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 × 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.

Thoracoscopy 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 tissue 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; 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 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.

At 53 year old patient underwent liver transplantation because of decompensated alcoholic cirrhosis. The patient was treated with antilymocyte globulins and prednisolone. Tacrolimus was added and antilymocyte 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/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 (ceftazidime, ciprofloxacin, teicoplanine, and fluconazole), the patient developed a diffuse bilateral interstitial pneumonitis with respiratory distress. On day 30 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 (pseudocytes 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. 1 It occurs very rarely after liver transplantation, and PCR can also be performed on BAL fluid or tissue samples. 2 The use of both morphology and PCR improves the sensitivity of the diagnosis. 3

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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). In this letter I report eight cases with this complication among 121 patients (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 rehydration and pamidronate 90 mg intravenously, with normalisation of the serum calcium level. The remaining three patients (cases 6–8) were not treated with pamidronate and had normalisation of the serum calcium level with treatment with denosumab.

Table 1: Details of the patients

<table>
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<tr>
<th>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Stage</th>
<th>B-NHL grade</th>
<th>Relapse</th>
<th>Richter’s syndrome</th>
<th>Median survival</th>
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One patient with low grade B-NHL developed hypercalcaemia at the time of relapse. This patient 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.

Three patients presented with hypercalcaemia (cases 1–5). The remaining three patients (cases 6–8) 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 calcium level. The remaining three patients (cases 6–8) were not treated with pamidronate and had normalisation of the serum calcium level with treatment with denosumab.

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Hypercalcaemia was found in some patients but not in all. A close correlation between the concentration of this protein and hypercalcaemia was also found in some patients, which strongly suggests a causal role. The importance of the other humoral mediators of bone resorption, such as tumour necrosis factor α and interleukin 6, is conjectural.

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
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 LGMD2B”. 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 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. The authors take no account of the importance of immunohistochemistry, 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 any conclusion is drawn.

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.

I illustrate excellent morphology of paraffin wax embedded material. However, fig. 1G, H shows rounded fibres that 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 520, adequate freezing, storage, and orientation of frozen material are 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 new 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 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 Sewry’s comments on 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; 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, enzymic, 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 colon 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?

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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 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.

In a further study, I compared FNAC cytology with NBC at several anatomical sites, including the breast. NBC 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 NBC 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 adequacy rate, sensitivity, and positive predictive value.

We believe that our use of FNAC, as used in routine clinical practice, is sufficient in the diagnosis of breast lesions.

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 (monclonal; 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. 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 bilateral 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. A separate case of mantle cell lymphoma involving both breasts was also reported last year.