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).

Histological examination of the resected material with haematoxylin and eosin stain 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; and (2) the 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. 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 intracytic haemorrhage as a result of idiopathic, chronic inflammation.

H Nomori, H Hori, K Suemasu
Department of Thoracic Surgery, Saiseikai Central Hospital, 1-4-17 Mita, Minato-ku, Tokyo 108-0073, Japan; hernomori@q9.so-net.ne.jp

H Orikasa, K Yamazaki
Department of Pathology, Saiseikai Central Hospital

K Nakano
Department of Internal Medicine, Tokyo Senbai Hospital, Tokyo, Japan

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 antilymphocyte globulins and prednisolone. Tacrolimus was added and antithymocyte globulin because of decompensated alcohol-specific IgG.

Liver transplantation was performed on day 14, and on day 17 the patient continued to have respiratory distress. On day 20, the patient developed fever and a multivisceral involvement. Physical examination was normal, and a blood analysis revealed leucopenia (leucocytes, 700/mm³), blood, urine, and bile cultures were repeatedly negative. Concentrations of antibodies against aspergillus and candida did not increase. Our patient was toxoplasma seropositive before the liver transplantation (specific IgG, 13 IU/ml) and the weekly serological follow up showed no rise in IgG titre and an absence of IgM.

Chest radiography, abdominal ultrasound, and transoesophageal ultrasonography revealed no abnormality. Ganciclovir was discontinued and leucocytes increased to 9400/mm³. Despite broad spectrum antimicrobial treatment (cefazidine, 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 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. It occurs very rarely after liver transplantation, 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 multisecral involvement. The organs most often involved are the lungs, heart, and brain. Visualization of tachyzoites in BAL fluid by Giemsa staining is difficult because of their small size. Immunostaining of tissues dramatically improves toxoplasma detection. The polymerase chain reaction (PCR) can also be performed on BAL fluid or blood samples. The use of both morphology and PCR improves the sensitivity of the diagnosis.

D Wendum, N Carbonell, M Svrek, O Chazoulières, J-P Fleju
Departments of Pathology and Hepatology, Hôpital Saint-Antoine, AP-HP, 184 Rue du Faubourg Saint-Antoine, 75571 Paris Cedex 12, France; dominique.wendum@atp-hop-paris.fr

References

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 IIIB and achieved complete remission with CHOP. However, the remission lasted for only three months and both lymphadenopathy and bone marrow involvement 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. ¹ No systematic study of hypercalcaemia in B-NHL has been published. Firkin and co-workers 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 have shown 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. 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.

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. ² A close correlation between the concentration of this protein and hypercalcaemia was also found in some patients, which strongly suggests a causal role. ³ The importance of the other humoral mediators of bone resorption, such as tumour necrosis factor α and interleukin 6, is conjectural. ⁴

Hypercalcaemia is usually associated with a poor prognosis in malignant diseases. ⁵ 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.

<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 IIIB</td>
<td>At diagnosis</td>
<td>4.05</td>
<td>No recurrence</td>
<td>DIXR</td>
<td>PR</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>9</td>
</tr>
<tr>
<td>4</td>
<td>70/F</td>
<td>IIB DLBL</td>
<td>At diagnosis</td>
<td>2.96</td>
<td>No recurrence</td>
<td>DIXR</td>
<td>NR</td>
<td>2</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>PR</td>
<td>9</td>
</tr>
<tr>
<td>6</td>
<td>57/M</td>
<td>IIB DLBL</td>
<td>24, at relapse</td>
<td>3.16</td>
<td>Recurred terminally</td>
<td>CIOP</td>
<td>PR</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>65/F</td>
<td>FCC</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 malignancy; FCC, follicular centre cell.

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

References
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 type of necrotic or dystrophic 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. The authors take no account of the importance of immunoblotting, which requires frozen tissue, and that some definitive 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 definitive proteins can only be studied on immunoblots (for example, calpain 3, responsible for limb girdle muscular dystrophy 2A).

Secondary abnormalities are also useful 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.

Laminin 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 frozen tissue is dispensed with.

The question of the ease of interpretation of paraffin wax embedded versus frozen tissue 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 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 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. The inadequacy rate, sensitivity, and positive predictive value for the symptomatic lesions were 4%, 92.2%, and 100%, respectively.1

In a further study, I compared FNAC cytology with NBC 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.2

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.3

FNAC is cost effective, with consistent results in experienced hands; sensitive, with relatively few false negative results; and highly specific.

I M Zardawi
Mayne Health, Newcastle Laboratory, PO Box 801, Newcastle, New South Wales, Australia; zardawi@hotmail.com

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.

S A Iversen
Brighton Healthcare NHS Trust, Eastern Road, Brighton BN2 5BE, UK; Andrew.Iversen@bsuh.nhs.uk

Reference

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.4 A separate case of mantle cell lymphoma involving both breasts was also reported last year.5

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 entire 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 MMH-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.6 These three cases show that mantle cell lymphoma should be included in that differential diagnosis.

O Fadare, P Shukla
Department of Pathology, Yale-New Haven Hospital/Yale University School of Medicine, 20 York Street, East Pavilion 2–631, New Haven, CT 06504, USA; Oluwole.fadare@yale.edu

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Skin tags and the atherogenic lipid profile

P Twomey

doi: 10.1136/jcp.55.8.639-a

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