Rheumatological conditions in critical care

Alex Bell MBChB BSc¹, Rachel Tattersall MBChB BMedSci FRCP PhD² and Tim Wenham MBChB FRCA DICM FFICM³,*

¹ST3 Anaesthesia. Hull Royal Infirmary, Hull and East Yorkshire NHS Trust, Anlaby Road, Hull HU3 2JZ, UK, ²Consultant in Adult and Adolescent Rheumatology, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK, and ³Consultant in Anaesthesia and Intensive Care Medicine, Barnsley Hospital NHS Foundation Trust, Gawber Road, Barnsley S75 2EP, UK

*To whom correspondence should be addressed. Tel: +44 1226 73 00 00; E-mail: t.wenham@nhs.net

Key points

- The management of rheumatological conditions now focuses on early, aggressive immunosuppression, using a variety of disease-modifying and biological agents.
- Rheumatological therapies can cause immunosuppression, and both specific and general side-effects of relevance to the intensivist.
- Atypical infection, such as Pneumocystis pneumonia, tuberculosis, and fungi, should be considered in all rheumatological patients on treatment who present to intensive care.
- Signs of underlying disease flare and sepsis are often indistinguishable; patients with rheumatological disease who are not responding to treatment on the intensive care unit may need further rheumatological/immunosuppressive treatment.
- Prompt rheumatology consultation is paramount.

Traditionally thought of as disorders of the joints and musculoskeletal system, rheumatological diseases (RDs) can affect any organ system and many have debilitating systemic effects. These conditions, and the sequelae of the immunosuppressive medications used to treat them, can also cause catastrophic complications and can pose many diagnostic and therapeutic challenges to the intensivist (Table 1). While RDs are relatively common in the general population, they remain a comparatively rare cause of intensive care admission. However, such patients have a reported intensive care unit (ICU) mortality of 15–55% and poor long-term outcomes.¹

The most common rheumatological causes for admission to the ICU include:²

- development of new manifestations/end-organ sequelae of RD,
- infection secondary to immunosuppressive treatment of RD,
- adverse effects of disease-modifying drugs,
- acute critical compromise unrelated to but exacerbated by the underlying RD.

In reality, these presentations tend to overlap, further complicating the ICU course. A common scenario, for example, would be attempting to differentiate between sepsis and a flare-up of underlying inflammatory disease. This can be a major diagnostic challenge, given that the management of infection differs substantially from control of the underlying disease. Early consultation with a rheumatologist is therefore paramount and treatment of both infection and the RD may be required in tandem.

Three-quarters of those patients admitted to the ICU because of RD have rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), or sclerderma. Other less prevalent conditions include antiphospholipid syndrome (APS), the vasculitides, and dermatomyositis.² There is not scope in this article to discuss every rheumatological condition and how it may present to the intensivist. Instead, we will concentrate on some important presentations that should not be missed, and critical problems potentially posed by the different therapies used within rheumatology.
Rheumatological presentations not to be missed

Macrophage activation syndrome (MAS)

Macrophage activation syndrome (MAS) is a rare, but potentially lethal complication of several rheumatological diseases and is one of the conditions grouped under the umbrella of ‘haemophagocytic lymphohistiocytosis’ (HLH). There is a significant mortality rate in MAS quoted between 15% and 20%, although a recent study demonstrated a mortality of 8%. In MAS/HLH, there is a loss of regulation within the immune system leading to inappropriate activity of macrophages and T-cells and a state of uncontrolled, self-perpetuating hyperinflammation. This ‘cytokine storm’ is characterized by unregulated release of tumour necrosis factor-α (TNF-α), IFN-γ, IL-6, IL-10, and IL-1β and marked decrease in natural killer cell activity.

Primary HLH is caused by genetic defects in perforin genes and presents mainly in infants. Secondary, acquired forms of MAS/HLH occur in malignant disease, those with acquired immune deficiency states, such as organ transplant recipients, and in those with RD. MAS/HLH is most often seen in association with systemic juvenile idiopathic arthritis (SJIA). It is also reported with SLE, adult-onset Still’s disease, and vasculitis and may occur at any stage of the disease; at onset, during periods of active disease or during periods when the underlying condition is quiescent. Importantly, MAS can also develop de novo in non-rheumatology patients on the ICU suspected to have sepsis and multi-organ dysfunction, or with commonly identified triggers such as lymphoma and Epstein-Barr virus infection.

Clinical features

Features are mainly due to the underlying hyper-inflammatory state:

- cytopaenias—often decreasing platelet count is the first abnormality noted,
- hyperferritinaemia,
- unremitting fever,
- coagulopathy/disseminated intravascular coagulation,
- splenomegaly and lymphadenopathy,
- hypertriglyceridaemia,
- neurological features, such as confusion, headache, seizures, and coma,
- multiple organ failure.

The most common presenting features in a recent multinational study were fever (96%), hepatomegaly (70%), and splenomegaly (58%).

Diagnosis

It is often difficult to differentiate MAS from underlying RD or overwhelming sepsis. Diagnosis requires a high degree of clinical suspicion and trends in serum values are more important than absolute values. High levels of serum ferritin and a low percentage of glycosylated ferritin have been shown to be useful in the diagnosis of MAS/HLH (hyperferritinaemia >10 000 µg litre⁻¹ is pathognomonic and levels >5000 very suggestive). Furthermore, there is evidence that consecutive ferritin levels can be used as a marker of response to therapy. Other serum markers showing marked change include aspartate and alanine aminotransferases (increased by 346 and 325%, respectively), D-dimer (122%), and lactate dehydrogenase (121%). C-reactive protein is expected to increase, while the erythrocyte sedimentation rate may decrease.

Treatment

While the majority of studies and recommendations for the treatment of MAS are in children, a multinational group proposed guidelines in 2005 for treatment in adults. These include:

- early, aggressive supportive therapy,
- high-dose corticosteroids, such as dexamethasone or methylprednisolone with escalation to additional immune suppression with ciclosporin,
- elimination of known or suspected triggers,
- infection control.

The use of i.v. immunoglobulin therapy (1 g kg⁻¹ for 2 days), plasma exchange, and treatment with biological agents have all been advocated in refractory cases of acquired MAS/HLH.

Minoia and colleagues documented that almost 98% of MAS patients received corticosteroids, ciclosporin (61.2%), and i.v. immunoglobulin (36.3%). Only 15.2% of the patients required biological agents, with anakinra being the most commonly selected agent.

Case report: MAS in a 17-yr-old male with arthritis

A 17-yr-old male with SJIA, controlled with methotrexate and tocilizumab, was admitted to the ICU with respiratory failure secondary to lobar pneumonia. His immunosuppression was stopped, he was sedated, his lungs mechanically ventilated, and he was turned prone for refractory hypoxaemia. Broad-spectrum antibiotics and antiviral drugs were commenced and his urine was positive for pneumococcal antigen.

After improvement in his respiratory parameters, a surgical tracheostomy was performed on day 11 because of repeated failed sedation holds. He then became more unwell, having developed a widespread rash and spiking temperatures. A full septic screen was undertaken and broad-spectrum antibiotics commenced to no avail. He was turned prone again for acute respiratory distress syndrome and worsening hypoxaemia.

Rheumatology review raised the possibility of MAS/HLH and suggested high-dose methylprednisolone if his platelet count decreased. Several days later, a blistering chest wall rash was noted, his platelets did decrease, he developed cerebral irritation, and then had a seizure. A diagnosis of MAS was made clinically and supported by laboratory features (ferritin >16 500 µg litre⁻¹, triglycerides 10.3 mmol litre⁻¹, and a pancytopaenia). Methylprednisolone was started after advice from a regional specialist rheumatologist and he was transferred to a regional centre for further treatment, including ciclosporin, IVIG, and etoposide and ultimately made a full recovery.

Scleroderma renal crisis

Systemic sclerosis is an autoimmune disease characterized by fibrosis and inflammation of internal organs and the skin. A life-threatening complication of this disease is scleroderma renal crisis (SRC), affecting 5–10% of patients with scleroderma.

Table 1 Why rheumatological diseases are important

<table>
<thead>
<tr>
<th>Predominantly affect young females</th>
<th>Multi-system diseases</th>
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<tbody>
<tr>
<td>Potential multi-organ failure</td>
<td>High mortality on ICU</td>
</tr>
<tr>
<td>Complicated pharmacotherapy</td>
<td>Result in immunocompromise, secondary to disease, medication, or both</td>
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<tr>
<td>Many rheumatological conditions coexist/overlap</td>
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</table>
SRC is characterized by a rapid-onset hypertension that becomes malignant, combined with acute oliguric/anuric renal failure. This is a true rheumatological emergency as rapid diagnosis and treatment may save lives and renal function. The pathogenesis is not fully understood, but is thought to involve thickening of the inter-lobar and arcuate arteries within the kidneys, leading to reduced renal perfusion and excessive renin release.

Risk factors include:
- corticosteroid therapy,
- rapidly progressive skin disease,
- diffuse cutaneous systemic sclerosis.

The male:female incidence of SRC is roughly 1:3, with an average age of 53 yr and a mean interval of 3.2 yr between diagnosis of systemic sclerosis and developing SRC. A proportion of patients (~10%) do not have hypertension and progressive fatigue and malaise may be the only symptoms, combined with renal failure; therefore, a high degree of clinical suspicion is required. Laboratory investigations show increased creatinine, thrombocytopenia, potentially a microscopic angiopathic haemolytic anaemia, and hyper-reninaemia.

Classically, patients present with headaches, visual disturbances, encephalopathy, and seizures. They may also have cardiac involvement leading to pulmonary oedema, arrhythmias, and myo/pericarditis. A proportion of patients (~10%) do not have hypertension and progressive fatigue and malaise may be the only symptoms, combined with renal failure; therefore, a high degree of clinical suspicion is required. Laboratory investigations show increased creatinine, thrombocytopenia, potentially a microscopic angiopathic haemolytic anaemia, and hyper-reninaemia.

Treatment
Aggressive management of hypertension is required to prevent irreversible renal damage. Angiotensin-converting enzyme inhibitors are the cornerstone of treatment and have achieved a decrease in acute mortality, but there is often resistance to their use in non-specialist ICUs because patients have renal failure. Further treatment may involve calcium channel blockers, labetalol, and nitrates (especially with pulmonary oedema) or plasma exchange if there is extensive thrombotic microangiopathy. Approximately 25% of SRC patients require dialysis in the short term; however, 40–66% of all SRC patients do not recover full renal function and require chronic dialysis, transplantation, or both. Recovery of renal function occurs slowly, taking up to 24–36 months, and prognosis is worse in those who are male, aged >53 yr, and those who are normotensive on presentation. The overall 5 yr survival for systemic sclerosis patients with full SRC remains low (65%), despite improving treatments.

Catastrophic antiphospholipid syndrome
APS is an autoimmune condition characterized by recurrent venous and arterial thrombosis, pregnancy disorders (miscarriage, preterm birth, and eclampsia), and the presence of antiphospholipid (APL) antibodies. It is most prevalent in women of reproductive age. There is also a higher incidence in Afro-Caribbean populations. APS is often found in conjunction with other inflammatory autoimmune conditions such as SLE, RA, systemic sclerosis, and Bechet’s disease. It is thought to account for 10–15% of recurrent miscarriages and 20% of recurrent thromboses in young people. Cardiac involvement in APS is common, with patients under 40 at increased risk of myocardial infarction and sudden death. These patients are also at high risk of re-stenosis after percutaneous intervention or coronary artery bypass grafting and can pose major therapeutic challenges.

The pathogenesis of APS is still not fully understood. It is thought that APL antibodies activate endothelial cells, monocytes, and platelets and a pro-coagulant state is induced. This appears to be primarily mediated by the increased production of tissue factor and thromboxane-A2.

Catastrophic APS (CAPS) is the rarer form, representing <1% of APS cases. In CAPS, there is an accelerated, widespread course of disease, leading to rapid multi-organ failure and over 50% mortality despite treatment. Histological studies show a thrombotic microangiopathy of small vessels, resulting in organ failure and a systemic inflammatory response syndrome (SIRS)-like state. The majority of CAPS events are preceded by a precipitating event which may be unknown. Identifiable triggers include infection, but also surgical procedures, trauma, and withdrawal of anticoagulation therapy.

Diagnosis
Diagnosis is challenging with many causes of false-positive and false-negative results, and validated diagnostic criteria are currently not available. Early recognition of CAPS is essential to ensure the best clinical course possible for the patient. Presentation may be suspected with clinical history and common clinical features (Table 2), but a high index of suspicion and early liaison with haematology/rheumatology specialists is vital.

Treatment
Treatment is not currently standardized due to the rarity of the condition. In addition to supportive care for specific organ involvement, it is important to recognize those at high risk (surgery/trauma) and aggressively treat any precipitating factors, for example infection. A three-pronged approach is then recommended:

1. Prevent and treat the ongoing thrombotic events, usually with i.v. heparin.
(ii) Consider IVIG and/or plasma exchange.
(iii) Suppress the excessive cytokine ‘storm’ with high-dose steroids and other immunomodulatory therapies if indicated.

**Anti-neutrophil cytoplasmic antibodies-associated vasculitides**

The anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitides (AAV) are a subgroup of multi-system, autoimmune diseases that affect small to medium-sized blood vessels and are characterized by the presence of ANCA in the circulation. In addition, there is an absence of immune deposits within vessel walls that differentiates AAV from other small vessel vasculitides.\(^1\)

The clinicopathological variants of AAV were revised in 2012\(^1\)\(^5\) and are as follows:

- microscopic polyangiitis (MPA),
- granulomatosis with polyangiitis (GPA, formerly Wegener’s),
- eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg–Strauss),
- single-organ AAV (e.g. renal-limited AAV).

It is important to note that AAV is not a single disease entity but rather a group of multi-system disorders that share certain features. The respiratory tract and kidneys are most commonly affected by AAV.

**Complications**

Many of these patients will be well established on corticosteroid therapy and other immunosuppressive drugs and as such are at high risk of opportunistic infections and overwhelming sepsis.

Pulmonary involvement is more frequent in GPA (90%) and EGPA (70%) and less frequent in MPA (50%).\(^1\)\(^6\) In granulomatosis with polyangiitis (Wegener’s), all parts of the respiratory tract can be affected from the nasal mucosa to the pleura and pulmonary artery. Complications of particular interest to the intensivist are the development of subglottic stenosis, leading to difficult tracheal intubation, and the potential for diffuse alveolar haemorrhage, requiring invasive ventilation. In EGPA (Churg–Strauss), there may be multiple nasal polyps and an eosinophilic asthma that progresses in severity with disease course.

Renal involvement occurs more frequently in MPA (90%) and in GPA (80%) and less frequently in EGPA (45%).\(^1\)\(^6\) Renal AAV can present as rapidly progressive glomerulonephritis, quickly leading to end-stage renal disease.\(^1\)

The heart is involved most commonly in EGPA, with presentations including heart blocks, myocarditis, pericarditis, and myocardial infarction. Gastrointestinal presentations include bowel perforation, resulting from vasculitic ulceration of the small and large intestine, and pancreatic or liver involvement.

**Systemic lupus erythematosus**

Systemic lupus erythematosus (SLE) is a complex, multi-system disease with numerous critical complications that may present to the intensivist. These range from common (coronary artery disease, overwhelming sepsis, and renal failure) to rare (peri-carditis, alveolar haemorrhage, and transverse myelitis). Owing to the vast scale of this disease, it is out of the scope of this review article.

**Rheumatological pharmacotherapies**

The pharmacological management of RD has changed dramatically over recent years. A paradigm shift has occurred where the ‘inflammatory burden’ a patient is exposed to is increasingly recognized; the greater the burden and the longer a patient’s exposure, the greater the risks of complications such as cardiovascular disease developing in later life. Therefore, by attenuating the inflammatory burden, the risks of associated complications are lowered. For example, suffering from RA is an independent risk factor in the ‘QRISK2 score’ (a widely used cardiovascular risk scoring algorithm for determining the likelihood of having a cardiac event within the next 10 yr).\(^1\)

In 2009, NICE recognized this and described the need for the early use of disease-modifying anti-rheumatic drugs (DMARDs) in their guidelines.\(^1\)\(^9\) This strategy is described as the ‘inverted pyramid approach’ (Fig. 1). Aggressive immunosuppressant therapy is now started early. Consequently, this means many more people are receiving DMARDs and often as dual- or triple-therapy. First-line DMARDS are usually started in combination as standard therapy for RA, e.g. methotrexate and sulphasalazine. For resistant disease, biological agents are usually given alongside an oral DMARD, e.g. methotrexate plus infliximab. Further biologics are then added as per NICE guidance. In other RDs such as SLE, hydroxychloroquine, azathioprine, or mycophenolate mofetil may also be used first line and again in combination (Table 3).

**Methotrexate**

Methotrexate is the most commonly used DMARD in the treatment of RA. It is an analogue of folic acid, with anti-proliferative, immunosuppressive, and anti-inflammatory properties. It is taken orally or subcutaneously once weekly. Methotrexate has many recognized side-effects including methotrexate pneumonitis (MX-P) and methotrexate-induced bone marrow failure.

**Methotrexate pneumonitis**

Methotrexate can cause pulmonary toxicity by exacerbating pulmonary fibrosis, the exact mechanism of which is unknown. One rare but important form of pulmonary toxicity is MX-P. The incidence of MX-P is between 2% and 7%, with the greatest risk being within the first year of treatment. Although rare, acute MX-P can have a mortality of up to 20%. Onset may be acute or subacute, within days to months of taking methotrexate.

Clinical features include:

- breathlessness,
- cough,
- fever,
- hypoxia,
- bibasal lung crackles.

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pulmonary function tests
Oxygen saturation
marked eosinophilia.

Diffusing capacity of lung for carbon monoxide (DLCO)
Non-productive cough
should be excluded. Several sets of diagnos-

Inhibitors have revo-
White cell count
Shortness of breath for <8 weeks
Radiological evidence of pulmonary interstitial or alveolar
Fl

MX-P is characterized as ≤
Hypersensitivity pneumonitis by histopathology without
Blood cultures (if febrile) and initial sputum cultures (if sputum is
Trans-bronchial tissue biopsy
Gas transfer usually decreased,
Em-

Table 3 Examples of common rheumatological drugs, classes, uses, and side-effects

<table>
<thead>
<tr>
<th>Drug type</th>
<th>Examples</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line DMARDS</td>
<td>Methotrexate, sulfasalazine, hydroxychloroquine</td>
<td>First-line RA treatment</td>
</tr>
<tr>
<td></td>
<td>Methotrexate agents, e.g., infliximab, etanercept, adalimumab</td>
<td>Used in combination with first-line DMARDs, for resistant RA</td>
</tr>
<tr>
<td></td>
<td>Methotrexate, adalimumab, etanercept</td>
<td>Methotrexate bone marrow toxicity</td>
</tr>
<tr>
<td></td>
<td>Anti-TNF agents, e.g., rilonizumab, tocilizumab, abatacept</td>
<td>SLE, granulomatosis with polyangiitis, rheumatoid arthritis</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide</td>
<td>Biologics</td>
</tr>
<tr>
<td></td>
<td>Ibuprofen, naproxen, celecoxib</td>
<td>NSAIDs</td>
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<tr>
<td></td>
<td>Steroids</td>
<td>Steroids</td>
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Investigations and the expected findings are:
• pulmonary function tests—gas transfer usually decreased,
• high-resolution CT—bilateral, patchy ground-glass opacities,
• trans-bronchial tissue biopsy—marked eosinophilia.

Diagnosis of MX-P can be challenging as MX-P is initially difficult to differentiate from acute pulmonary infection, and organisms such as Pneumocystis should be excluded. Several sets of diagnostic criteria have been developed; the one most commonly used is Searles’ criteria (Table 4).²⁰ MX-P is characterized as ‘definite’ if one of the major criteria is present in conjunction with three minor criteria. ‘Probable’ MX-P is present if major criteria 2 and 3 plus two of the five minor criteria are present.

Treatment of MX-P involves simply discontinuing methotrexate therapy and this may be enough to halt the pathological process and improve the clinical condition. In those who do not respond to the cessation of methotrexate, high-dose corticosteroid therapy may be required (e.g. methylprednisolone 1 mg kg⁻¹ initially). Empirical antibiotics should be commenced in those in whom infection, especially with pneumocystis, cannot be ruled out. In severe cases, inotropic and ventilatory support may be required.

Patients usually improve clinically within days of cessation of methotrexate and radiologically within weeks to months. Premethotrexate screening with pulmonary function tests and chest X-ray are standard to ensure if the rare complication of MTX pneumonitis is encountered, the patient has sufficient respiratory reserve to recover when MTX is withdrawn.

Methotrexate bone marrow toxicity
Methotrexate bone marrow toxicity may present as a moderate to severe pancytopenia. Risk factors include impaired glomerular filtration rate, advanced age, low serum albumin levels, and concurrent liver disease. Treatment begins with cessation of methotrexate, organ support, and administration of folinic acid. Appropriate replacement of red blood cells and platelets, granulocyte colony-stimulating factor, and i.v. methylprednisolone may also be required.

Biological agents
The ‘biologics’ are usually second-line treatments and fall into four broad categories.

Anti-TNF agents
TNF is a family of cytokines that have key functions in immunity, cell proliferation, and inflammation. TNF-α inhibitors have revolutionized the treatment of RA and other inflammatory diseases.

Table 4 Searles criteria for diagnosis of MX-P²⁰

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hypersensitivity pneumonitis by histopathology without evidence of pathogenic organisms</td>
<td>• Shortness of breath for &lt;8 weeks</td>
</tr>
<tr>
<td>• Radiological evidence of pulmonary interstitial or alveolar infiltrates</td>
<td>• Oxygen saturation ≤90% on room air at the time of initial evaluation</td>
</tr>
<tr>
<td>• Blood cultures (febrile) and initial sputum cultures (if sputum is produced) that are negative for pathogenic organisms</td>
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</table>

Satisfactory i.v. methylprednisolone is often enough to halt the process, but severe, persistent cases may require additional immunosuppressive therapy. Biologics have some place in the treatment armamentarium, but there is little evidence that they improve survival in MX-P.

Table 5 New-generation biologics for the treatment of RA

<table>
<thead>
<tr>
<th>Biologics</th>
<th>Examples</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-TNF agents</td>
<td>Infliximab, etanercept, adalimumab</td>
<td>Rheumatological conditions in critical care</td>
</tr>
<tr>
<td></td>
<td>Rilonizumab, tocilizumab</td>
<td>Anti-TNF agents, e.g., rilonizumab, tocilizumab</td>
</tr>
<tr>
<td></td>
<td>Methotrexate bone marrow toxicity</td>
<td>Biologics</td>
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</tbody>
</table>

TNF is a family of cytokines that have key functions in immunity, cell proliferation, and inflammation. TNF-α inhibitors have revolutionized the treatment of RA and other inflammatory diseases.
Owing to their powerful inhibitory action on TNF-α, they suppress the immune system significantly and are relatively contraindicated in those already at risk of infection, e.g. patients with uncontrolled diabetes or those on high-dose steroid therapy. Currently, they can only be given under specialist supervision. Infliximab, adalimumab, certolizumab, and golimumab are monoclonal antibodies, while etanercept is a construct of TNF-α receptors, coupled to a human monoclonal antibody.

As patients may be admitted to the ICU already taking these agents, it is useful to know dosing schedules. Broadly, these drugs are usually given subcutaneously weekly (etanercept), fortnightly (certolizumab), or monthly (golimumab). Infliximab is given 8-weekly by i.v. infusion. This should allow ample time to gain rheumatology involvement to discuss dosing and whether to continue administration or not.

Anti-TNF agents put patients at risk of atypical and opportunistic infections. Examples include:

- bacterial, e.g. Listeria, Salmonella,
- mycobacterial, e.g. Mycobacterium tuberculosis,
- viral, e.g. varicella,
- fungal, e.g. Pneumocystis jirovecii (previously Pneumocystis carinii pneumonia), Aspergillus.

B-cell depleters

Rituximab is a monoclonal antibody against CD20, a protein found on the surface of B-lymphocytes. It therefore has potent anti-B-cell action. It is licensed for the treatment of resistant RA in combination with methotrexate. It is given 6–12 monthly as two i.v. infusions 2 weeks apart.

Antibody depletion confers a high risk of the reactivation of latent infections such as tuberculosis. Reactivation of the John Cunningham virus can lead to the serious and potentially fatal progressive multifocal leukoencephalopathy.

IL-6 antagonists

Tocilizumab is a monoclonal antibody licensed for the treatment of juvenile idiopathic arthritis and RA that has failed to respond to DMARDs and a TNF-α inhibitor. It is administered by monthly i.v. infusion and weekly s/c injection.

T-cell co-stimulators

Abatacept is a fusion protein that binds to CD80 and CD86 receptors on the surface of T-cells, thus preventing T-cell activation. It is licensed for resistant RA and polyarticular juvenile idiopathic arthritis. It is usually given by monthly i.v. infusion.

Conclusions

The recent paradigm change in rheumatology where inflammatory disease is treated early with combination immunosuppressant therapies means patients are more susceptible to sepsis including atypical and opportunistic infection. Rheumatological disease flares can cause acute illness or can be a sequelae of acute illness, especially sepsis. In patients on intensive care who initially improve with antibiotics but then worsen, there should be consideration that a flare of the underlying rheumatic disease is responsible and requires treatment. Intensivists should be aware of hyper-inflammatory states such as MAS and CAPS as these are treatable when recognized. Intensivists should be aware of the rare but specific rheumatological emergencies.

Acknowledgement

Mrs Julie Alexander is acknowledged for her assistance with the diagrams.

Declaration of interest

None declared.

MCQs

The associated MCQs (to support CME/CPD activity) can be accessed at https://access.oxfordjournals.org by subscribers to BJA Education.

References

