A case of rapidly enlarging unilocular thymic cyst

Thymic cysts occur relatively rarely and account for only about 3% of all anterior mediastinal masses. Although thymic cysts usually grow very slowly, there have been three reported cases of unilocular thymic cysts that enlarged rapidly as a result of intra-cystic haemorrhage: two cases occurred in children with aplastic anaemia and one occurred in a 13 year old boy with no other symptoms. Here, we present a case of a unilocular thymic cyst, which appeared within one year, was associated with chronic inflammation, and had findings different from the cases reported previously.

The patient was a 63 year old man, who had been well with no apparent symptoms of disease. There was no history of trauma. He complained of dull anterior chest pain in April 2001, and a chest x-ray film showed an abnormal shadow in the left mediastinum. A chest x-ray that had been taken one year before for a routine medical examination had shown no abnormality (fig 1). Computed tomography and magnetic resonance imaging showed a unilocular cyst measuring 8 × 6 cm in the left side of the anterior mediastinum (fig 2). The cyst was sharply demarcated from the mediastinal fat. Haematological and laboratory examinations showed no inflammation.

Thoracoscopic surgery, with a left thoracic approach, was conducted on 8 May 2001. The cyst originated in the thymic tissue and adhered extensively to the left upper lobe of the lung. The cyst and its neighbouring thymic tissue were resected completely.

The cyst contained a brownish fluid, the cytology of which showed numerous old red blood cells with some lymphocytes and macrophages. On gross macroscopic examination, the cyst was unilocular and the cyst wall was of varying thickness up to 5 mm. The whole of the resected material was examined histologically by making 22 sliced sections. The cyst wall was lined mostly with cuboidal epithelium, but without respiratory type epithelium. There were scattered thymic tissues and also elongated branching strands of thymic tissues within the wall (small arrows) (haematoxylin and eosin stain; original magnification, ×36).

The main histological features of the MTCs included multiple cystic cavities partially lined by squamous, columnar, or cuboidal epithelium; scattered nests of non-neoplastic thymic tissue within the cyst walls; and severe acute and chronic inflammation accompanied by fibrovascular proliferation, necrosis, haemorrhage, and granulation tissue formation. They concluded that the MTCs probably resulted from cystic transformation in the ductal epithelial formations of the branchial pouch or from a related process induced by acquired inflammation. Our present case showed pathological findings similar to those of MTC except...
that it was unilocular. We believe that, although our present case was not an MTC, it could have originated from a process similar to that leading to MTC development, and could have been enlarged by intracystic haemorrhage as a result of idiopathic, chronic inflammation.

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References

Fatal disseminated toxoplasmosis in a toxoplasma seropositive liver transplant recipient

Disseminated toxoplasmosis is a severe disease that occurs in immunocompromised patients but has been rarely reported after liver transplantation. We describe the first case of fatal disseminated toxoplasmosis in a toxoplasma seropositive liver transplant recipient with a documented lack of a rise in specific IgG.

A 53 year old patient underwent liver transplantation because of decompensated alcoholic cirrhosis. The patient was treated with antimycotic globulins and prednisolone. Tacrolimus was added and antithymocyte treatment stopped. Oral ganciclovir was given to prevent cytomegalovirus infection. On day 22, the patient developed fever with chills. Physical examination was normal and blood analysis revealed leucopenia (leucocytes, 700/22,000). Despite broad spectrum antimicrobial treatment and extracerebral toxoplasmosis.

Liver involvement: gondii

Liver (fig 1). Tachyzoites were also identified in the liver (fig 2), kidneys (endothelial cells), pancreas (acinar cells), and spleen on immunostaining using a specific anti-toxoplasma antibody (Biogencex, San Ramon, California, USA). Re-examination of the BAL revealed very rare tachyzoites.

Disseminated toxoplasmosis is a severe disease with a very high mortality rate, but treatment with pyrimethamine sulfadiazine or clindamycin can sometimes be effective.1 It occurs very rarely after liver transplantation,2,3 and can result from pri-


Incidence and prognostic significance of hypercalcaemia in B-cell non-Hodgkin’s lymphoma

Hypercalcaemia is considered to be rare in B-cell non-Hodgkin’s lymphoma (B-NHL).2 In this letter I report eight cases with this complication among 62 (7.1%) diagnosed with B-NHL over a period of five years. The diagnosis of B-NHL was established by morphology and immunohistochemistry of biopsy specimens, and staging was done by computed tomography scans of the chest and abdomen, together with bone marrow aspirate and trephine biopsy. There were 70 patients with high grade B-NHL, 32 of whom had advanced disease (stage III/IV). The remaining 42 had low grade B-NHL.

Five patients with high grade B-NHL presented with hypercalcaemia and another patient developed hypercalcaemia at the time of relapse. One patient with low grade B-NHL developed hypercalcaemia at the time of transformation to Richter’s syndrome. One other patient with low grade B-NHL developed hypercalcaemia at the time of relapse. All patients had advanced disease. Table 1 shows the details of the patients.

Median survival of the five patients with high grade B-NHL presenting with hypercalcaemia was 10 months. This was significantly shorter than the 47 other patients with advanced disease (21 months; p < 0.05) who did not present with hypercalcaemia. The median survival of all eight patients from the time of developing hypercalcaemia was only nine months.

All five patients (cases 1–5) presenting with hypercalcaemia initially responded to rehy-

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calcium concentration. Parathyroid hormone was undetectable in one patient and low normal in the other four. None of the patients had a paraprotein in the serum or urine or had bone marrow plasmacytosis. No lytic bone lesions were seen on skeletal survey. Once the diagnosis of B-NHL was established they were treated with standard chemotherapy protocols. None of these five patients achieved complete remission with the standard protocol or with further intensive chemotherapy and/or radiotherapy. During the course of the disease one patient had recurrent hypercalcaemia and required intravenous infusion of pamidronate on four occasions.

One patient (case 6) with high grade B-NHL presented in stage IIb and achieved complete remission with standard chemotherapy. He relapsed after 24 months in stage IVb with bone marrow involvement and hypercalcaemia. There was no plasmacytosis in the bone marrow and no paraprotein was detected. He was treated with intravenous pamidronate infusion with normalisation of serum calcium concentration. He showed only a partial response to intensive chemotherapy. Hypercalcaemia recurred terminally.

None of the 42 patients with low grade B-NHL presented with hypercalcaemia. One of these patients (case 7) transformed to high grade lymphoma (Richter’s syndrome) after 49 months. She presented initially with generalised lymphadenopathy and bone marrow involvement and achieved partial remission with chlorambucil. Her disease relapsed after 24 months but she again achieved partial remission with the same drug. She developed hypercalcaemia at the time of transformation. Hypercalcaemia did not respond to repeated intravenous infusion of pamidronate. Her disease showed no response to intensive chemotherapy and she died within two months.

The last patient (case 8) of this series presented with low grade B-NHL in stage IVa with bone marrow involvement. He was initially treated with chlorambucil and achieved partial remission. His disease relapsed after 15 months with hypercalcaemia. Repeat biopsy showed no change of the histological type and serum parathyroid hormone was low normal. Hypercalcaemia responded to intravenous pamidronate 90 mg and he achieved partial remission with CHOP. However, the remission lasted for only three months and both lymphadenopathy and hypercalcaemia recurred. He died of chest infection shortly afterwards. None of the eight patients had renal failure at the time of developing hypercalcaemia, although three of them developed renal impairment in the terminal stages of their disease.

Hypercalcaemia is supposed to be rare in B-NHL but several individual case reports have appeared over the years.9 No systematic study of hypercalcaemia in B-NHL has been published. Finkin and co-workers9 reported an 8.5% incidence of hypercalcaemia in newly diagnosed patients with high grade B-NHL. This incidence was similar to the present study (7%). Some patients in other reports showed radiological evidence of bone destruction but none of the patients in the present series had this feature.

Transformation of low grade lymphoma into high grade (Richter’s syndrome) is a rare and usually terminal complication. Hypercalcaemia has been reported previously in only one patient with Richter’s syndrome.10 The patient reported here showed total resistance to bisphosphonate treatment for hypercalcaemia, in addition to no response to intensive chemotherapy. This is not unusual for Richter’s syndrome and this patient died within a short period.

Hypercalcaemia appears to be rare in low grade B-NHL. None of the patients in the present series presented with this complication and only one patient with follicular centre cell lymphoma developed hypercalcaemia during the course of the disease. There appear to be no other reported cases of hypercalcaemia in patients with follicular centre cell lymphoma, although it has been reported in some patients with Waldenstrom’s macroglobulinaemia (lymphoplasmacytic lymphoma), another subtype of low grade B-NHL.11

The cause of hypercalcaemia in B-NHL appears to be humoral. A raised concentration of parathyroid hormone related protein was found in some patients but not in all.12 A close correlation between the concentration of this protein and hypercalcaemia was also found in some patients, which strongly suggests a causal role.13 The importance of the other humoral mediators of bone resorption, such as tumour necrosis factor α and interleukin 6, is conjectural.14 Hypercalcaemia is usually associated with a poor prognosis in malignant diseases. B-NHL appears to be no exception. It is concluded that hypercalcaemia is not rare in B-NHL, particularly in the high grade type, and carries a poor prognosis.

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References

Table 1 Details of the clinical and laboratory findings of the patients with hypercalcaemia and non-Hodgkin’s lymphoma (NHL)

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/ Sex</th>
<th>Type of NHL and stage at diagnosis</th>
<th>Time (months) from diagnosis to hypercalcaemia</th>
<th>Highest calcium value (mmol/l)</th>
<th>Recurrence of hypercalcaemia</th>
<th>Treatment</th>
<th>Response</th>
<th>Survival (months) from developing hypercalcaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>51/M</td>
<td>DLB IIB</td>
<td>At diagnosis</td>
<td>3.08</td>
<td>Recurred terminally</td>
<td>CIDEBOM</td>
<td>NR</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>23/M</td>
<td>DLBC</td>
<td>At diagnosis</td>
<td>4.05</td>
<td>No recurrence</td>
<td>DXR</td>
<td>NR</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>71/F</td>
<td>HGGM IVB</td>
<td>At diagnosis</td>
<td>4.16</td>
<td>Recurrent</td>
<td>CHOP</td>
<td>PR</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>70/F</td>
<td>DLBC IIB</td>
<td>At diagnosis</td>
<td>2.96</td>
<td>No recurrence</td>
<td>CIOP</td>
<td>NR</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>61/F</td>
<td>HGGM IVB</td>
<td>At diagnosis</td>
<td>2.92</td>
<td>No recurrence</td>
<td>CIOP</td>
<td>NR</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>57/M</td>
<td>DLBC IIB</td>
<td>24, at relapse</td>
<td>3.16</td>
<td>Recurred terminally</td>
<td>CIOP</td>
<td>CR</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>65/F</td>
<td>FCC IVA</td>
<td>49, at the time of transformation</td>
<td>3.02</td>
<td>No response to treatment</td>
<td>Chlorambucil</td>
<td>PR</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>74/M</td>
<td>FCC IVA</td>
<td>15, at relapse</td>
<td>3.27</td>
<td>Recurred terminally</td>
<td>Chlorambucil</td>
<td>PR</td>
<td>9</td>
</tr>
</tbody>
</table>

Normal calcium range, 2.2–2.6 mmol/l. Type of B-NHL: DLBC, diffuse large B cell; HGGM, high grade gastric maltoma; FCC, follicular centre cell. Chemotherapy protocols: C, cyclophosphamide; I, idarubicin; D, dexamethasone; E, etoposide; B, bleomycine; O, vincristine; M, methotrexate in BOM, melphalan in mini-BEAM, H, doxorubicin; P, prednisolone; A, ARA-C; DXR, radiotherapy. Response: CR, complete response; NR, no response; PR, partial response.
Paraffin wax embedded muscle is suitable for the diagnosis of muscular dystrophy

The article by Sheriff et al. on the use of paraffin wax embedded muscle for the diagnosis of muscular dystrophy illustrates some valid points, but some are questionable. Excellent results are illustrated and some retrospective studies of archival material will clearly be possible. However, many of us in the field of muscle pathology will be alarmed at the statement in the discussion that “...frozen muscle tissue is no longer necessary for the diagnosis of muscular dystrophy, with the exception of LGMD2F”. This statement is premature, inaccurate, and only deals with a limited number of muscular dystrophies. It also takes no account of the fact that the technique of neuromuscular disorder is not known before a biopsy is taken, so tissue must be prepared for all possible studies.

Enzyme histochemistry still has an important role, and requires frozen tissue.6 The authors take no account of the importance of immunoblotting, which requires frozen tissue, and that some defective proteins can only be studied on immunoblots (for example, calpain 3, responsible for limb girdle muscular dystrophy 2A).

No evidence of the diagnostic use of the technique is shown; only the known localisation of antibodies in control muscle. No assessment of reduced or partial protein expression is shown although this, in contrast to absent protein, occurs in many muscular dystrophies. It is essential that reduced expression is fully assessed in fixed material before fixation material is dispensed with.

Secondary abnormalities are also useful1 and the value of paraffin wax sections for the assessment of these is not known, or not possible. For example, the commercial antibodies to fetal myosin (Novocastra MHCn) and to laminin β1 (Chemicon) produce negative results with antigen retrieval, but both are important in muscular dystrophies.

The figures illustrate excellent morphology of paraffin wax embedded material. However, fig 1G,H shows rounded fibres which may be pathological or artefact; in frozen muscle of dystrophic muscle this is an important pathological feature, in addition, it is well known that wax embedding can cause unacceptable artefacts, and results differ from sample to sample and from laboratory to laboratory.

The number of gene defects responsible for a muscular dystrophy is increasing rapidly. It is not possible to know the type of material that will be required in the future, but a bank of frozen muscle will probably be the most versatile. Contrary to the comments on page 529, adequate freezing, storage, and orientation of frozen material is all possible with care, and fixed frozen sections give equivalent morphology of inflammatory cells.

It has taken decades to ensure that muscle samples are kept out of formalin so that a wide range of techniques can be applied. The role of antigen retrieval will probably increase, but the stage when everything, both now and in the future, can be performed on paraffin wax embedded material has not yet been reached. I hope all clinicians and muscle pathologists will take note of this and not set the clock back.

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References

Authors’ reply
The purpose of our article was not to belittle the value of frozen material in the advancement of muscle pathology diagnosis (that is, for western blotting), but to stress that we should not ignore humoral paraffin wax embedded sections. It is vital to emphasise that with the help of immunohistochemistry they facilitate the accurate diagnosis of many muscular dystrophies and other muscle pathologies, such as nemaline myopathy.

Dr Sewry’s comments point to negative results for laminin β1 and fetal myosin on paraffin wax embedded sections is currently valid, but antigen retrieval techniques are evolving and new antibodies are being developed, allowing larger antibody panels to be used on paraffin wax embedded tissue.

The question of the ease of interpretation of paraffin wax embedded versus frozen tissue is partly a matter of re-education. Adequate freezing, storage, and orientation of frozen material is no problem in specialist centres; freezing, storage, and orientation of frozen tissue is clearly valid, but antigen retrieval techniques are evolving and new antibodies are being developed, allowing larger antibody panels to be used on paraffin wax embedded tissue.

The question of the ease of interpretation of paraffin wax embedded versus frozen tissue is partly a matter of re-education. Adequate freezing, storage, and orientation of frozen material is no problem in specialist centres; freezing, storage, and orientation of frozen tissue is clearly valid, but antigen retrieval techniques are evolving and new antibodies are being developed, allowing larger antibody panels to be used on paraffin wax embedded tissue.

We are not turning back the clock, merely we are increasing the range of tissues that can be used for the diagnosis of muscular dystrophy.


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Author’s reply
I was very interested in Dr Twomey’s letter suggesting that growth hormone may be a possible link between skin tags and the atherogenic lipid profile. Unfortunately, we do not have growth hormone determinations in our patients so we are unable to test his hypothesis, although presumably it would not be too difficult to design such studies. The cutaneous manifestations of lipid disorders are relatively unexplained and unexplored. Why—for example, do xanthelasma or eruptive xanthoma appear at certain sites and not in every patient with lipid abnormalities? Interestingly, one of the patients in our study who had an atherogenic lipid profile also manifested bilateral ear lobe creases. The importance of this is unclear and also merits further study, particularly because these are thought to be associated with cardiovascular disease.”

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References

The role and histological classification of needle core biopsy in conjunction with fine needle aspiration cytology in the preoperative assessment of impalpable breast lesions

I read with interest the article on the role and histological classification of needle core biopsy (NCB) in conjunction with fine needle aspiration cytology (FNAC) in the preoperative assessment of impalpable breast lesions by Ibrahim et al. in the February 2001 edition of the journal.

These findings are at variance with the published literature. My own research on
FNAC of impalpable breast lesions was non-diagnostic (no epithelial cells) in 14% of cases. When this was combined with imaging (ultrasound) all of the non-diagnostic cases were resolved, with 70% showing no change on follow up, 17% producing benign histology, and 13% yielding a malignant outcome.

In a further study, I compared FNAC cytology with NCB at several anatomical sites, including the breast. NCB was only marginally better, occasionally offering additional information. This slight advantage resulted from the availability of tissue from the first and often the only pass for assessment of architecture and the performance of ancillary tests.

The main reasons for the abandonment of FNAC in favour of NCB in the preoperative management of patients with breast lesions are failure of the aspirator to produce diagnostic material and unfamiliarity of the interpreter with the subtleties of breast FNAC.

I believe that by taking an active role with on site management of the FNAC material and discussion with radiological colleagues, the cytopathologist could offer an FNAC service comparable to surgical pathology in sensitivity and very similar to frozen sections in specificity.

FNAC is cost effective, with consistent predictive value for the symptomatic lesions and very similar to frozen sections in ice comparable to surgical pathology in sensitivity.

We read with great interest the recently published article by Windrum et al about a mantle cell lymphoma presenting as a breast mass.1 A separate case of mantle cell lymphoma involving both breasts was also reported last year.

We wish to report the third case of a mantle cell lymphoma involving the breast, in this case presenting as bilateral breast masses. The patient is a 77 year old woman whose bilateral masses were palpated on routine physical examination. Core biopsies were performed and the biopsied tissues were processed routinely in our laboratory. All microscopic patterns were identical bilaterally. The entirety of the specimen consisted of a diffuse monomorphic population of small lymphocytes. Adipose tissue or residual ductal units were not identified. The immunohistochemical profile of the tumour was evaluated on 1 µm thick, dewaxed sections using the standard streptavidin–biotin immunoperoxidase technique with diaminobenzidine as chromogen.

The cells were strongly positive for CD5 (clone 54/F6; dilution, 1/80; Dako, Carpinteria, California, USA), cyclin D1 (clone AB-1; dilution, 1/100; Neomarkers, Fremont, California, USA), and bcl-2 (monoclonal; dilution, 1/40; Dako), but were negative for CD23 (clone MHM-6; dilution, 1/100; Dako). We interpreted this immunophenotypic profile as being most consistent with mantle cell lymphoma. Several types of lymphoma have been reported in the breast, with diffuse large B cell non-Hodgkin’s lymphoma being the most common.1 These three cases show that mantle cell lymphoma should be included in that differential diagnosis.

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References

Another case of mantle cell lymphoma presenting as breast masses

We read with great interest the recently published article by Windrum et al about a mantle cell lymphoma presenting as a breast mass.1 A separate case of mantle cell lymphoma involving both breasts was also reported last year.

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