Case report: A rare case of eosinophilic cholecystitis presenting after talc pleurodesis for recurrent pneumothorax

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Abstract
Eosinophilic cholecystitis (EC) is a rare inflammatory condition of the gallbladder, confirmed by a cellular infiltrate comprised of more than 90% eosinophils in the gallbladder wall on histological examination. Although the etiology of EC is largely unknown, local autoimmune reactions within the gallbladder wall to inflammatory mediators from distal sites of inflammation have been hypothesized. Talc pleurodesis (TP) is a common clinical procedure used within respiratory medicine. However, it is associated with activation of systemic acute inflammatory responses including an increase in serum interleukin-8 (IL-8), which is a potent mediator of eosinophil chemotaxis. We report a case of EC following a TP procedure for persistent, secondary pneumothorax.

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1. Introduction

First described in 1949 [1], EC is a rare and poorly understood inflammatory condition of the gallbladder [2], with fewer than 30 cases described in the literature [3]. Clinically indistinguishable from other causes of cholecystitis, diagnosis is based on histological examination of the surgical specimen (following cholecystectomy) and confirmed when cellular infiltrate of the gallbladder wall is composed of more than 90% eosinophils [4]. It can occur with or without an associated peripheral hypereosinophilia. The etiology of EC is unknown but links have been hypothesized between local autoimmune reactions to inflammatory mediators, hyper-eosinophilic syndromes, eosinophilic gastroenteritis, parasitosis, drugs and medicinal herbs [5,6]. Occasionally, apparent precipitating etiology is absent and idiopathic EC is described [3]. We report the case of a 52 year old lady who presented with EC following TP for a persistent, secondary pneumothorax.

2. Case report

A 52 year old lady with a background of chronic obstructive pulmonary disease (COPD), secondary to a heavy smoking history, presented with severe right upper quadrant pain and nausea.

3 weeks prior to admission, talc slurry pleurodesis was performed to treat a chronic left-sided secondary pneumothorax. The procedure was well tolerated with no adverse effects documented. Retrospective review of blood tests prior to pleurodesis demonstrated normal inflammatory markers, no eosinophilia and no hepatic or biliary abnormalities. Previous CT imaging did not highlight any hepatic or biliary pathology.

Her past medical history included a total abdominal hysterectomy for menorrhagia and recurrent COPD exacerbations. She smoked 10 cigarettes a day but did not drink alcohol and denied use of illicit drugs or herbal supplements. Medications consisted of salbutamol and Spiriva inhalers, she had no known allergies and had not received recent courses of antibiotics or steroids. Furthermore, no infective focus was identified and she had no symptoms consistent with gastroenteritis. An eosinophil count was normal (0.3 × 10^9/L, Reference Interval < 0.6 × 10^9/L), however, a raised value (1.0 × 10^9/L) was noted on routine bloods two weeks post TP.

Bloods on admission are outlined in Table 1. Of note, a mildly elevated IgE level was recorded (115 IU/mL). Although mildly elevated, this value is not in keeping with a parasitic process or Eosinophilic Granulomatosis with Polyangiitis (formally known as Churg Strauss Syndrome) in which higher IgE levels would be expected. In addition, whilst both conditions have been linked to EC, our patient did not demonstrate symptoms consistent with these diagnoses.

An abdominal CT scan showed an acalculus gallbladder with inflammation consistent with cholecystitis (Fig. 1). Therefore, a
was identified a diagnosis of EC. No evidence of epithelial dysplasia or malignancy was noted. Magnification of the gallbladder wall (5mm) with a dense eosinophilic infiltrate (Fig. 2), confirming a diagnosis of EC. No evidence of epithelial dysplasia or malignancy was identified.

Table 1
Table of patient blood test results on admission (3 weeks post talc pleurodesis).

<table>
<thead>
<tr>
<th>Blood test</th>
<th>Result</th>
<th>Normal reference interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>5 μmol/L</td>
<td>2–20 μmol/L</td>
</tr>
<tr>
<td>ALP</td>
<td>174 U/L</td>
<td>30–150 U/L</td>
</tr>
<tr>
<td>GGT</td>
<td>160 U/L</td>
<td>10–35 U/L</td>
</tr>
<tr>
<td>ALT</td>
<td>68 U/L</td>
<td>0–30 U/L</td>
</tr>
<tr>
<td>AST</td>
<td>53 U/L</td>
<td>10–50 U/L</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>129 g/L</td>
<td>115–155 g/L</td>
</tr>
<tr>
<td>WBC</td>
<td>4.8 × 10³/L</td>
<td>4–11 × 10³/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>263 × 10³/L</td>
<td>150–400 × 10³/L</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>2.9 × 10³/L</td>
<td>1.9–7.5 × 10³/L</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0.3 × 10³/L</td>
<td>&lt;0.6 × 10³/L</td>
</tr>
<tr>
<td>CRP</td>
<td>8 mg/L</td>
<td>&lt;5 mg/L</td>
</tr>
<tr>
<td>Renal function tests</td>
<td>unremarkable</td>
<td>–</td>
</tr>
<tr>
<td>IgE</td>
<td>115 IU/mL</td>
<td>&lt;100 IU/mL</td>
</tr>
</tbody>
</table>

Fig. 1. CT scan demonstrating thickening of the gallbladder wall (green arrow), consistent with acute inflammation/cholecystitis. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

laparoscopic cholecystectomy was performed. No intra- or postoperative complications were encountered and she was discharged two days later.

Gallbladder histology showed no gallstones and a thickened wall (5mm) with a dense eosinophilic infiltrate (Fig. 2), confirming a diagnosis of EC. No evidence of epithelial dysplasia or malignancy was identified.

Fig. 2. Histology slide demonstrating dense eosinophilic infiltration of the gallbladder wall. Magnification ×400. Stain – hematoxylin and eosin stain.

3. Discussion

TP is a procedure that can be used to treat persistent pneumothorax [7]. With a high efficacy rate (90%), talc is the agent of choice for chemical pleurodesis [8]. Predominantly composed of hydrated magnesium silicate (Mg₃Si₄O₁₀(OH)₂), talc stimulates an intrapleural inflammatory reaction that causes pleural fibrosis and scarring, leading to obliteration of the pleural space and prevention of recurrent pneumothoraces [9]. However, despite its widespread use, TP is associated with multiple side effects including pain, fever, dyspnoea and systemic conditions including acute respiratory distress syndrome [8].

The mechanisms underlying the systemic responses associated with TP are poorly understood [9]. However, widespread systemic absorption of talc particles can occur following intra-pleural administration [8]. Considering the extensive surface area of the pleural cavity and abundance of lymphatic and vascular vessels, the hypothesis that talc particle migration plays a role in the genesis of systemic effects should be considered [10]. Indeed, distant embolization of talc particles to multiple sites, including the lungs, liver, spleen and brain have been demonstrated in both animal and human models [8,11,12]. Furthermore, autopsy results have found systemic talc distribution to every organ of the body, including the gallbladder [11].

It is thought that after infiltration of the pleural cavity with talc slurry, an acute pleural inflammatory response occurs leading to scarring and fibrosis of the pleura. This process affects the integrity of the alveolar-capillary barrier, leading to spilling of inflammatory mediators into the lymphatic or blood system. Although, there is no firm consensus on the major signaling mechanism for eosinophil activation [13], TP has been shown to cause an acute systemic response, including an increase in serum IL-8 [14], a potent mediator of eosinophil chemotaxis [15]. This mechanism could have occurred in our case, with increased IL-8 levels from pleural cavity inflammation stimulating a systemic response via increased vascular permeability post pleurodesis [9]. Therefore, in the absence of a definitive cause for this presentation of EC, the hypothesized presence of intravascular inflammatory mediators post-pleurodesis could explain the subsequent serum eosinophilia and eosinophilic gallbladder infiltration.

EC has been linked to allergies, parasitic infections, cephalosporin use, hypereosinophilic syndromes and eosinophilic gastroenteritis [3]. However, clinical examination, history and investigation for such causes of EC were unremarkable in our case. Additionally, no gallstones were identified during imaging or histology, and whilst acalculous cholecystitis has been linked to eosinophilic cholecystitis, with EC three times more common in patients with acalculous cholecystitis than with cholelithiasis, EC should be considered a separate diagnosis [2]. Furthermore, there was no clinical evidence of Crohn’s disease, sarcoidosis, Sjogren’s syndrome or Polyarteritis Nodosa which have also been implicated in previously reported acalculous cholecystitis cases [6].

Although no definitive link can be drawn between TP and EC, given the rare and uncertain etiology of EC, we believe it is highly plausible that the two events are more than coincidental. Due to the short time period between TP administration and subsequent EC diagnosis, it seems there is reasonable evidence in the existing literature to suggest that talc particles or inflammatory mediators from pleural inflammation can indeed enter the systemic circulation and stimulate eosinophilic activation with subsequent end-organ deposition. Consequently, we would like to highlight this case and the potential risk of eosinophilic cholecystitis post TP to inform future practice.
Conflict of interest

All specified authors have read and understood the Respiratory Medicine Case Reports policy on declaration of interests and declare that we have no competing interests.

Disclosure

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Prior publications

I can confirm that this case report has not been copyrighted or published previously and is not currently under consideration for publication elsewhere. Additionally this manuscript will not be copyrighted, submitted, or published elsewhere, while acceptance by the Journal is under consideration.

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References