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 film taken one year before presentation (left) shows no abnormality, whereas the film taken at presentation (right) shows the abnormal shadow at the left mediastinum.

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 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 antiretroviral globulins and prednisolone. Tacrolimus was added and antithymocyte treatment stopped. Oral ganciclovir was given in spite of the ganciclovir treatment, may have contributed to the heavy immunosuppression, as in our patient. In addition to the heavy immunosuppression, leukopenia, probably related to the ganciclovir treatment, may have contributed to the heavy immunosuppression as 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 multisystemic 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.

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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 (7.1%) diagnosed with B-NHL over a period of five years. The diagnosis of B-NHL was established by morphology and immunohistochernistry 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 dehydration and pamidronate 90 mg intravenously, with normalisation of the serum
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 II B and achieved complete remission with standard chemotherapy. He relapsed after 24 months in stage IV B 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 showed radiological evidence of bone destruction 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. No systematic study of hypercalcaemia in B-NHL has been published. Firkin and co-workers’ reported an 8.9% 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. 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 macro-globulinemia (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. 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 alpha 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

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>NHL type and stage</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>DLB IIIB</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>M</td>
<td>DBBC</td>
<td>At diagnosis</td>
<td>4.05</td>
<td>No recurrence</td>
<td>DEXR</td>
<td>NR</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>HGGM</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>F</td>
<td>DBBC</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>F</td>
<td>HGGM</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>M</td>
<td>DBBC</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>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>M</td>
<td>FCC</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 NHL: DLBC, diffuse large B cell; HGGM, high grade gastric malignancy; FCC, follicular centre cell.

Chemotherapy protocols: C, cyclophosphamide; I, ifosfamide; D, dexamethasone; E, etoposide; B, bleomycin; 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 type of neuro- muscular 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 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 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.

Dr Sewry’s comment about 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 antibodys 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 (immunohistochemical, enzymic, protein, DNA, and RNA analyses). However, we live in a world with constraints. Given a choice of badly frozen/patchily 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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References

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. 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

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. 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.

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References


CSF spectrophotometry in the diagnosis of subarachnoid haemorrhage

The recent “Best Practice” article by Dr Cruickshank1 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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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.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 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.3 These three cases show that mantle cell lymphoma should be included in that differential diagnosis.

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References
