomas on the decision whether to undertake future pelvic ileal reservoir surgery and we are uneasy about the last sentence of Lee *et al*'s paper "...the presence of pericryptal granulomas should signal a warning to surgeons that ileoanal pouch construction might have unwelcome consequences". We have observed a number of patients with such lesions in mucosal biopsies or in colectomy specimens who have proceeded to successful pelvic ileal reservoir surgery when careful preoperative review of the whole clinicopathological picture has identified no other suggestion of Crohn's disease. We therefore consider that pericryptal granulomas alone cannot be sufficient reason to deny a patient the benefit of a successful restorative operation when it is otherwise appropriate.

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1 Lee FD, Maguire C, Obeidat W. Russell RI. Importance of cryptolytic lesions and pericryptal granulomas in inflammatory bowel disease. *J Clin Pathol* 1997;**50**:148–52.
2 Warren BF, Shepherd NA. Pouch pathology. In: Nicholls RJ, Bartolo DCC, Mortensen NJMcC, eds. *Restorative proctocolectomy.* Oxford: Blackwell Scientific Publications, 1993:147–62.
3 Warren BF, Shepherd NA, Bartolo DCC, Bradfield JWB. The pathology of the defunctioned rectum in ulcerative colitis. *Gut* 1993;**34**:514–16.

Professor Lee et al comment:

I was most interested to read the comments made by Warren and his distinguished colleagues regarding our article on cryptolytic lesions and pericryptal granulomas in colorectal biopsies. We are of course well aware of the conventional view of such lesions, which many consider to be too widespread to have any serious diagnostic significance. We are also interested to hear that patients whose biopsies showed pericryptal granulomas have proceeded to ileoanal pouch construction without further incident.

Other patients may not however have been quite so fortunate as is illustrated by the following case, which also addresses many of the issues raised by Warren and colleagues. The patient in question, a 28 year old man, experienced rupture of an ileoanal pouch 14 months after pouch construction that was done following a diagnosis of severe ulcerative colitis. Review of the histological sections from the previous colectomy specimen revealed numerous pericryptal granulomas, which had been attributed to crypt rupture and discounted because the generality of the histological changes favoured a diagnosis of ulcerative colitis. Histological examination of the ruptured pouch also revealed numerous

pericryptal granulomas. There are thus reasonable grounds for supposing that this patient had been suffering from Crohn's disease from the outset. In this case at least a warning to the surgeons that ileoanal pouch construction might have unwelcome consequences would have been entirely justified.

The received wisdom is that the presence of a pericryptal granuloma regardless of the context in which it arises is a diagnostic pitfall; but perhaps as the above case illustrates, the pitfall may be the other way round.

Colorectal cancer reporting

The article by Shepherd and Quirke[1] is timely and publication coincided with the completion of our own colorectal cancer reporting sheet (fig 1). This was designed for in-house use to supplement a laboratory protocol for handling and reporting colorectal malignancy resection specimens and to improve the accuracy and consistency of reporting. The top part of the sheet is filled in by the surgeon in the operating theatre and the specimens are handled according to ACP guidelines.[2] Together with the separate free text histology report, the sheet will be filed in the patient's clinical case notes and will be the source of the histopathological data that will be used, eventually, in the multidisciplinary database that we hope to have available for colorectal cancer patients in this unit.

The general layout of our form owes much to the "Sloane" forms for the reporting of breast screening histopathology and we are pleased to see that Professor Sloane is to chair the forthcoming Royal College of Pathologists' working party. However, unlike breast screening, reduction of mortality and morbidity from colorectal cancer is not a *Health of the Nation* target. For colorectal cancer this cancer unit is going to need at least one clerk to help gather and correlate data from several different sources including outpatients, radiology, operating theatres, histopathology, and oncology. The clinical audit committee at the Peterborough Hospitals NHS Trust has decided that cancer database entry is not an appropriate use of clinical audit facilitator time or audit funds. The decision was based on the fact that the clinical audit department is unlikely to be able to cope with the vast amount of data that will need to be collected for multiple cancers from several locations across a trust that is split between two sites. The department will continue to support data analysis and audit project presentation. We are exploring other means of collecting the data.

Any recommendations of the proposed Royal College of Pathologists working party must give consideration to a coordinated and multidisciplinary approach to the diagnosis and treatment of this important neoplasm and to the provision of software packages and support staffing.

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1 Shepherd NA, Quirke P. Colorectal cancer reporting: are we failing the patient? *J Clin Pathol* 1997;50:266–7.
2 Sheffield JP, Talbot IC. ACP Broadsheet 132. Gross examination of the large intestine. *J Clin Pathol* 1992;45:751–5.

PETERBOROUGH HOSPITALS NHS TRUST

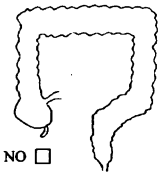
COLORECTAL CANCER HISTOPATHOLOGY REPORTING SHEET

SURNAME | FORENAME(S) | D.O.B

HOSPITAL NO. P | SURGEON | DATE OF OPERATION

SPECIMEN | NO. OF TIES | SITE OF TUMOUR(S)

L HEMICOLECTOMY ☐
ANTR. RESECTION ☐
A-P RESECTION ☐
OTHER (SPECIFY) .....



PREVIOUS COLORECTAL BIOPSIES YES (give Histol. No.) ☐ NO ☐

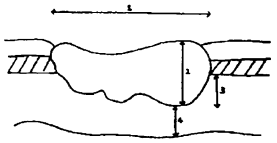
MALIGNANT LESIONS (use a separate sheet for each tumour)

NUMBER PRESENT ☐

ENDS CLEAR? PROXIMAL ☐ DISTAL ☐ CLOSEST (CM) ☐ DO'NUTS CLEAR? N/A ☐ YES ☐ NO ☐

MEASUREMENTS (CM) + RADIAL MARGINS

1 WIDTH/AXIAL LENGTH ☐
2 THICKNESS ☐
3 "MESORECTAL" SPREAD ☐
4 CLOSEST RADIAL MARGIN (Zero if involved) ☐



IS THIS PERITONEAL YES ☐ NO ☐
IS THIS ANTR ☐ POSTR ☐ RIGHT ☐ LEFT ☐

HISTOLOGICAL TYPE ADENOCARCINOMA ☐ SPECIAL TYPE (SPECIFY) .....
OTHER (SPECIFY) .....

NODES: TOTAL ☐ INVOLVED ☐ HIGH NODES: CLEAR ☐ INVOLVED ☐

GRADE; WELL ☐ MOD ☐ POOR ☐ STAGE; A ☐ B ☐ C1 ☐ C2 ☐ D ☐

VASCULAR INVASION; YES ☐ NO ☐ SATELLITES; YES ☐ NO ☐

BENIGN LESIONS; YES/NO

ADENOMA - NUMBER ☐ MAX SIZE (CM) ☐

METAPLASTIC POLYP ☐ OTHER (SPECIFY) .....

PATHOLOGIST ☐ REPORT NO ☐ DATE ☐

Figure 1 Colorectal cancer reporting sheet from the Peterborough Hospitals NHS Trust.

Dr Shepherd and Professor Quirke comment:
We welcome Womack *et al*'s adoption of a proforma and congratulate them on its design. We would, however, like to avoid a plethora of forms emerging. We are currently aware of a number of forms, all of which are slightly different with more in the pipeline. The value of Professor Sloane's breast cancer form is its national use and apparent acceptability; this will allow comparison of the quality of surgical reporting, the type and quality of treatment, and patient outcome on a national level. We have been involved in the generation of the UKCCCR Colorectal Cancer Subcommittee forms[1] and the pathology form of the Royal College of Surgeons Colorectal Cancer Guidelines[2]: we are now convinced that what is required is a basic minimum dataset of information on colorectal cancer that will be collected throughout the United Kingdom. The current Joint National Guidelines (fig 1) have been extensively discussed and approved by the Royal College of Pathologists, the Royal College of Surgeons (England), the Scottish Intercollegiate Guidelines Network, the Welsh CROPS Project, the Association of Clinical Pathologists, the Association of Coloproctology, and the Pathology Committee of the British Society of Gastroenterology. It has also been discussed extensively among British gastrointestinal pathologists. Professor Geraint Williams and Professor Ian Talbot have also played a major part in developing the proforma, as did Dr Judy Wyatt and Dr Michael Dixon in developing the Yorkshire proforma.

The major difference between the Joint National Guidelines and the Peterborough proforma is that the Joint National Guidelines have included TNM staging alongside Dukes's. We believe this is important as many international trials report their data in the context of TNM staging. This is most relevant in respect of stage pT1 for local excision studies and stage pT4 for adjuvant therapy studies. Subdividing nodal involvement into pN1 (1–3 nodes) and pN2 (4 or more nodes) is also important as this may