Rare presentation of intestinal amyloidosis with acute intestinal pseudo-obstruction and perforation

Gastrointestinal manifestations of amyloidosis include dysmotility and pseudo-obstruction.1 Here, we report an exceptional case of acute small bowel obstruction followed by perforation in a patient with documented light chain amyloidosis (AL). A 39 year old Chinese woman had a 10 year history of xerostomia, night sweats, and weight loss after the age of 30. She had a family history of amyloidosis and a paternal grandmother suffering from primary amyloidosis (AA) was asymptomatic. Twelve years previously, she had received six months of weekly injections of alternaria, cladosporium, helminthosporium, and stemplyum as immunotherapy in France. She had no pets, but had noticed mould on her bedroom and bathroom windows.

Skin prick testing and specific IgE results suggested type 1 hypersensitivities to Quorn, Alternaria alternata, Aerobasidium pullulans, cat dander, and grass pollen (table 1). Scrapings from her bathroom and bedroom windows grew heavy growths of Cladosporium sphaerospermum, Rhodotorula sp, Aerobasidium pullulans, and fewer numbers of non-sporing mould (Mycology Reference Laboratory, Bristol, UK). The patient's rhinitis symptoms improved with the regular use of long acting antihistamines, replacing her windows, and controlling humidity at home. She has tried to avoid fungi-contaminated food and has had no further episodes of angio-oedema.

Quorn mycoprotein is produced by Marlow Foods Ltd, from the fungus Fusarium venenatum.2–4 Approximately 1/140 000 consumers report adverse reactions after eating Quorn. Ten such complainants had negative skin prick tests to an aqueous extract of fresh Quorn.3 Thirty three Quorn production workers did not have high titres of IgE specific to Quorn, although six known mould allergic subjects did.1 This study suggested that the risk of sensitisation to Quorn was low, but that patients who were allergic to mould might react adversely to inhaled or ingested mycoprotein. Crossreactivity studies showed that Quorn shared multiple allergenic determinants with Aspergillus fumigatus, Cladosporium herbarum, and Alternaria alternata.1 Allergen preparations for skin prick testing and specific IgE tests are poorly standardised, and may differ in their potency as much as possible.

Sensitivity to Quorn mycoprotein (Fusarium venenatum) in a mould allergic patient

A 27 year old female civil servant presented with five episodes of peri-orbital, tongue, and neck angio-oedema with wheeze and shortness of breath. One of these episodes occurred a few minutes after eating a Quorn burger. She had a 20 year history of perennial sneezing, rhinorrhea, and itchy throat, occurring throughout the day and night, but no cough or wheezing. While on holiday in Mauritius she was asymptomatic. Twelve years previously, she had received six months of weekly injections of alternaria, cladosporium, helminthosporium, and stemplyum as immunotherapy in France. She had no pets, but had noticed mould on her bedroom and bathroom windows.

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Table 1 Allergy testing results

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Skin prick testing</th>
<th>Specific IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wheal (mm)</td>
<td>Flare</td>
</tr>
<tr>
<td>Grass pollen mix</td>
<td>3</td>
<td>++</td>
</tr>
<tr>
<td>Cat dander</td>
<td>4</td>
<td>++</td>
</tr>
<tr>
<td>Dermatophagoides pteron conspirus</td>
<td>0</td>
<td>ND</td>
</tr>
<tr>
<td>Dermatophagoides fariniae</td>
<td>0</td>
<td>ND</td>
</tr>
<tr>
<td>Fresh Quorn mixed with saline</td>
<td>7</td>
<td>++</td>
</tr>
<tr>
<td>Alternaria alternata</td>
<td>2</td>
<td>4.1</td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Cladosporium herbarum</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Aerobasidium pullulans</td>
<td>ND</td>
<td>0.8</td>
</tr>
</tbody>
</table>

In the skin prick test histamine produced a 6 mm wheal and + + flare, and saline produced a 0 mm wheal and no flare. Results were those seen 15 minutes after using AUK standardised lancets and skin prick test reagents. The specific IgE tests were performed by Sheffield Protein Reference Unit. When Quorn was used as the allergen a small piece of fresh quorn burger was mixed with saline, and a single drop of liquid from the mixture was put on the patient’s forearm as with the other skin prick reagents. No specific IgE was detected to two other fusarium species, F culmorum and F oxysporum. Alternaria alternata, Aspergillus fumigatus, and Cladosporium herbarum are reported to crossreact with Quorn. There was a heavy growth of Aerobasidium pullulans in the patient’s home (no tests available to other species isolated).

ND, not done.
200–3000 fold. The diversity of fungal allergens is a challenge for successful immunotherapy. A reduction in occupational exposure to fungi may be achieved using helmets with filtered air (which may remove up to 98% of spores), improving ventilation, and controlling humidity. Fungi in dwellings generally have no specialised spore liberation mechanisms and largely depend on disturbance. Spore wall structure determines whether allergens are already available on the surface, and whether the spores can remain airborne.

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References

Tumour cells produce receptor activator of NF-κB ligand (RANKL) in skeletal metastases

Osteolytic bone destruction is a common complication of tumours that metastasise to bone. Several solid tumours, most notably breast carcinoma, lung carcinoma, and prostate carcinoma, commonly metastasise to bone in patients with advanced disease, where they cause osteolysis and associated pain, hypercalcaemia, and fracture. It is generally accepted that osteoclasts are the only cells capable of destroying mineralised bone. In osteolytic metastases, it has been shown that tumour cells directly stimulate bone resorption by a vicious cycle: in particular, tumour cell produced parathyroid hormone related protein (PTH-rP) facilitates bone resorption and, as a consequence, transforming growth factor β is released from the bone matrix and promotes the progression of bone metastases by further inducing PTH-rP production by tumour cells. Other tumour cell products, such as macrophage colony stimulating factor, interleukin 6 (IL-6), IL-11, and tumour necrosis factor α, have also been reported to be associated with tumour induced osteolysis.

However, with the identification and characterisation of a direct stimulator of osteoclastogenesis—the receptor activator of NF-κB ligand (RANKL) formerly known as ODF, OPGL, and TRANCE—a possible final common pathway for osteoclastic bone destruction has emerged. A variety of osteotropic factors such as l-2,3-dihydroxyvitamin D3, prostaglandin E2, parathyroid hormone, IL-6, and IL-11, have been shown to mediate osteoclast differentiation through the upregulation of RANKL expression or the downregulation of osteoprotegerin (OPG), the decoy receptor of RANKL expression in osteoblast/stromal cells. There is also experimental evidence that tumour produced PTH-rP may stimulate osteoclastic bone resorption by enhancing RANKL expression and reducing OPG expression in the osteoblast. However, whether tumour cells directly produce RANKL, which then stimulates osteolysis in metastatic skeletal lesions, has not been determined.

To this end, we have investigated the expression of RANKL in the skeletal lesions of patients with carcinomas that had metastasised to bone. Sixteen cases, including breast carcinoma (four cases), lung carcinoma (six cases), prostate carcinoma (two cases), and follicular thyroid carcinoma (four cases), were collected during surgical pathological procedures. Histological confirmation of the diagnosis in each case was based on the review of routinely prepared paraffin wax embedded tissue sections in conjunction with knowledge of the clinical and radiological findings. All patients presented with aggressive osteolytic lesions and pathological fracture. The expression of RANKL in the skeletal lesions of patients with carcinomas that had metastasised to bone.

<table>
<thead>
<tr>
<th>Case Primary site Diagnosis</th>
<th>RANKL immunoreactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Breast Adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>2 Breast Adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>3 Breast Adenocarcinoma</td>
<td>95% Intense</td>
</tr>
<tr>
<td>4 Breast Adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>5 Lung Adenocarcinoma</td>
<td>90% Intense</td>
</tr>
<tr>
<td>6 Lung Adenocarcinoma</td>
<td>95% Intense</td>
</tr>
<tr>
<td>7 Lung Adenocarcinoma</td>
<td>90% Intense</td>
</tr>
<tr>
<td>8 Lung Adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>9 Lung Adenocarcinoma</td>
<td>100% Intense</td>
</tr>
<tr>
<td>10 Lung Adenocarcinoma</td>
<td>95% Intense</td>
</tr>
<tr>
<td>11 Prostate Adenocarcinoma</td>
<td>90% Intense</td>
</tr>
<tr>
<td>12 Prostate Adenocarcinoma</td>
<td>85% Faint</td>
</tr>
<tr>
<td>13 Thyroid Follicular ade</td>
<td>90% Intense</td>
</tr>
<tr>
<td>14 Thyroid Follicular ade</td>
<td>95% Faint to intense</td>
</tr>
<tr>
<td>15 Thyroid Follicular ade</td>
<td>85% Faint</td>
</tr>
<tr>
<td>16 Thyroid Follicular ade</td>
<td>100% Intense</td>
</tr>
</tbody>
</table>

Acknowledgements
This study was fully supported by a grant of the Research Grants Council of the Hong Kong SAR (CUIK/4142/00M).

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References

Are coroners’ necropsies necessary? A prospective study examining whether a “view and grant” system of death certification could be introduced into England and Wales

The paper by Rutty and colleagues’ fails to focus upon the key issues raised by the question it seeks to answer. Those issues are: (1) What is the “primary purpose” of coroners’ necropsies? (2) Is the “information available at the time of necropy” adequate? (3) What is meant by postmortem examination? Does it only mean dissection of the whole body? (4) Under what circumstances should a necropsy be performed without regard to the views of the next of kin?

Figure 1Expression of RANKL mRNA and protein in bone metastatic tumours. Signals are dark blue in colour. RANKL mRNA was present in the neoplastic cells of various metastatic tumours. Positive signals are brown in colour. RANKL protein was present at different intensities in the cytoplasm of the neoplastic cells of various metastatic tumours. All images are at x200 magnification. In addition, when present in surrounding tissues, osteoblasts and fibroblasts also expressed RANKL mRNA and protein (indicated by arrows). H&E, haematoxylin and eosin staining; ISH, in situ hybridisation; IHC, immunohistochemistry.

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In our view, this last issue is the most important and other issues should be dealt with within that context: none of these issues can be dealt with meaningfully without informed public debate. The authors pay lip service only to this question and reach a conclusion that we consider that necropsies still have an essential role within the coroner’s enquiry” that is self-evident but superficial.

The paper seems to be based on a false premise—that the “view and grant” facility could replace necropsies. In this study, the causes of death were predicted in 61–74% of deaths where there is no suspicion or evidence of criminality to be certified without a necropsy.

The authors acknowledge that “the most important” factor in a pathologist’s ability to “predict a cause of death before necropsy” is “the quality of the information available to the pathologist”. However, there is no assessment of the quality of information provided in this study, despite a publication by one of the authors indicating the relatively poor quality of such information. A key question raised is: “Was there, in fact, no clinical information available or was the absence of information a reflection of inadequate enquiry on the part of the department of forensic medicine concerned. This procedure is regarded as an “alternative”, an adjunct to a detailed review of the circumstances of death, allowing deaths where there is no suspicion or evidence of criminality to be certified without a necropsy.

We welcome the opportunity afforded by the authors to add to the debate regarding the role and future of the coroner system. The authors’ implicit support for more detailed investigation of the circumstances of death before postmortem examination sits well with the “radical option”—foreshadowing a “medical examiner” system—detailed in the Home Office consultation document produced in the first phase of its Review of Death Certification, and with recommendation 11—“the feasibility of establishing a new system of death certification involving a medical examiner should be explored”—in recent advice from the chief medical officer.

**References**


**Androgen receptor expression in ductal carcinoma in situ of the breast: relation to oestrogen and progesterone receptors**

We wish to add a reference to the list included in the paper of Selim and colleagues’ concerning androgen receptors in ductal carcinoma in situ (DCIS) of the breast that appeared in the *Journal of Clinical Pathology* in the first issue of 2002. Although the authors state that androgen receptors in DCIS have not been reported previously, we had studied this and published a paper dealing with our observations, in addition to CAG repeat lengths in the androgen receptor in DCIS.

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**References**


**Authors’ reply**

Thank you for this information and the opportunity to reply. Unfortunately, the study of androgen receptor (AR) CAG repeats by Kasami and colleagues’ is not included in the usual searches and this appears to be the reason for overlooking this reference. In this study, cases of fibroadenoma, ductal carcinoma in situ (DCIS), and invasive mammary carcinoma were included. Twenty four cases of DCIS were tested for AR CAG repeats and 10 were tested for AR expression immunohistochemically. Two of 10 cases were positive for AR and these two cases were the only cases with apocrine morphology. However, in our study, we found that 19 of 37 cases of DCIS expressed AR. Thirteen of those 19 cases were of non-apocrine morphology. In addition, of the nine morphologically apocrine cases, three lacked AR expression. It seems to be that AR is expressed in a subset of DCIS even without an apocrine morphology, but it is necessarily true that all morphologically apocrine cases of DCIS will express AR. In Kasami and colleagues’ study, none of the cases of invasive mammary carcinoma was tested for AR expression, but other studies 4 have found that a subset of invasive breast carcinomas expresses AR. We feel that a study of AR CAG repeats in benign apocrine metaplasia, which is always immunohistochemically positive for AR, together with and without cases of apocrine and/or non-apocrine in situ and invasive breast carcinoma, would be valuable in highlighting the importance of CAG repeats and apocrine differentiation.

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Sensitivity to Quorn mycoprotein (*Fusarium venenatum*) in a mould allergic patient

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