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Langerhans' cell histiocytosis: possible association with malignant germ cell tumour

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Abstract

A rare case of adult onset Langerhans' cell histiocytosis associated with dysgerminoma in a 35 year old Chinese woman is reported. The patient had a history of dysgerminoma of left ovary 15 years previously and had undergone surgery followed by radiotherapy and an uneventful recovery. She presented again in March 1994, this time with a left clavicular mass, which was shown histologically to be Langerhans' cell histiocytosis. The report illustrates the probable association between the two lesions, with some discussion on the underlying pathogenesis.

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Keywords: Langerhans' cell histiocytosis, malignant germ cell tumour.

Langerhans' cell histiocytosis, previously known as histiocytosis X, consists of a group of clinicopathological disorders characterised by proliferation of Langerhans' cells. It may

sometimes occur in association with various types of malignant neoplasms.¹ Several case reports have been published concerning the possible association between Langerhans' cell histiocytosis and malignant lymphoma, especially Hodgkin's disease.²⁻⁴ de Camargo *et al*⁵ also described the coexistence of osteosarcoma, lymphoma, or medulloblastoma and Langerhans' cell histiocytosis in the same patient. Malignant germ cell tumour (MGCT) is associated with haematological neoplasia, mainly leukaemia.⁶⁻⁹ However, Langerhans' cell histiocytosis was not known to associate with MGCT, until a recent case report by Mandel *et al*,¹⁰ describing a family with clustering of MGCT and Langerhans' cell histiocytosis. We report a rare case of dysgerminoma and Langerhans' cell histiocytosis in a Chinese woman, which may give some clues to the possible association between the two disease entities.

Case report

A 35 year old Chinese woman first presented in 1979 with a left ovarian mass. Laparotomy revealed a dysgerminoma of the left ovary with metastasis involving the rectal wall. Total abdominal hysterectomy and bilateral salpingoophorectomy, together with partial resection of the rectum, were performed. There was no clinical evidence of other distant metastases. She was then given postoperative radiotherapy for one year. No adjuvant chemotherapy was given.

The postoperative course was uneventful until March 1994 when she noticed pain and swelling over left clavicle for two months. On x ray examination, a 1.5 cm diameter osteolytic lesion was observed in the left clavicle. The clinical diagnosis at that time was metastatic dysgerminoma. Curettage of the lesion was carried out, yielding several small fragments of brownish tissue. The specimen was promptly fixed in 10% neutral formalin and embedded in paraffin wax. Sections, 3 µm thick, were cut and stained with haematoxylin and eosin. The sections were then stained with a polyclonal antibody (diluted 1 in 200; Dako, Copenhagen, Denmark) directed against S-100 protein using the Streptavidin-biotin complex technique. A representative area was also selected from the paraffin wax block, dewaxed, rehydrated, post-fixed in 1% osmium tetroxide, embedded in epoxy resin, sectioned, and stained with uranyl acetate-lead citrate for subsequent ultrastructural study.

Histological examination of the left clavicular lesion revealed aggregates of ovoid cells ad-

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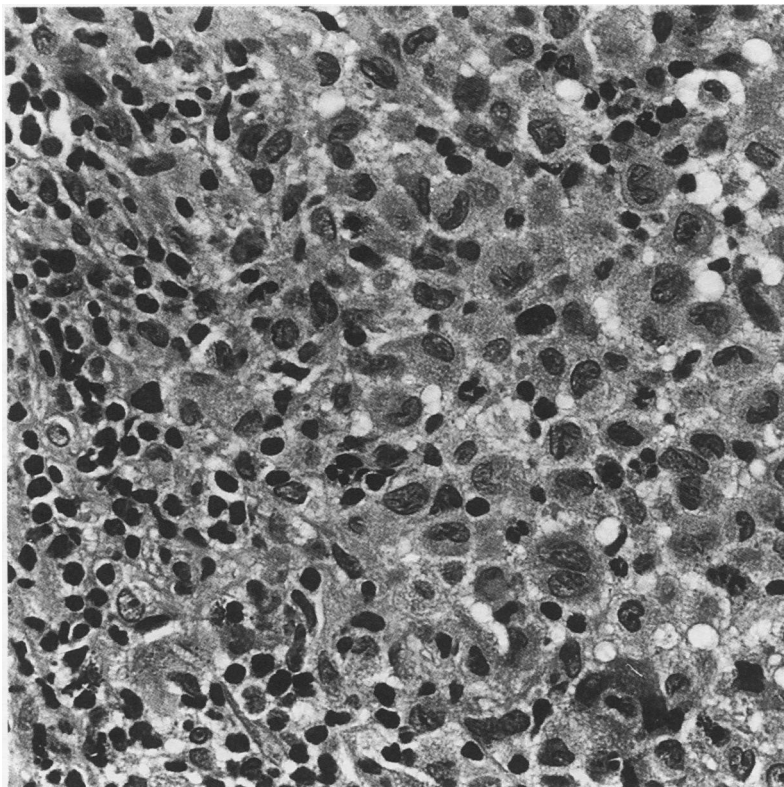


Figure 1 Histological section of the left clavicular bony curettage showing Langerhans' cell histiocytosis. Note the characteristic folded nuclei of Langerhans' cells. (Haematoxylin and eosin; × 500.)

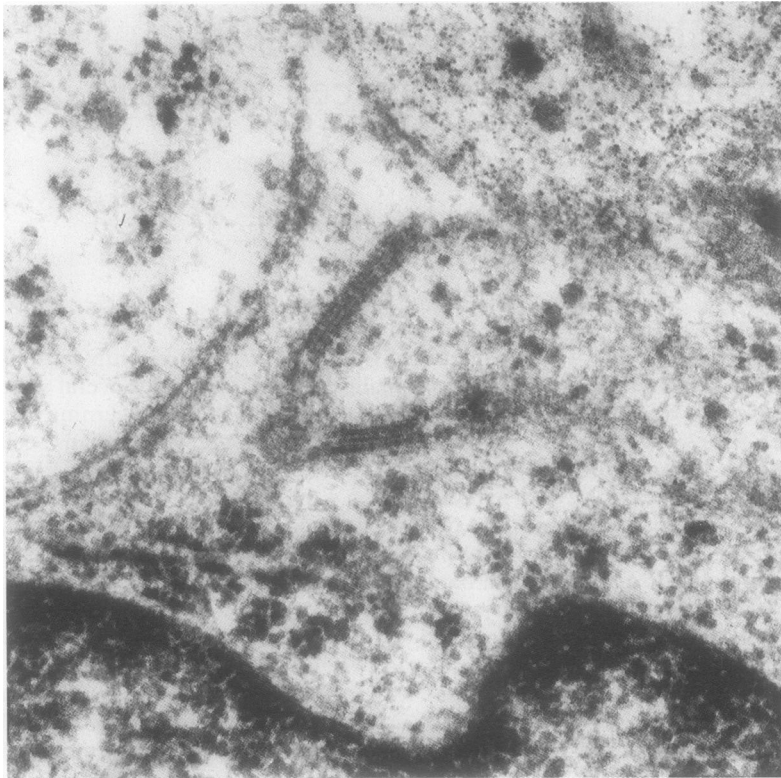


Figure 2 Electron micrograph of a Langerhans' cell showing characteristic intracytoplasmic Birbeck's granules in the perinuclear region. Note the barely discernible "zip-like" periodic core of the granules with terminal expansion. (Uranyl acetate-lead citrate; $\times 40\,000$.)

mixed with small lymphocytes and occasional eosinophils. The ovoid cells had deeply folded nuclei with a characteristic "coffee bean" appearance, fine chromatin, inconspicuous nucleoli, eosinophilic cytoplasm, and ill-defined cell borders (fig 1). Many of these cells expressed S-100 protein. Ultrastructural examination revealed the presence of intracytoplasmic Birbeck's granules in the perinuclear region of some of the Langerhans' cells (fig 2). The overall features were those of Langerhans' cell histiocytosis. Bone scan and skeletal x ray showed no other bony lesions and there was no other evidence of systemic involvement by Langerhans' cell histiocytosis. The peripheral blood examination was unremarkable. There was no clinical evidence of recurrence of dysgerminoma.

Discussion

Langerhans' cell histiocytosis is now considered by some authors to be a probable non-neoplastic reactive proliferation of Langerhans' cells.^{11,12} The nature of the underlying stimuli is not known, though immune dysfunction and viral infections have been postulated.¹³ The diagnosis of Langerhans' cell histiocytosis is based mainly on the characteristic cellular morphology, appearances on immunohistochemistry, and the ultrastructural identification of Birbeck's granules in the cytoplasm. Occasional cases of Langerhans' cell histiocytosis associated with malignant lymphoma, especially Hodgkin's disease, have been reported,²⁻⁴ mainly coexisting with lymphoma

in the same lymph nodes. One possible explanation is that the lymphoma cells may provide a direct or indirect stimulus for the proliferation of these Langerhans' cells.

MGCT, as the name implies, is a malignancy arising from germ cells which may have the potential to differentiate along different lines including yolk sac, trophoblasts and embryonic tissue. Occasional cases of mediastinal, non-seminomatous MGCT associated with haematological malignancies have been reported.⁶⁻⁹ Three hypotheses have been put forward^{6,7,14}: (1) leukaemic differentiation of the malignant germ cells; (2) induction of leukaemia by an unknown factor secreted by the germ cell tumour; and (3) the leukaemia and the germ cell tumour may arise independently of each other. In 1989 Chaganti *et al*⁸ described a case of mediastinal yolk sac tumour with later leukaemic differentiation, as both tumours showed identical cytogenetic changes. Their results were in agreement with the first hypothesis. Mediastinal yolk sac tumour may also be associated with malignant histiocytosis, which may be related to the secretion of macrophage colony stimulating factor or a similar substance by the yolk sac elements.¹⁴ However, there is no previous reported case in the English literature mentioning the occurrence of Langerhans' cell histiocytosis and MGCT in the same patient. Our case represents a rare case documenting an occurrence of adult onset Langerhans' cell histiocytosis 15 years after the diagnosis of dysgerminoma.

In 1994 Mandel *et al*¹⁰ described a family with MGCT and Langerhans' cell histiocytosis occurring in different family members. The patient with Langerhans' cell histiocytosis shared an identical haplotype with her two sisters who had a yolk sac tumour and dysgerminoma, respectively. Their postulation of an association between Langerhans' cell histiocytosis and MGCT is in agreement with our observation. It is possible that Langerhans' cell histiocytosis, like leukaemia, can share a common stem cell with MGCT; or else the histiocytosis may be the result of stimulation by a "factor" secreted by an occult focus of residual dysgerminoma. Alternatively, the Langerhans' cell and germ cell proliferations may be triggered by a common stimulus that acts on both types of cells. The occurrence of the two may also be coincidental. Detailed cytogenetic and molecular studies in the future may help to clarify the underlying pathogenic relationship.

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Papillary mucinous adenoma arising in adenomyomatous hyperplasia of the gall bladder

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Abstract

A case of papillary mucinous adenoma arising in adenomyomatous hyperplasia (AMH) of the gall bladder is reported. The lesion was unsuspected and discovered by routine palpation of the gall bladder during laparotomy. The adenoma developed within fundal AMH and showed cytological atypia. This case illustrates that neoplastic proliferation is indeed possible in AMH and challenges the classical opinion that AMH is devoid of neoplastic potential.

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Keywords: Gall bladder, cancer, adenomyomatous hyperplasia, adenomyomatosis, mucinous adenoma.

Methods

Sections of the gall bladder were fixed in 10% buffered formalin and embedded in paraffin wax. Paraffin wax sections 4 µm thick were stained with haematoxylin phloxine saffron. Histochemical stains including periodic acid Schiff (PAS), with and without diastase pretreatment, mucicarmine, and alcian blue were applied to the sections. Sections were also stained immunohistochemically with chromogranin (Boehringer Mannheim, Indianapolis, Indiana, USA) monoclonal antibodies using the avidin-biotin peroxidase technique, as described previously.⁹

Results

PATHOLOGICAL FINDINGS

On gross examination, the fundus of the acalculous gall bladder showed a dome shaped, cystic lesion measuring 2 × 1.3 × 1 cm. Microscopically, the gall bladder mucosa showed normal luminal folds lined by a single layer of columnar epithelium. The stroma was slightly fibrotic and contained lymphocytes in small clusters. AMH was identified within the wall of the fundus as the typical multiple anastomosing, epithelium lined extrusions extending between bundles of hyperplastic smooth muscle. Foveolar type mucinous metaplasia of the hyperplastic epithelium was also present. A large cyst measuring 11 × 5 mm was observed in continuity with AMH. Its lining was composed of tall mucinous cells with focal formation of papillae (figs 1 and 2). A large villous polypoid lesion formed of anastomosing fronds protruded into the cystic space. The fibrovascular stroma of the papillae was infiltrated by lymphocytes and plasma cells. Most of the fronds were lined by a single layer of benign mucus cells, although focal cellular tufting and nuclear atypia were present.

Adenomyomatous hyperplasia (AMH), also known as adenomyomatosis, is the most frequently diagnosed pseudotumour of the gall bladder.¹ Although classically considered to be a hyperplastic lesion, recent reports showed not only a causative relation between AMH and gall bladder carcinoma, but also actual neoplastic degeneration arising in AMH.²⁻⁸ Here, we report a unique case of adenomatous changes and evidence of neoplastic potential in AMH.

Case report

An 86 year old woman was admitted for surgery following a diagnosis of adenocarcinoma of the left colon. A preoperative workup showed no evidence of metastatic tumour and a left hemicolectomy was performed. At surgery, palpation of the gall bladder revealed a small soft mass at the tip of the fundus and a cholecystectomy was performed. The postoperative course was uneventful and the patient is alive and well 17 months after surgery.

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