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 intracystic 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 x 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 externally to the left upper lobe of the lung. The cyst and its neighboring 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 tissue within the wall [small arrows] (haematoxylin and eosin stain; original magnification, x36).

The wall of the cyst contains thymic tissues (large arrow) and also elongated branching strands of thymic tissues within the wall (fig 3). Reactive lymphoid hyperplasia with a germinal centre was not seen in the thymic tissue. In most areas, the cyst wall was thickened with granulation. The granulation tissue just below the intraluminal wall consisted mostly of newly formed blood vessels with lymphocyte and macrophage infiltration. There were few neutrophils. Some areas of the cyst wall showed abundant deposits of haemosiderin pigments. Immunohistochemical examination using anti-CD3 and anti-CD79a antibodies showed that the infiltrating lymphocytes were a mixture of both T and B cells. There was no indication of caseous necrosis or Langhans giant cells. The patient is now doing well without recurrence of the cyst four months after surgery.

Most thymic cysts are found incidentally during chest x-ray or computed tomography procedures, and they usually do not enlarge in a short period. The pathogenesis of thymic cysts is currently thought to be congenital, originating from branchial pouch remnants. However, in our present case the thymic cyst was different from the congenital form because it enlarged rapidly. The cytological and histological findings were also different from those of congenital thymic cysts in the following respects: (1) the fluid within the cyst showed numerous old red blood cells with some lymphocytes and macrophages; (2) cyst wall showed non-specific chronic inflammation.

Although the cyst in our present case was unilocular, its pathological features were something like those of a multilocular thymic cyst (MTC), as reported by Suster and Rosai. They reported the clinical and pathological features of 18 cases of anterior mediastinal MTC, collected from personnel consultant files. 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.
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 intracytic 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 antibiotics (vancomycin and prednisolone). Tacrolimus was added and antithymocyte globulin and cidofovir were added and leucocytes increased to 9400/mm³. Ganciclovir was discontinued and leucocytes increased to 9400/mm³. A 53-year-old patient underwent liver transplantation because of decompensated alcoholic cirrhosis. The patient was treated with antibiotics (vancomycin and prednisolone). Tacrolimus was added and antithymocyte globulin and cidofovir were added. Ganciclovir was discontinued and leucocytes increased to 9400/mm³. Despite broad spectrum antimicrobial treatment (cefazidime, ciprofloxacin, teicoplanine, and fluconazole), the patient developed a diffuse bilateral interstitial pneumonitis with respiratory distress. On day 30 a bronchoalveolar lavage (BAL) was performed but no pathogens were identified. On day 36 the patient died of refractory septic shock. Necropsy revealed disseminated toxoplasmosis. Lesions were identified on haematoxylin and eosin stained sections within the heart (pseudocysts in myocytes and foci of necrotic myocytes with free tachyzoites) and the lungs (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 gondii antibody (Biogenex, 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 primary infection or reactivation, as in our patient. In addition to the heavy immunosuppression, leucopenia, probably related to the ganciclovir treatment, may have contributed to this reactivation in our patient.

The diagnosis of toxoplasmosis infection is difficult. Indeed, serological changes (rise in baseline antibody titres or the development of antibodies) are frequently lacking in immunocompromised patients. So far, our case is the only one described in a toxoplasma seropositive liver transplant recipient with no increase in antibodies titres, which were regularly measured. This clearly shows that serological data are unreliable in liver transplant recipients, as in other immunocompromised patients.

Disseminated toxoplasmosis is associated with fever and a multivisceral involvement. The organs most often involved are the lungs, heart, and brain.4,5 Visualization of tachyzoites in BAL fluid by Giemsa staining is difficult because of their small size. Immunostaining of tissues dramatically improves toxoplasma detection.6 The polymerase chain reaction (PCR) can also be performed on BAL fluid or blood samples.6 The use of both morphology and PCR improves the sensitivity of the diagnosis.6

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References

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).1 In this letter I report eight cases with this complication among 112 patients infected with the human immunodeficiency virus (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 scan of the chest and abdomen, together with bone marrow aspirate and trephine biopsy. There were 70 patients with high grade B-NHL, 52 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 rehydration and pamidronate 90 mg intravenously, with normalisation of the serum levels within three days. Although the management of hypercalcaemia in B-NHL is not well documented, it is generally recommended that initial therapy involves hydration and pamidronate, with or without a bisphosphonate. Our patients were treated as described above and all responded as expected. However, despite relapse at the site of the primary lesion and palliative chemotherapy, three patients died from progressive disease within six months. The remaining two patients required further treatment for hypercalcaemia and have now been treated with pamidronate or ibandronate, with normalisation of serum calcium levels.

Five patients with low grade B-NHL presented with hypercalcaemia and all responded to hydration and pamidronate 90 mg intravenously, with normalisation of serum calcium levels. Two patients died from progressive disease within 10 months. The remaining three patients required further treatment for hypercalcaemia and have now been treated with pamidronate or ibandronate, with normalisation of serum calcium levels.

The use of both morphology and PCR improves the sensitivity of the diagnosis.

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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>Sex</th>
<th>Age/</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>M</td>
<td>51</td>
<td>DLB IIIB</td>
<td>At diagnosis</td>
<td>3.08</td>
<td>Recurred terminally</td>
<td>CIDEBOM</td>
<td>NR</td>
<td>11</td>
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<tr>
<td>2</td>
<td>M</td>
<td>23</td>
<td>DLBC</td>
<td>At diagnosis</td>
<td>4.05</td>
<td>No recurrence</td>
<td>DIXR PR</td>
<td>PR</td>
<td>10</td>
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<tr>
<td>3</td>
<td>F</td>
<td>71</td>
<td>HGGM IVB</td>
<td>At diagnosis</td>
<td>4.16</td>
<td>Recurrent</td>
<td>CHOP PR</td>
<td>PR</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>70</td>
<td>DLBC</td>
<td>At diagnosis</td>
<td>2.96</td>
<td>No recurrence</td>
<td>CIOP PR</td>
<td>NR</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>61</td>
<td>HGGM IVB</td>
<td>At diagnosis</td>
<td>2.92</td>
<td>No recurrence</td>
<td>CIOP PR</td>
<td>PR</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>57</td>
<td>DLBC</td>
<td>24, at relapse</td>
<td>3.16</td>
<td>Recurred terminally</td>
<td>CIOP PR</td>
<td>CR</td>
<td>5</td>
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<tr>
<td>7</td>
<td>F</td>
<td>65</td>
<td>FCC</td>
<td>49, at the time of transformation</td>
<td>3.02</td>
<td>No response to treatment</td>
<td>Chlorambucil PR</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>74</td>
<td>FCC</td>
<td>15, at relapse</td>
<td>3.27</td>
<td>Recurred terminally</td>
<td>Chlorambucil PR</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

Normal calcium range, 2.2–2.6 mmol/l. Type of B-NHL: DLB, diffuse large B cell; HGGM, high grade gastric mantle; FCC, follicular centre cell. 

References
Paraffin wax embedded muscle is suitable for the diagnosis of muscular dystrophy

The article by Sheriff et al.1 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 type of neuropathy or 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.1 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 account is taken 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).

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 MHC11) and to laminin β1 (Chemicon) produce negative results with antigen retrieval, but both are important in muscular dystrophies.

I am interested in 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 in conjunction with fine needle aspiration cytology in the preoperative assessment of impalpable breast lesions. 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 xanthelasmas or eruptive xanthomas 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 carotid lobe creases. The importance of this is unclear and also merits further study, particularly because these are thought to be associated with cardiovascular disease.1

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 humble 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 Twomey’s comments are to be welcomed; we agree that 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 case 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; however, referred frozen tissue from centres unaccustomed to dealing with them is often inadequate, and in those situations paraffin wax embedded tissue can provide the diagnosis.

Moreover, there is an opportunity to study archival tissue or tissue taken at necropsy when there has been no clinical suspicion of muscle disease.

We are not turning back the clock, merely suggesting that much can be achieved using routinely processed tissue. In an ideal world, any tissue should be preserved for many different techniques (morphological, enzymatic, protein, DNA, and RNA analyses). However, we live in a world with constraints. Given a choice of badly frozen/partially thawed muscle or paraffin wax embedded sections for morphological interpretation (with the help of immunohistochemistry) the latter is more likely to be helpful.

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Skin tags and the atherogenic lipid profile

I read the short report by MA Crook on “Skin tags and the atherogenic lipid profile” with interest. Multiple skin tags are frequently found in patients with acromegaly and may predict colonic polyps.1 Hypersecretion of growth hormone induces insulin resistance, with glucose intolerance occurring in 29–45% and clinical diabetes mellitus in 10–20% of cases. Hypertriglyceridaemia occurs in 19–44% of patients with acromegaly and is probably the result of decreased hepatic triglyceride lipase and lipoprotein lipase activities because the activities of these enzymes rise after successful lowering of hormone values. Could increased growth hormone concentrations be the link between skin tags, insulin resistance, and the atherogenic lipid profile in these four cases?

References

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 xanthelasmas or eruptive xanthomas 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 carotid lobe creases. The importance of this is unclear and also merits further study, particularly because these are thought to be associated with cardiovascular disease.

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

References
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 79% showing no change on follow up, 17% producing benign histology, and 13% yielding a malignant outcome. The inadequacy rate, sensitivity, and positive predictive value for the symptomatic lesions were 4%, 92.2%, and 100%, respectively.

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 results in experienced hands; sensitive, with relatively few false negative results; and highly specific.

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References

CSF spectrophotometry in the diagnosis of subarachnoid haemorrhage

The recent “Best Practice” article by Dr Cruickshank does not mention pseudoxanthochromia caused by contamination of the cerebrospinal fluid (CSF) with iodine solution at the time of sample collection. The problem seems to occur when iodine solution is applied to the patient’s skin and the operator’s glove, and then the specimen is contaminated. When combined with a traumatic tap in a normal patient, this technique can mimic the appearance of subarachnoid haemorrhage. Clues to the presence of pseudoxanthochromia are iodine staining around the outside of the specimen container, and the absorbance maximum of iodine is typically 445 nm compared with bilirubin at 450–460 nm. Preparation of the skin with chlorhexidine instead of iodine avoids this source of potential confusion.

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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.2

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 4 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 HM-H-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.3 These three cases show that mantle cell lymphoma should be included in that differential diagnosis.

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