CASE REPORT

Vasculitis of the gallbladder in early rheumatoid arthritis

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SUMMARY

Vasculitis secondary to rheumatoid arthritis (RA) usually occurs in patients with high circulating titres of rheumatoid factor and established, chronic disease. Vasculitis of the gallbladder causing acute cholecystitis is an extremely rare manifestation of rheumatoid vasculitis. To our knowledge, this is the first case in which vasculitis occurred early in the course of disease. We report the case of a localised gallbladder vasculitis in a 74-year-old, newly diagnosed male patient with RA. He presented with acute abdominal pain, a history of constitutional symptoms and a 1-week history of polyarthritis of his wrist and hands. Cholecystitis was diagnosed clinically and radiologically and he underwent a laparoscopic cholecystectomy. Histopathology of the gallbladder confirmed cholecystitis and gallstones but in addition found small vessel vasculitis and rheumatoid nodules. This case illustrates that rheumatoid vasculitis can occur early in the onset of RA. Additionally, although rare, the gallbladder can be a site of localised rheumatoid vasculitis.

BACKGROUND

Rheumatoid vasculitis occurs in approximately 1% of people with rheumatoid arthritis. It usually occurs in patients with chronic disease in association with active inflammation and high circulating titres of rheumatoid factor in their blood. Vasculitis in early rheumatoid arthritis is rare and vasculitis of the gallbladder of sufficient severity to cause acute cholecystitis is an extremely rare manifestation of rheumatoid vasculitis.

To the best of our knowledge, this is only the fourth such reported case; and the only reported case in which the vasculitis occurred early in the course of disease.

CASE PRESENTATION

We report the case of a 74-year-old Caucasian man who initially presented to our institution with a 1-month history of constitutional symptoms including sweats, fatigue, anorexia and 30 pound weight loss in 1 month. This was associated with generalised myalgia and shortness of breath on exertion. He had not noticed any abdominal pain or change in bowel habit. He was an ex-smoker of 25 years. He had a medical history of dyslipidaemia and type 2 diabetes mellitus. He had no cough, chest pain, palpitations, orthopnoea or paroxysmal nocturnal dyspnoea and no peripheral oedema. His only medication was metformin 500 mg twice daily. He had no known drug allergies.

Physical examination revealed that he was haemodynamically stable and afebrile. He had bibasilar inspiratory crackles on respiratory examination. Remaining system examinations including the neurological and musculoskeletal examinations were normal. He was admitted to the hospital to facilitate further investigation of his constitutional symptoms.

INVESTIGATIONS

Initial investigations revealed elevated inflammatory markers; C reactive protein 190 mg/L, erythrocyte sedimentation rate 46 mm/h, ferritin 1029 µg/L. Complete blood count revealed an elevated white cell count of 23.3×10^9/L, haemoglobin 129 g/L and platelet count 408×10^9/L. The differential white cell count revealed an elevated neutrophil count of 18.4×10^9/L, remaining differential within normal limits. His albumin was low at 28 g/L. Creatine kinase, thyroid stimulating hormone, serum creatine and electrolytes were normal. Investigations for infection, including three sets of blood cultures, urine and stool cultures were negative. Hepatitis B and C serology were negative. Rheumatoid factor was elevated at 111 IU/mL (normal <20 IU/mL), antinuclear antibody positive at 1:80 dilution, speckled. Anti-citrullinated protein antibodies, anti DNA, extractable nuclear antigens and antineutrophil cytoplasmic antibodies were negative. C3 and C4, urinalysis and urine microscopy were normal. Chest X-ray revealed reticular-nodular opacities in the left lower lobe. A chest CT revealed bilateral pulmonary emphysema, mild interstitial fibrosis and scattered small pulmonary nodules. An abdomen CT revealed gallstones but no evidence of intra-abdominal malignancy. Transthoracic echo and oesophagogastroduodenoscopy were unremarkable. In short, investigations did not reveal any evidence of malignancy or source of sepsis.

An initial presumptive diagnosis of polymyalgia rheumatica was made by the attending physician and the patient was started on prednisone 15 mg/day prior to discharge. He was referred to rheumatology and was seen as an outpatient 4 days after discharge. He reported 70% improvement in myalgia and improved energy. He remained without any joint discomforts but in view of his elevated rheumatoid factor, elevated inflammatory markers, hypoalbuminaemia and a subsequent normochromic normocytic anaemia (haemoglobin 103 g/L); a presumptive diagnosis of likely early rheumatoid arthritis was made. Two weeks later, he developed joint swelling with synovitis affecting his

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right wrist, bilateral index and middle metacarpophalangeal joints and right proximal interphalangeal joints. X-rays of his hands and feet showed soft tissue swelling of the right wrist and no evidence of any erosive changes.

He was initially started on sulfasalazine. Unfortunately this caused severe nausea. He was subsequently started on azathioprine 50 mg twice daily and prednisone 15 mg/day was continued.

One week after the onset of his arthritis, he developed acute periumbilical and right upper quadrant pain and a 12 h history of recurrent emesis. A CT abdomen and confirmatory ultrasound scan of abdomen revealed distention of the gallbladder with gallbladder wall thickening, pericholecystic fluid and gallstones.

A diagnosis of acute cholecystitis was made and he was admitted to the hospital, where he was treated conservatively and settled overnight. A laparoscopic cholecystectomy was performed electively, 3 weeks later. Surgical pathology report confirmed cholecystitis and gallstones. In addition, vasculitic changes with fibrinoid necrosis in the small arteries of the gallbladder were noted (figure1). Nodules of histiocytic inflammatory cells surrounding a necrobiotic centre were also present (figure 2), in keeping with rheumatoid nodules.

OUTCOME AND FOLLOW-UP

The patient made a good recovery postoperatively. He had been closely followed for the past 15 months. He currently remains on azathioprine 50 mg twice daily and prednisone 5 mg/day with no evidence of active joint disease or peripheral nodulosis. He has not developed any other extra-articular manifestations of his rheumatoid arthritis. There has been no evidence of systemic vasculitis or localised vasculitis affecting any other sites.

DISCUSSION

Rheumatoid vasculitis is a necrotising vasculitis, usually affecting small and occasionally medium-sized blood vessels. It is a rare but well-described manifestation, of rheumatoid arthritis[1] and has been associated with a number of predisposing factors including smoking,[2] male sex, high rheumatoid factor titres, erosive joint disease and the presence of other extra-articular manifestations of disease including rheumatoid nodules.[3] It usually occurs in established disease, one study reporting the average the onset to be 13.6 years after diagnosis of disease.[4] Rheumatoid vasculitis is very rare in early disease.[5]

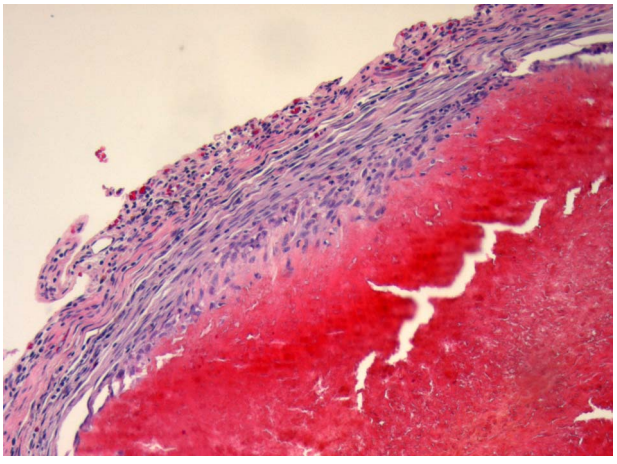

Figure 1 Vasculitic changes with fibrinoid necrosis in small arteries of the gallbladder.

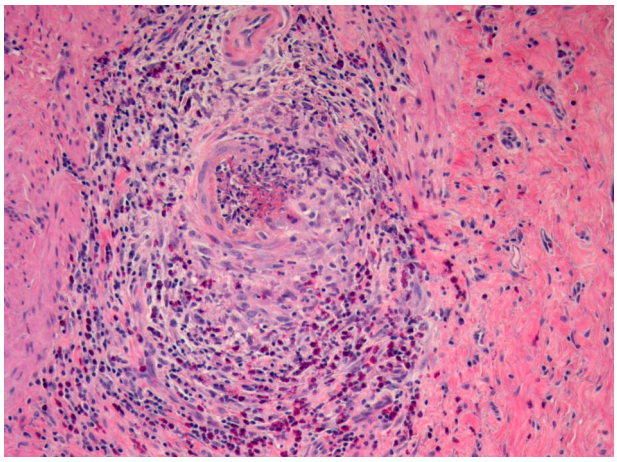

Figure 2 Nodules of histiocytic inflammatory cells surrounding a necrobiotic centre in keeping with rheumatoid nodules.

Acute cholecystitis due to vasculitis has been reported in the past, most commonly in the setting of systemic vasculitis.[6] Localised rheumatoid vasculitis of the gallbladder is extremely rare and to our knowledge, there have only been three previously reported cases in the literature. However, ours is the first such case where localised vasculitis of the gallbladder presented so early in the course of disease.

In all three previously reported cases,[7–9] the vasculitis occurred in the setting of established rheumatoid arthritis (30 years, 11 years and 3 years duration, respectively). Cholecystitis was associated with gallstones in one of the cases, while the other two reported cases presented with alithiasic cholecystitis. All three underwent cholecystectomy with the diagnosis of rheumatoid vasculitis made on histological examination.

Interestingly, our patient presented with localised gallbladder vasculitis less than 3 months after the onset of his constitutional upset and 1 week after the onset of arthritis. Extensive investigations did not reveal any evidence of malignancy or source of sepsis. Other than the gallbladder, there was no evidence of rheumatoid nodulosis elsewhere. There has been no evidence of systemic or generalised vasculitis throughout the course of his illness. He currently remains on imuran 50 mg twice daily and prednisone 5 mg/day with no evidence of active joint disease or peripheral nodulosis and no evidence of vasculitis affecting any other sites.

While the majority of patients with rheumatoid arthritis present at the onset with arthritis of the small joints of the hands or feet, atypical presentations have been described. These include the polymyalgic onset of rheumatoid arthritis, usually in elderly patients with predominant pelvic and shoulder girdle involvement; the palindromic onset with short-lived episodes of arthritis affecting one or more joints at a time; the systemic onset where patients present with constitutional symptoms and where arthritis may be absent to begin with or a persistent monoarthritis usually involving one large joint.

Our patient fulfilled the ACR/EULAR 2010 classification criteria for rheumatoid arthritis.[10] This is a score-based algorithm. Patients with synovitis of one or more joints and whose synovitis is not better explained by another disease, are scored based on joint distribution, serology, duration and acute phase reactants. A score of 6 or more is classified as definite rheumatoid arthritis. Our patient score 7 of 10 based on his joint involvement, high rheumatoid factor (>3× upper limit of normal) and

elevated acute phase reactant, in keeping with definite rheumatoid arthritis.

This case illustrates the fact that rheumatoid vasculitis can occur early in the onset of rheumatoid arthritis and may predate the onset of joint disease. It also reinforces the fact that rheumatoid arthritis may present atypically with the systemic onset. In addition, although rare, the gallbladder can be a site of rheumatoid vasculitis and as such, vasculitis of the gallbladder should be considered in patients with rheumatoid arthritis presenting with acute cholecystitis.

Learning points

- Rheumatoid arthritis may present atypically, with systemic symptoms preceding the joint symptoms.
- Contrary to traditional teaching, rheumatoid vasculitis can occur early in the onset of rheumatoid arthritis.
- The suspicion of vasculitis in a patient with rheumatoid arthritis should prompt a thorough search for other organ system involvement.
- Acute cholecystitis in a patient with rheumatoid arthritis may be secondary to vasculitis of the gallbladder.

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Competing interests None.

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