CASE REPORT

Ascites and other incidental findings revealing undiagnosed systemic rheumatoid arthritis

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Accepted 13 May 2015

SUMMARY

We describe a case of a 43-year-old man presenting to the gastroenterology outpatient department with exudative ascites. Mediastinal lymphadenopathy, pericardial effusion and pleural effusion were detected on further imaging. Further clinical examination revealed subcutaneous nodules on the left arm, which were confirmed to be rheumatoid nodules on histology. Inflammatory markers were elevated with positive serology for rheumatoid factor and anticyclic citrullinated protein antibody. Our investigations excluded tuberculosis, pancreatitis and malignancy in the patient. Following review by a rheumatologist, a diagnosis of systemic rheumatoid arthritis (RA) was made. Pleuritis and pericarditis are well recognised as extra-articular manifestation of RA. Ascites, however, is rarely recognised as a manifestation of RA. Our literature search revealed two other cases of ascites due to RA disease activity, and both patients had long-standing known RA. This case adds to the discussion on whether ascites and peritonitis should be classified as extra-articular manifestations of RA.

BACKGROUND

Rheumatoid arthritis (RA) is recognised as a systemic disease with a multitude of extra-articular manifestations.[1] It is also known that extra-articular manifestations can be present in early RA.[1 2] Therefore, patients with RA may present to many specialties beyond rheumatology. These patients should be promptly identified, and referred on to a rheumatologist, as extra-articular manifestations of RA are associated with a worse prognosis.[3 4]

There is currently no consensus for the classification of extra-articular manifestations of RA,[5] which present a diagnostic challenge to clinicians. Pleural and pericardial effusions secondary to serositis in RA are well recognised,[1 5] but ascites is rarely described.

We report this case to further the discussion on whether exudative ascites should be considered as an extra-articular manifestation of RA.

CASE PRESENTATION

A 43-year-old man was referred to the gastroenterology clinic with a 3-week history of intermittent abdominal pain and progressive distension. He reported poor appetite and weight loss of around 10 kg over the last 4 months.

He had a history of alcohol excess, previously drinking up to 90 units of alcohol per week. He had since reduced his alcohol intake to 12 units over the weekends. He was a smoker with a 13-pack-year history. His general practitioner had recently started him on vitamin B complex, spironolactone and codeine phosphate. There was no family history of note.

On subsequent system review, the patient reported intermittent arthralgia and swelling of wrist, metacarpophalangeal and proximal interphalangeal joints in both hands in the previous 5 years. The distal interphalangeal joints were not involved. There was associated early morning joint stiffness lasting up to 2 h. This had not been previously investigated.

Examination revealed no peripheral stigmata of chronic liver disease. He had clinical signs of ascites. There were subcutaneous nodules on his left forearm and elbow. No swollen joints were found but five tender joints were detected when examining his hands and wrists.

INVESTIGATIONS

An ultrasound scan of the abdomen showed the presence of ascites. There was an incidental finding of bilateral pleural effusions. The liver was enlarged (18.9 cm in long axis) but hepatic and portal blood flows were normal.

A CT of the thorax, abdomen and pelvis detected no solid malignancy nor peritoneal thickening. However, numerous enlarged mediastinal lymph nodes were identified (largest 1.5 cm in short axis). There were also moderate left and small right pleural effusions, and a small pericardial effusion.

Liver function tests showed raised alkaline phosphatase (213 U/L), γ glutamyl transferase (165 U/L) and lactate dehydrogenase (312 U/L). Bilirubin and alanine aminotransferase were within normal limits. Serum albumin was 34 g/L and total protein 84 g/L. Renal and thyroid function tests were normal. Tests for viral and metabolic causes of liver disease were negative. There was an elevated serum IgA level (3.07 g/L). There was no serological evidence of active infection with hepatitis B virus, hepatitis C virus, Epstein-Barr virus, cytomegalovirus or HIV. α-1-Antitrypsin level was normal (2.30 g/L).

Further serological tests found rheumatoid factors of 128 kU/L and anticyclic citrullinated protein antibody of >340 kU/L. C reactive protein was elevated at 91 mg/L. Antinuclear antibody, antidouble-stranded DNA antibody and antineutrophil cytoplasmic antibody were negative. C3 and C4 levels were normal as were serum ACE level (33 μg/L).

Ascitic fluid analysis (table 1) showed ascites protein level of 51 g/L, lactate dehydrogenase level of 378 U/L and amylase of 12 IU/L. This is consistent with an exudate,[6] but inconsistent with pancreatitis. Ascitic fluid albumin level testing was not

To cite: Szeto MCH, Disney B, Perkins P, *et al*. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2014-207142

Table 1 Biochemistry analyses of serum, ascites fluid and pleural fluid

	Serum	Ascites fluid	Pleural fluid
Total protein (g/L)	83	51	38
Fluid:serum protein ratio	NA	0.61	0.46
Lactate dehydrogenase (U/L)	312	378	220
Fluid:serum lactate dehydrogenase ratio	NA	1.21	0.71

NA, not applicable.

performed. Cytology was negative for malignant cells. Bacterial and acid-fast bacilli were negative by microscopy and extended cultures.

Pleural fluid analysis (see table 1) showed a total protein level of 38 g/L and lactate dehydrogenase level of 220 U/L. This was also consistent with an exudate. There was no evidence of malignancy or infection. Pleural biopsy showed chronic inflammation and fibrosis on histology. It was also negative for acid-fast bacilli after extended culture.

The largest mediastinal lymph node was excised, and it showed follicular hyperplasia only. Excision biopsies of the two subcutaneous nodules on the patient's left arm were also performed. These were reported to be consistent with classical rheumatoid nodules on histology. Plain radiograph of the hands and wrists did not show erosive lesions.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for an exudative ascites include solid malignancy, lymphoma, pancreatitis, tuberculosis, hypothyroidism and primary inflammatory diseases.[7] The results of the investigations pointed towards a primary inflammatory disease.

Although joint swelling was not detected on clinical examination, this was reported in the patient's history. Applying the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA,[8] he scored 8 of 10. It was on this basis that the diagnosis of RA was made. The diagnosis was further supported by the presence of rheumatoid nodules, which was a diagnostic feature under previous American Rheumatism Association 1987 revised criteria for RA.[9]

The findings of hepatomegaly, abnormal liver function tests and raised serum IgA level was likely due to excessive alcohol intake.[10] They subsequently normalised following further reduction in alcohol use.

TREATMENT

Therapeutic drainage of ascites and pleural effusion was performed.

The patient was referred to a rheumatologist. Treatment with naproxen, prednisolone (10 mg once daily) and methotrexate (7.5 mg once weekly) was initiated.

OUTCOME AND FOLLOW-UP

The dose of methotrexate was titrated to 15 mg once weekly and the patient was successfully weaned off prednisolone. He reported improvement in arthralgia and early morning joint stiffness. The articular disease was kept in remission with a disease activity score (DAS28) between 1.69 and 2.50.[11]

The ascites and pleural effusion have not recurred. The patient was discharged from gastroenterology service 2 years after initial presentation.

DISCUSSION

Our patient presented to gastroenterology service with ascites and other incidental findings. Our diagnostic work up was highly suggestive of undiagnosed underlying RA and the patient was referred on to rheumatology service.

Our case is limited by the lack of serum-ascites albumin gradient, which would have allowed for better classification of ascites. Ascites fluid albumin level was not part of the work up in our hospital when this patient presented.

Based on the biochemistry analyses, both the ascites and pleural fluid were likely exudate, suggestive of pleural and peritoneal inflammation. We feel that the patient's undiagnosed RA could be responsible for the underlying inflammatory process.

Our literature search found 12 reports of ascites associated with RA.[12–21] The most common causes are drug-related hepatotoxicity (4 cases)[12–14] and reactivation of peritoneal tuberculosis due to biological therapy (4 cases).[15–17] There are two further reported cases of ascites attributed to RA disease activity.[20 21] In both of these cases, the patient had long-standing RA.

There is currently no randomised trial evidence available for management of extra-articular RA.[4 5] Had therapeutic drainage not been performed, it is uncertain whether the ascites and pleural effusion would have resolved with methotrexate and prednisolone.

There is a need for a consensus in the classification of extra-articular manifestations of RA, so that optimal management strategies can be systemically studied.[4 5] The classification will also serve to remind clinicians that RA should be considered as a differential diagnosis in a wide range of presentations, allowing for prompt referral and diagnosis.

The Malmo criteria[1] is a commonly used classification for extra-articular manifestations of RA. It only recognises pleuritis and pericarditis under the heading of 'serositis'. Together with the two previous reports, our case raises the question of whether peritonitis and ascites should also be considered as extra-articular manifestation of RA.

Learning points

- Rheumatoid arthritis (RA) is a systemic disease that can present to many specialties.
- There needs to be further discussion on whether peritonitis and ascites should be classified as extra-articular manifestations of RA.
- RA may form part of the differential diagnoses when investigating an exudative ascites.
- Alternative causes of exudative ascites require significantly different management. These need to be excluded before initiating or escalating treatment for RA.

Contributors MCHS reviewed the literature, and wrote and revised the paper. BD and GW revised the paper and took consent from the patient. All authors reviewed and analysed the clinical aspect of the case.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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