Necrobiotic granulomas of the urogenital system

Recently, Akosa and Boret1 described the condition of four patients who complained of menorrhagia which was treated by laser ablation of the endometrium. Treatment failed in these patients and hysterectomy was performed. Necrotising histiocytic granulomas were found in the endometria of all the four cases.

We have recently investigated nine similar hysterectomy specimens which were subjected to laser ablation of the endometrium (unpublished data, 1994, Aqel et al). We found scattered histiocytes and/or multinucleated giant cells in the endometria of eight of the nine cases. Some of the histiocytes formed necrotising granulomas. In all cases histiocytes showed intracytoplasmic black and golden-brown pigment; in addition, residual endometria contained variable quantities of haemosiderin (Perl’s positive) which suggested past injury and haemorrhage in the basal layer of the endometrium.

We have also recently examined a urinary bladder biopsy specimen which was removed three months after diathermy resection of a transitional cell carcinoma. This biopsy specimen showed necrotising granulomas with deposition of intracytoplasmic black pigment (figure). The pigment in the hysterectomy specimens and in the bladder biopsy specimen was not birefringent and did not stain with haematoxylin, Perl’s (iron), Masson-Fontana (melanin), Gram (bacteria), or Zielh-Neelsen (acid-alcohol fast bacilli). It seemed to be composed of non-degradable products of carbonised tissue, resulting from injury by laser or cautery.

Similar black or golden-brown “diathermy pigment” was reported following laser ablation or diathermy resection of endometrium and ovary.1,2 As histiocyte and granulomatous inflammation of the urogenital system can be a component of a wide range of pathological conditions including infections, infestations, and systemic diseases, such as sarcoidosis,3 it is important to recognise the presence of “diathermy pigment” and haemosiderin in these lesions. Such observations should prompt the histopathologist to consider the possibility of previous cautery or laser treatment, and so enquire further about the past surgical history. This will save unnecessary histological and clinical investigations to rule out infectious or systemic diseases.4

Correspondence

Necrobiotic granulomas of the urogenital system

Recently, Akosa and Boret1 described the condition of four patients who complained of menorrhagia which was treated by laser ablation of the endometrium. Treatment failed in these patients and hysterectomy was performed. Necrotising histiocytic granulomas were found in the endometria of all the four cases.

We have recently investigated nine similar hysterectomy specimens which were subjected to laser ablation of the endometrium (unpublished data, 1994, Aqel et al). We found scattered histiocytes and/or multinucleated giant cells in the endometria of eight of the nine cases. Some of the histiocytes formed necrotising granulomas. In all cases histiocytes showed intracytoplasmic black and golden-brown pigment; in addition, residual endometria contained variable quantities of haemosiderin (Perl’s positive) which suggested past injury and haemorrhage in the basal layer of the endometrium.

We have also recently examined a urinary bladder biopsy specimen which was removed three months after diathermy resection of a transitional cell carcinoma. This biopsy specimen showed necrotising granulomas with deposition of intracytoplasmic black pigment (figure). The pigment in the hysterectomy specimens and in the bladder biopsy specimen was not birefringent and did not stain with haematoxylin, Perl’s (iron), Masson-Fontana (melanin), Gram (bacteria), or Zielh-Neelsen (acid-alcohol fast bacilli). It seemed to be composed of non-degradable products of carbonised tissue, resulting from injury by laser or cautery.

Similar black or golden-brown “diathermy pigment” was reported following laser ablation or diathermy resection of endometrium and ovary.1,2 As histiocyte and granulomatous inflammation of the urogenital system can be a component of a wide range of pathological conditions including infections, infestations, and systemic diseases, such as sarcoidosis,3 it is important to recognise the presence of “diathermy pigment” and haemosiderin in these lesions. Such observations should prompt the histopathologist to consider the possibility of previous cautery or laser treatment, and so enquire further about the past surgical history. This will save unnecessary histological and clinical investigations to rule out infectious or systemic diseases.4

Dr Harach comments:

Dr Woyke and colleagues raise the interesting point that it may be possible to separate needle biopsy specimens of papillary microcarcinomas from those of clinically significant carcinomas by the admixture of benign follicular cells in the specimen. In our own report of needle biopsy specimens diagnosed as papillary carcinoma, found on operation to be papillary microcarcinomas, both cases contained non-neoplastic follicular cells as well as the typical cells of papillary carcinoma. However, I have also seen numerous examples where needle biopsy specimens contained both non-neoplastic and neoplastic follicular cells, and at surgery a clinically significant papillary carcinoma was found. The proposal to use repeat aspirations is also difficult, unless there is proof that the aspirate is restricted to the nodule. A possible strategy would be to carry out a second biopsy with ultrasound, when the first biopsy of a palpable nodule produces abundant non-neoplastic follicles and a minor papillary carcinoma component.


2 Department of Pathology, Kuwait Cancer Control Centre, Kuwait.

3 UK LUTHRA A SHERIF

4 Department of Cytology, Mubarak Hospital, Kuwait.


Dr Harach comments:

Dr Woyke and colleagues raise the interesting point that it may be possible to separate needle biopsy specimens of papillary microcarcinomas from those of clinically significant carcinomas by the admixture of benign follicular cells in the specimen. In our own report of needle biopsy specimens diagnosed as papillary carcinoma, found on operation to be papillary microcarcinomas, both cases contained non-neoplastic follicular cells as well as the typical cells of papillary carcinoma. However, I have also seen numerous examples where needle biopsy specimens contained both non-neoplastic and neoplastic follicular cells, and at surgery a clinically significant papillary carcinoma was found. The proposal to use repeat aspirations is also difficult, unless there is proof that the aspirate is restricted to the nodule. A possible strategy would be to carry out a second biopsy with ultrasound, when the first biopsy of a palpable nodule produces abundant non-neoplastic follicles and a minor papillary carcinoma component.

One should not lose sight of the scale of the problem. We only found two cases in 1756 biopsy specimens where the diagnosis of papillary carcinoma led to resection. Microcarcinomas as well as the benign nodule which was the palpable lesion. Any procedure that increases the chance of finding a clinically insignificant microcarcinoma, such as multiple blind biopsies of non-nodular thyroid tissue or of ultrasonic detected lesions of less than 1 cm in diameter, should be very carefully evaluated before being introduced into routine use. Multiple blind needle biopsies obviously increase the chance of detecting clinically insignificant lesions—microcarcinomas may occur in as many as 34% of adult thyroids when they are histologically examined in 2 to 3 mm steps. If those thyroids were thoroughly examined histologically, it was estimated that about 300 microcarcinomas would have been found. The prevalence of thyroid cancer will increase still further with an increasing number of sections studied per gland. Not to mention the primary thyroid lesions where fine needle aspiration cytology, serum calcitonin levels or genetic studies helped to yield a diagnosis of an unsuspected medullary microcarcinoma where thyroidectomy should be advocated.

H RUBEN HARACH
Department of Histopathology, Addenbrooke’s Hospital, University of Cambridge, Hills Road, Cambridge CB2 0QQ

Leukaemia immunophenotyping: effect of antibody source and fluorochrome on antigen detection

We read with interest the recent publication by Howard et al in which the authors highlight discrepant findings of myeloid antigen expression in cases of childhood acute lymphoblastic leukaemia (ALL). They concluded that the detection of antigens CD13 and/or CD33 may be dependent upon both the commercial source of antibody and the type of fluorochrome used. We wish to add support to their conclusions by reporting results from the United Kingdom National External Quality Assurance Scheme (UK NEQAS) for leucocyte immunophenotyping, in addition to data from our own investigations.

Results from UK NEQAS surveys have frequently shown variability in antigen detection attributable, in part, to the use of different commercial monoclonal antibodies. In survey 935, for example (acute biphenotypic leukaemia), the following mean values for CD13 expression were obtained for each reagent: Becton Dickinson (LeuM7) 15% (n = 15), Diemert et al 16% (n = 15), Coulter 24.5% (n = 8), Serelab 3% (n = 2), Ortho 0.5% (n = 2), and Serotec 89% (n = 1). In addition, the scheme has consistently shown statistically significant differences between samples analysed with fluorescein isothiocyanate (FITC) conjugated antibodies for the following antigens: CD3, CD5, CD13, CD14, CD19, and CD33. In survey 2031, investigating CD13 detection in a case of acute myeloid leukaemia, eight laboratories using FITC conjugated antibodies obtained values less than 50% (overall mean 58%), of which three were negative results, as defined as less than 20%.

In contrast, all 12 laboratories using PE conjugated antibodies obtained results greater than 50% (mean 77%). This variation may be as a result of PE having a higher quantum yield than FITC, thus potentially increasing sensitivity.

In a parallel study to that of Howard and colleagues we have recently determined the expression of myeloid antigens in B cell chronic lymphocytic leukaemia (B-CLL). As with childhood ALL, such “aberrant” myeloid expression has been reported to be of prognostic significance. To confirm these findings we examined 53 cases of B-CLL (stages 0 to IV), using Becton Dickinson PE conjugated anti-CD13 and anti-CD33 (clones L138 and P6-7, respectively), by whole blood lysis and triple colour staining. In 51 cases fewer than 4% of B cells expressed either CD13 or CD33 (6% in two cases) when compared with iso-type matched controls. Mean fluorescence staining intensity (MFSI) for both CD13 and CD33 expression did not differ significantly from the negative controls. Previous studies, reporting positive myeloid antigen expression, predominantly used Coulter anti-CD13 (MY7) and anti-CD33 (MY9) thus raising the possibility that these discrepant findings may relate to antibody source. To confirm this hypothesis we re-examined 15 of the B-CLL cases with PE conjugated MY7 (CD13) and MY9 (CD33). Of these, nine expressed the CD33 antigen on ≥10% of the leukaemic B cells, with five cases being regarded as positive (>20% expression); results in agreement with previous studies. The MFSI values showed a significant increase when compared with controls (p < 0.001). No sample expressed CD13 on >20% of the leukaemic B cells (one had 12%) although the values were significantly raised when compared with those obtained using Becton Dickinson antibodies (p < 0.001). We feel, therefore, that antibody source and also the fluorochrome used should be taken into account when comparing reports studying “aberrant” myeloid antigen expression.

Data from UK NEQAS, together with our own studies and those of Howard and colleagues, support the concerns of Howard and colleagues and raises several important issues. Firstly, which result is right? This question may only be answered if all commercially available reagents are standardized and calibrated. This is considered to be of great importance when collecting immunophenotypic data in multicentre trials, particularly if meaningful diagnostic and prognostic information is to be obtained.

The development of a newer and more sensitive fluorochrome, coupled with multiparameter technology, will increase the dilemma as to what should be regarded as positive. The simplistic approach using an arbitrary cut off point, as suggested in the recent BSCH guidelines, will probably not be applicable in the future. Data analysis procedures which currently employ the placement of a cursor at the boundary of the negative population are likely to be inappropriate. More biologically relevant procedures, such as antigen density quantification using calibrated flow cytometers, may yield more meaningful data. Finally, despite the experience of a number of quality control schemes worldwide, there is no consensus as to the best antibody within a CD group for diagnostic use. Such evaluations would require the production of reference materials for which there is no biological or clinical importance. Research in this area is currently under way, although the technical difficulties must not be underestimated.

J T REILLY
V GRANGER
P TEMPERTON
D BARNETT
UK NEQAS for Leucocyte Immunophenotyping, Department of Haematology, Northern General Hospital, Herrison Road, Sheffield, S5 7AU

Recurrent thrombotic occlusions of arteries and veins caused by intravascular metastatic adenocarcinoma

I refer to the case reported by Levi et al of a young woman with recurrent vascular occlusions found at necropsy to be caused by microscopic metastatic adenocarcinoma. They rightly suspected the presence of malignant disease during life, but despite wide-ranging investigative and laboratory investigations were unable to confirm their clinical suspicion. In their last sentence, the authors speculate that postmortal examination of the brain using specific markers for malignant cells, might have detected the adenocarcinoma cells; this may have been so, but I wonder if they performed bone marrow trephine biopsy as it is not mentioned in their investigation. Nevertheless, this is an important study and deserves the recognition that they have given it in their paper. Similarly, no mention was made of bone marrow studies carried out on post-mortem tissues.

It is thought that one large trephine biopsy or bilateral biopsies can provide a detection rate of metastatic disease somewhere in the region of 60%. Certainly, it is a worthwhile investigation in the type of case reported by Levi et al if performed might have resulted in 1 Howard MR, Thomas L, Reid MM. Variable detection of myeloid antigens in childhood acute lymphoblastic leukaemia. J Clin Pathol 1993;46:126-9.