PostScript

**MATTERS ARISING**

**Refractory leg infection as an inducer of the catastrophic antiphospholipid syndrome**

In their report Yoo et al describe a 72 year old woman who presented with fever and symptoms typical of the fingers and toes despite intact peripheral arterial pulses. Klebsiella pneumoniae grew both from blood and liver biopsy aspirates. Treatment with antibiotics, prostaclin, tissue plasminogen activator followed by warfarin and aspirin was beneficial and led to the regression of almost all the lesions. The authors state that “Although Amital et al reported that amputation could induce remission of the systemic illness, some reports have recommended that non-surgical management is preferable if there is an intact pulse in the affected limb”.

The term “catastrophic” antiphospholipid syndrome (CAPS) is used to define an accelerated form of antiphospholipid syndrome (APS) resulting in multiorgan failure. These patients have clinical evidence of multiple organ involvement, which develops within a short period of time, in addition to histopathological evidence of multiple small vessel thrombotic occlusion and high titres of antiphospholipid antibodies. The most common precipitating factor of CAPS is infection, appearing in 35% of patients.

We previously described two patients with APS with severe leg infections who developed a fulminant course of CAPS with acute renal failure, adult respiratory distress syndrome, central nervous system involvement, and the emergence of gangrenous lesions in both legs. After conservative treatment failed both patients had both legs amputated and recovered. Recently, we encountered two patients with systemic lupus erythematosus and secondary CAPS who were less fortunate. Both had severe leg infections refractory to antibiotic, vasodilator, and anticoagulant treatment. Both refused bilateral leg amputation and after a short period died owing to multiple thrombi and multiorgan failure.

CAPS differs from APS by its systemic involvement and down hill progression ending in multiorgan failure and death. Kitchens reasoned that a “fibrinolytic shutdown” might be caused during infections as they induce a transitory increase in plasminogen activator inhibitor concentrations. This especially when another thrombophilic conditions is present may lead to a “thrombotic storm”. We believe that the patient described by Yoo et al does not comply with the definitions of CAPS. Therefore their citation of our previous work, underlining the importance of eradicating the source of infection even at the cost of amputating both legs (in case the infection cannot be conservatively controlled), is inaccurate. The two unfortunate new cases we mentioned clearly demonstrate how critical these conditions may be and how essential it is to reach a decisive mode of action.

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References


Authors’ reply

We thank Dr Amital and his colleagues for their valuable opinions about important guidelines for treatment of catastrophic antiphospholipid syndrome (CAPS). We think there are two points which were raised by Dr Amital and colleagues: one is whether our case is strictly consistent with the criteria of CAPS, the other is to decide between the surgical and non-surgical intervention in cases of gangrenous extremities.

CAPS was initially defined as an accelerated APS with multiorgan failure. This definition has been refined to be classified as the definite and probable category through the consensus workshop of the 10th International Congress on antiphospholipid antibodies (aPL) on 29 September 2002.

According to these new preliminary criteria, the patient presented by us belongs to the category of probable CAPS: shock, acute respiratory distress syndrome, stuporous mentality, and multiorgan failure as well as the gangrenous extremities were the initial manifestations shown simultaneously (we had to omit these findings from the initial manuscript owing to the length of letters allowed in this journal). The presence of aPL was confirmed on two occasions 6 weeks apart. However, histopathological confirmation was not obtained. Therefore, there is no doubt that the patient had probable CAPS. As Ashton et al commented in the new preliminary criteria, the optimal management of CAPS is to date not firmly established. In fact, we agree with Dr Amital’s opinion that it is important to eradicate the infectious source even at the cost of amputation in case the infection is intractable. However, we do not think that amputation should be performed in all cases of CAPS. If peripheral arterial pulses are intact, as they were in our patient, non-surgical management may be initially preferred to allow the chance that the patient’s lesion may improve. In addition, the new treatment algorithm presented by Ashton et al also recommends medical management as an initial treatment (anti-coagulation plus high doses of steroid plus intravenous immunoglobulin and plasma exchange). In our opinion, there is no absolute rule for the management of gangrenous condition in CAPS. We also think that the decision to amputate should be individualised and remains to be elucidated in the further consensus study.

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References


**Hepatic manifestations of autoimmune rheumatic diseases**

We read with interest the recent review by Abraham et al. Other uncommon conditions of the liver have been described in association with rheumatic diseases.

One case report detailed the presence of rheumatoid nodules in a patient with active rheumatoid arthritis complicated by amyloidosis and chronic renal failure. Postmortem findings disclosed numerous nodules scattered throughout the liver of maximum diameter 5 mm. Histological examination of these showed a central zone of cell necrosis...
interstitial lung disease, a common manifestation of newly diagnosed polymyositis and dermatomyositis

We read with interest the article by Fathi et al. We agree with the main message of this study and we would like to comment on the serological findings of the patients with polymyositis (PM) and dermatomyositis (DM).

Both PM and DM are associated with the production of autoantibodies against intracellular antigens. The prevalence of anti-Ro antibodies in PM and DM patients has been reported to be between 14% and 70%.

In this study, the authors found a higher frequency of anti-Ro antibodies in the sera of patients with PM and DM, with a prevalence of 44%. This result is consistent with previous studies, which have shown that anti-Ro/SSA antibodies are more common in PM than in other inflammatory myopathies.

However, the authors also identified a lower frequency of anti-Ro antibodies in the sera of patients with DM. This finding is in agreement with previous studies, which have reported a lower prevalence of anti-Ro antibodies in DM patients compared to PM patients.

The authors mention that the low frequency of anti-Ro antibodies in the sera of patients with DM may be due to the fact that the disease is more often diagnosed in a later stage, when the antibodies are less likely to be detected.

In conclusion, the study by Fathi et al. highlights the importance of considering anti-Ro antibodies in the diagnostic workup of PM and DM patients, especially when the disease is suspected in a later stage. Further research is needed to better understand the role of anti-Ro antibodies in the pathogenesis of PM and DM.

References


Authors’ reply

We thank Drs Sandhu and Jawad for highlighting additional hepatic pathologies associated with rheumatoid arthritis. Our review was specifically aimed at highlighting liver involvement primarily due to autoimmune rheumatic disease and not as a result of pharmacotherapy.

Unfortunately, the authors did not present any details of the antibody detection methods, which are of the utmost significance. Owing to many different to the detection of autoantibodies against intratireal antigens, several options are available, ranging from “in-house” methods to commercial kits. The choice may be crucial in considering those 

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agree that these numbers are higher than expected in comparison with most previously published myositis cohorts. 2 Notably, we had excluded patients with other defined rheumatic diseases.

The analyses for anti-SSA/Ro and anti-SSB/La antibody detection that were used in our study were performed with an enzyme linked immunosorbent assay (ELISA) containing both Ro52 and Ro60 recombinant antigens. These autoantibody tests were performed at the time of the diagnostic check up for each person as part of the routine procedure at the Karolinska University Hospital, Solna, Sweden. The laboratory procedures were performed at the Department of Clinical Immunology, which is ISO/IEC certified for autoimmune analyses.

To further confirm the anti-SSA/Ro positive results we have retested the anti-SSA and anti-La positive sera with two other assays—immunodiffusion from Immunogenetics. We could confirm the anti-SSA/Ro positivity from the ELISA tests with immunodiffusion in three of the six cases. The three additional cases were negative for anti-SSA using immunodiffusion, but were positive for Ro52 with the immunoblot technique. None of the six cases was positive for Ro60. Two cases had anti-La antibodies, both in addition to anti-SSA antibodies, using the ELISA test. The anti-La positivity was in one case confirmed by immunodiffusion, the other was not.

The discrepancy between the results in our patients and previously presented data is likely to depend on the different methods that have been used in different studies. The patient cohort presented in our study is small, which makes analyses from stratified patient groups into subgroups such as polymyositis or dermatomyositis uncertain. Both ELISA and line immunodiffusion tests are generally more sensitive than immunodiffusion and counter-immunoelectrophoresis. Moreover, the sensitivity threshold of various immunodiffusion tests varies with the manufacturer's content of specific antigens, like the Ro52 antigen. The assay used for immunodiffusion is, in our hands, less likely to detect Ro52 positive sera than other assays and, consequently, likely to overlook anti-SSA autoantibody reactivity if used alone. On the other hand, the higher sensitivity of ELISA and the line immunodiffusion tests may be at the cost of a weaker clinical specificity for the detection of anti-SSA antibodies associated with disease.

We still believe that our data are valid as similar results were achieved by both the ELISA and the line immunodiffusion assay recombinant Ro52 antigen from different sources and even confirmed by immunodiffusion in three of the six cases. Another possible explanation for the lower frequency of anti-SSA antibodies in patients with polymyositis in older studies might be that patients with inclusion body myositis were not excluded, as autoantibodies seem to be less common in this disease entity.

Based upon the validating laboratory procedures presented above, we believe that anti-SSA/Ro and anti-SSB/La antibodies may be more common in pure polymyositis and dermatomyositis than previously recognised. This hypothesis remains to be tested in a larger cohort of patients with myositis, particularly with regard to Ro52 alone.

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References

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ACR/ARHP 68th Annual Scientific Meeting
16–21 October 2004; San Antonio, Texas, USA
Website: www.rheumatology.org/annual/index.asp

Osteoarthritis Research Society International
2–5 December 2004; Chicago, USA
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International Society for the Study of the Lumbar Spine Instructional Course
27, 28 March 2005; Nairobi, Kenya
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Future EULAR congresses
8–11 June 2005; EULAR 2005; Vienna, Austria
21–24 June 2006; EULAR 2006; Amsterdam, The Netherlands