Cholecystitis associated with myelomatosis

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Summary

A case of myeloma presenting as acute cholecystitis unresponsive to conventional management is reported. The impairment of the immunological response is a well-known aspect of myeloma, although this usually takes the form of recurrent respiratory infections. It is unusual for acute on chronic cholecystitis, a predominantly Gram-negative infection, to present in this way.

KEY WORDS: immunoglobulins, Gram-negative infection, cholelithiasis.

Introduction

The majority of cases of acute cholecystitis respond to conservative treatment with intravenous fluids and antibiotic administration. The reasons for failure of these measures have been largely attributed to the severity and extent of the inflammation, but it is equally likely that a failure of the body's immune response might be responsible.

We report a patient with acute on chronic cholecystitis who failed to respond to conservative management, and who was subsequently found to have myelomatosis.

Case report

A 41-year-old man presented with a 2-week history of right hypochondrial pain, typical of biliary colic. He had been vomiting repeatedly and complained of lassitude. Clinically, he was pyrexial and dehydrated, but was not jaundiced. He was acutely tender in the right hypochondrium, and initial investigations showed a normal haemoglobin (12.4 g/dl) and normal white cell count ($8.9 \times 10^9/l$), with 80% neutrophils. Both blood urea and creatinine levels were raised (25.4 mmol/l and 319 mmol/l respectively), but his liver function tests, including serum albumin, were normal. Ultrasound scanning showed the presence of a thick-walled gall bladder containing

stones, and blood cultures demonstrated *Escherichia coli* infection.

Conservative management was instigated, consisting of rehydration and parental cephalosporins. The blood urea fell towards normal and he symptomatically improved over the initial 24 hr, but subsequently the pain and tenderness became more pronounced. Six days after admission, he underwent cholecystectomy, an acutely inflamed, thickened gall bladder, with small stones in the neck, being removed. Histology confirmed an acute on chronic cholecystitis and microscopy of the bile, a moderate growth of *E. coli*.

Postoperatively, he improved rapidly with relief of his abdominal pain. Subsequently, however, his haemoglobin and white count began to fall and he developed increasing lethargy. Electrophoresis at this time revealed a broad M band and he was hypercalcaemic (4.72 mmol/l). Bone marrow aspiration showed an overwhelming preponderance of abnormal cells, analysis of the immunoglobulins being as follows: IgA = 47 g/l (normal 0.9-5.2) (Monoclonal IgAk); IgG = 2.65 g/l (normal 6.0-16.0); IgM = 0.15 g/l (normal 0.25-1.6).

IgA Kappa paraproteins were detected in the urine and a radiolucent defect was found in his 6th rib posteriorly. A diagnosis of IgA myelomatosis was made and the patient commenced on appropriate chemotherapy.

Discussion

Myeloma is known to have protean manifestations, but cholecystitis has not previously been reported in association or as a presenting symptom. For chronic histological changes to be apparent in the gall bladder, previous episodes of infection must have occurred, possibly as a result of his diminished immune response. This is an important aspect of myeloma, infection in one series being the major cause of death (Anon, 1964).

It is the Gram-negative enteric organisms which predominate in cholecystitis, *Escherichia coli* being

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the most common as in this case, and is secondary to cholelithiasis. In the present case the relationship between cholecystitis and the myeloma is conjectural, but Seligmann (1968, 1973) has produced evidence that recurrent infections may predispose to malignant transformation of a susceptible subclone.

Although pulmonary infections with pneumococcus predominate and are the commonest cause of morbidity and mortality, both Meyers (1972) and Twomey (1973) have noted an increasing trend in myeloma patients to develop Gram-negative infections. However, the majority of these commenced as urinary tract infections, the biliary system previously being unreported as a site of origin of infection in myeloma patients.

Several factors attribute to the increased susceptibility to infection. Impaired neutrophil function occurs in patients with paraproteinaemia. Penny, Castaldi and Whitsed (1971) have shown defective skin window responses, reduced adhesiveness to glass beads and impaired phagocytic capacity of neutrophils in these patients. Furthermore, neutropenia, either due to marrow infiltration or later as a result of chemotherapy can occur. In the reported case the initial white count, although in the normal range, was disproportionate to the degree of infection resulting from the acute cholecystitis. Functional hypogammaglobulinaemia is a common feature of the disease, and is associated with the presence of the large amount of paraprotein. This is thought by Salmon (1974) to be due to the suppression of the normal plasma cell population of the marrow by the myelomatous clone. This would also explain the poor antibody response to antigenic stimulation, and it is

these defects which result in susceptibility to the polysaccharide encapsulated organisms, pneumococcus, meningococcus and *Haemophilus influenzae*. Norden (1980) has observed that the serum bactericidal activity against Gram-negative organisms involves both complement and IgM, the latter being depressed in most myeloma patients, and also in this reported case.

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