

Correspondence

Defining epithelioid cell granulomas

A journal of evidence-based health care recently featured an editorial¹ 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 (microgranulomas² and pericryptal granuloma³) composed of histiocytes lacking cytoplasmic features of activation. Both epithelioid cell granulomas² and microgranulomas³ 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 epithelioid cells (EC) by two consultant pathologists

Observer	Epithelioid granuloma		Microgranuloma	
	BSG initiative (fig 2b) ²	Lee <i>et al</i> (fig 1) ³	BSG initiative (fig 2c) ²	Lee <i>et al</i> (fig 3) ³
1	GC 0 EC 44	GC 8 EC 6	GC 5 EC 5	GC 0 EC 9
2	GC 0 EC 61	GC 6 EC 55	GC 1 EC 16	GC 1 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 initiative. *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 colleagues¹ 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 pouchitis² 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