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Case report

Solitary Langerhans' cell granulomatosis of the stomach associated with gastric carcinoma

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Summary. A case of Langerhans' cell granulomatosis associated with gastric adenocarcinoma is reported. A review of the literature demonstrate an association of this entity with Hodgkin or non-Hodgkin lymphomas alone. The discussion is centred on differential diagnosis from the pseudo-sarcoid granulomatous reaction. Further reports may assist in classifying the granulomatous reaction to tumours into two types, epithelioid and Langerhans.

Key words: Langerhans' cell granulomatosis – Stomach – Gastric cancer

Introduction

The relationship of Langerhans' cells to neoplasia may be demonstrated in two main groups. A first, non-granulomatous type, is characterized by the simple presence and co-existence of Langerhans' cells and neoplastic cells. This is well known to occur in a number of epithelial neoplasms, mainly of epidermoid or squamous variety (Basset et al. 1974; David and Buchner 1980).

The second type is represented by Langerhans' cell granulomatosis, associated with lymphoid tumours (Kjedlsberg and Kim 1980; Hoste et al. 1982; Burns et al. 1983). To our knowledge this combination has not been reported in relation to carcinomas.

We report Langerhans' cell granulomatosis associated with gastric carcinoma. The differential diagnosis between this entity and the granulomata of the pseudo-sarcoid reaction to tumours will be discussed.

Material and methods

The patient was a 49-year-old male, with a diffuse gastric carcinoma involving the full thickness of the wall and metastatic to six lesser curvature and one greater curvature nodes. There was no evidence of metastatic disease beyond the local lymph nodes. Radiosotopic bone scan-

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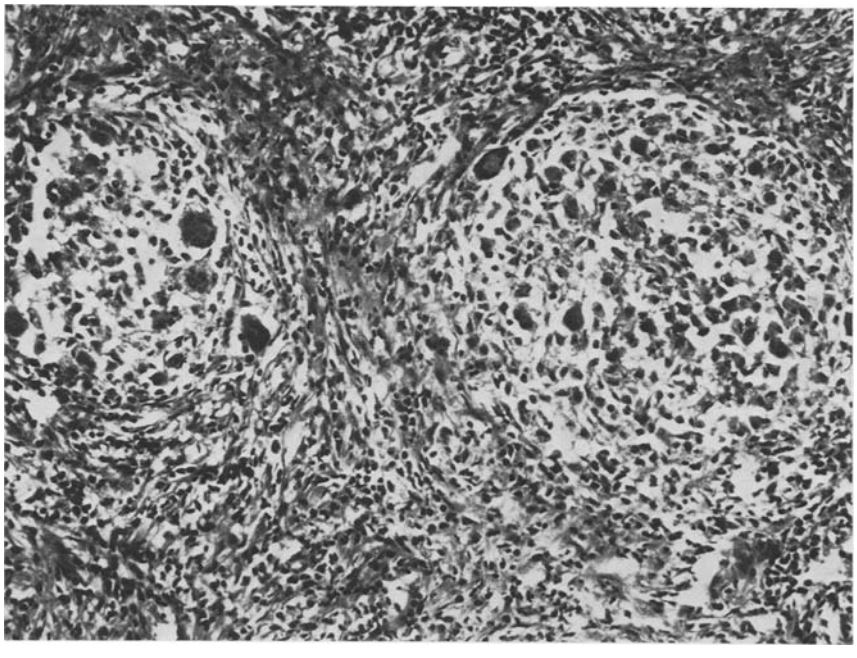

Fig. 1. Langerhans' cell granulomas. Notice giant cells and neatly bound periphery. (HE, ×200)

ning was negative. The rest of the clinical history, exploratory and analytical data were unremarkable and non-contributory. The resected specimen consisted of a total gastrectomy, omentectomy and splenectomy.

Multiple tissue blocks obtained from an ulcerated antral gastric cancer and from three randomly selected cases of pseudo-sarcoid granulomatous reactions to breast and lung carcinomata were routinely processed for conventional histopathological studies. Paraffin sections were stained with H&E, PAS, alcian blue, Gomori, methenamine silver, Ziehl-Nielssen and Fite-Faraco.

The PAP technique was used on 5-μm-thick paraffin sections. All reagents were diluted with phosphate-buffered saline (PBS 05 M). Peroxidase activity was visualized with 3,3 diaminobencidine-tetrahydroclorhide (0.05% w/v) hydrogen peroxide (0.01 v/v) in Tris-HCL buffer (0.05 M, pH 7.2). The following antibodies were used: anti S-100 protein (DAKO), anti Lisozyme (DAKO) and anti alpha 1 antitrypsin (DAKO).

For EM, observations, formaldehyde-fixed tissue recovered from the gastric cancer paraffin blocks was fixed in glutaraldehyde after previous washing in phosphate buffer, post-fixed in osmium tetraoxide and embedded in araldite. Semithin sections were stained with toluidine blue and the thin sections with lead citrate.

Results

The most significant morphological finding was the presence of several granuloma-like nodules intimately associated to the adenocarcinomatous growth, which otherwise did not reveal any remarkable features. The nodules were also seen in one of the lymph nodes free of metastasis and also in the muscularis and serosa of the gastric wall at several centimetres from the tumour. Each granuloma-like nodule (Fig. 1) was composed by a central proliferation of large to medium size histiocytic cells, with abundant pale eosinophilic cytoplasm and markedly indented lobular nucleus (Fig. 2). Oc-

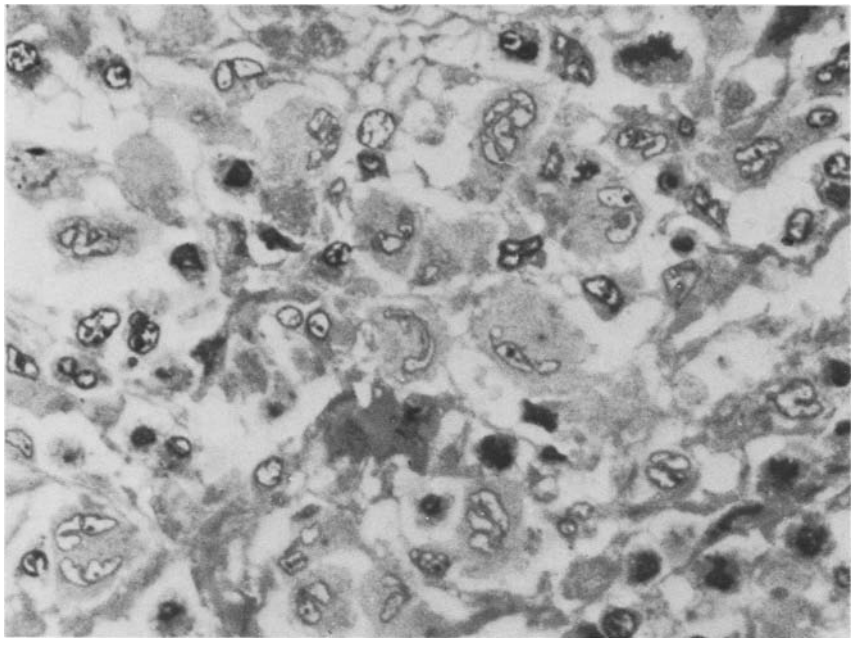

Fig. 2. Langerhans' cells. Notice abundant cytoplasm and markedly lobular indented nuclei. (Toluidine blue, ×400)

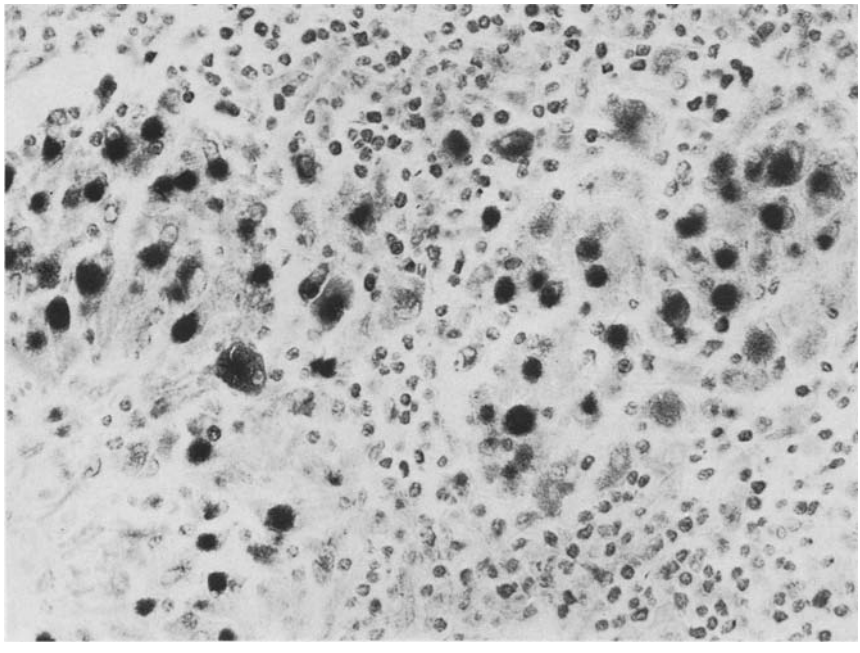

Fig. 3. Pseudosarcoid reaction strongly positive for lysozyme. (PAP lysozyme stain, ×200)

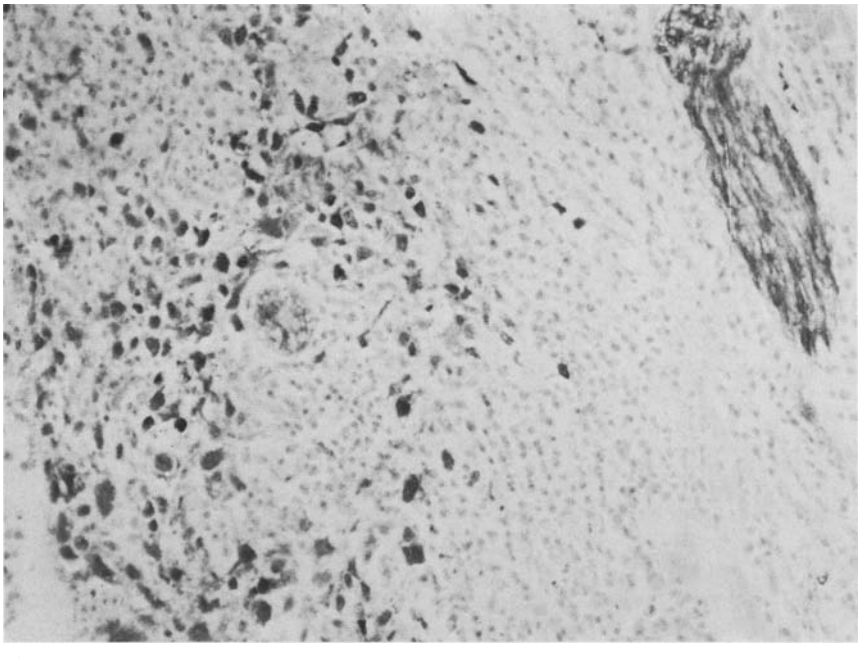

Fig. 4. Langerhans' cells. Strong positive cytoplasm staining to S-100 protein. Notice positive stain of Schwann cells on large nerve trunk. (PAP S-100 stain, ×100)

casionally, multinucleated giant cells displaying a similar type nuclei intermingled with the mononuclear cells. The periphery included lymphocytes, plasma cells and abundant eosinophils. Some of the granulomata showed necrotic centers. Stains for microorganisms were negative. The ultrastructure confirmed the lobular deeply indented nucleus and showed cytoplasm containing phagolysosomes, Charcot-Leyden crystals, lamellar myeline-like bodies and Birbeck's granula. Langerhans' cells were not observed in the midst of the tumour cells.

The granulomatous pseudo-sarcoid reactions displayed predominantly epithelioid cells with rare giant cells, both lacking indented nuclei. Eosinophils were absent. The epithelioid cells were consistently negative for the S-100 protein and strongly positive for the lysozyme (Fig. 3). The gastric granulomata included abundant eosinophils and significant numbers of giant cells intermingled with the histiocytic population, which typically revealed lobated nuclei. All of these cells were strongly positive for S-100 protein (fig. 4). The lysozyme only stained ocassional histiocytic non-lobated cells. A poor staining reaction was obtained with the alpha 1 antitrypsin technique, which was not discriminatory.

Discussion

Comparative analysis of the results shows significant differences between the two types of granulomata investigated. The presence of abundant eosino-

phils, the markedly lobated nuclei of the monuclear and multinuclear cells together with positivity for the S-100 protein and the negative staining for the lysozyme are demonstrative of Langerhans' cell granulomatosis (Motoi et al. 1980; Kahn et al. 1983; Favara et al. 1983; Siegal et al. 1985). The lack of eosinophilis, the absence of grooved and infolded histiomonocytic cell nuclei, the negative stain for the S-100 protein and the positive reaction for the lysozyme antibody, characterize the pseudo-sarcoid granulomatous inflammation. Thus, the present work suggests a relatively simple work-up method to differentiate between the two types of granulomatous inflammation. The usefulness of the alpha 1 antitrypsin antibody in the differentiation of both types of macrophages (Isaacson et al. 1981) could not be confirmed in our material.

Involvement of the gastric wall in cases of diffuse histiocytosis X is rare and is only occasionally mentioned in the literature (Robbins and Cotram 1979; Kjeldsberg and Kim 1980). A still more unusual entity is the presence of isolated Langerhans' granulomata of the gastric wall (Vanek 1949; Vazquez and Ayestaran 1975). Although no explanation is given to account for the presence of this process, the most widely held opinion when the change is associated to lymphomas is that it represents a peculiar and poorly understood reaction to an unknown antigenic stimulus (Burns et al. 1983). A similar opinion is maintained in the case of Langerhans' cell granulomatosis of bone in adults (Wester et al. 1982).

This case may not be unusual. Further cases are needed to permit classification of the granulomatous reactions to tumours into two main categories: the common pseudo-sarcoid and the Langerhans' cell type.

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