Wegener’s granulomatosis (WG) was made. The patient was started on antibiotics and transferred to a renal unit where he was treated with plasma exchange followed by prednisolone and cyclophosphamide. He made a good recovery and returned to work 3 months later.

Cardiac involvement in WG was first described by Wegener in 1936 [1]. Abnormalities reported in this and subsequent case studies include myocarditis, pericarditis, valvular defects, vegetations, conduction defects and coronary arteritis, caused by either granulomatous infiltration or vasculitis [1–3]. The incidence of cardiac disease in WG is unclear. In one of the largest studies, where 158 patients with WG were followed up for an average of 8 years, 6% had disease affecting the heart, with only a third of these having involvement of the coronary arteries [3]. However, there are several reports of patients developing ‘silent’ MIs, often only identified following post mortem or during routine investigations [2, 4–6]. This calculation of the incidence of coronary arteritis could, therefore, be an underestimate.

Surprisingly, there are only three reports of patients with WG developing MIs with symptoms of chest pain [7–9]. In all three cases, the MI occurred early in the course of the disease and approximately a week after the diagnosis of WG was made. One patient died from the MI before immunosuppressive treatment could be started [7]. Post mortem examination revealed all three arteries to be thrombosed at the distal segments. With the other two cases, the MI occurred after commencing immunosuppressive treatment [8, 9]. Both patients underwent coronary angiography and were both found to have significant stenotic lesions in the LAD artery requiring stenting. They both made a good recovery. There has also been a case report of a patient with WG developing pulmonary oedema with ST changes consistent with an MI, but who did not experience chest pain [10]. The MI also occurred early in the course of the disease, soon after diagnosis and once steroid therapy had been started. He died shortly after. Post mortem examination reported diffuse coronary arteritis with arterial occlusion, although did not specify which artery.

Our case is unique in that this is the first reported case of a patient presenting with a symptomatic MI as the initial presenting symptom of their WG. Wegener’s granulomatosis classically presents with granulomatous disease of the respiratory tract (localized WG) followed by inflammation of the small- to medium-sized blood vessels (generalized WG) [11]. Interestingly, in our case, the coronary angiogram showed that our patient had developed a coronary vasculitis, whilst having only mild upper respiratory tract symptoms and few of the constitutional symptoms typical of generalized WG. It is possible that the pre-existing atherosclerosis in our patient led to symptoms of myocardial ischaemia in the early stages of the vasculitis. However, it is noted that of the eight previous reports of MIs in patients with WG, several also appear to have occurred during an early stage of the disease, suggesting that this is the period in which patients with WG may be most susceptible to coronary arteritis [4–10].

This is only the third coronary angiogram reported in a patient with active WG. Like the other two angiograms [8, 9], this showed no abnormalities diagnostic of vasculitis, as is often seen in other systemic vasculitides such as polyarteritis nodosa, but did show an unusual distribution of occluded small- and medium-sized vessels, particularly at the cardiac apex. Involvement of the distal segments was also seen in one of the otherwise previously reported angiograms [9] and has also been seen during post-mortem examination [7]. These observations would seem to reflect the fact that WG is a vasculitis that predominantly affects the smaller blood vessels first [11], with the distal branches possibly being more likely to be affected in WG because of their smaller diameter. It is also noted that all three angiograms identified stenoses in the LAD artery rather than the other main branches but we cannot provide an explanation for this.

In conclusion, we report a unique case of a young man with multiple cardiac risk factors, who presented with an apparently straightforward acute inferior MI who subsequently developed symptoms, signs and serological evidence of WG. We have observed that coronary arteritis may occur early in WG and suggest careful cardiac screening of all patients with newly diagnosed WG.

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Severe infections following leflunomide therapy for Rheumatoid Arthritis

Sir, We read with great interest the report by Hocevar et al. [1] about the association of pulmonary tuberculosis with leflunomide therapy in rheumatoid arthritis (RA). We face a similar problem in our rheumatology practice. The average prevalence of all forms of tuberculosis in India is estimated to be 5.05 per thousand [2], so it is not surprising that the commonest infectious complication of disease-modifying anti-rheumatic drug (DMARD) therapy that we see is tuberculosis (TB). We find most cases of TB in patients


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receiving methotrexate, a possible reflection of its use as a first-line drug in our practice. Leflunomide has fast risen in popularity as a preferred drug for combination therapy in patients with poor response to methotrexate alone. Although most of our patients tolerate it well, and respond favorably to its addition, there have been infectious complications including TB in some. What concerns us more is the severity of infections that occasionally occur while patients are receiving these therapies. We report here two patients with RA who had atypical and severe infectious complications while they were receiving leflunomide.

The first patient was a 48-yr old lady who first came to the rheumatology clinic of our institute 6 months back. She had symmetric polyarthritis for last 5 yrs and had a RF positive and erosive disease. She had not received any DMARDs previously. At presentation her Disease Activity Score 28 (DAS28) score was 6.4. She was managed with a short course of steroids (depomedrol 80 mg i.m. weekly for 4 weeks) along with oral methotrexate 10 mg weekly (titrated upwards to 20 mg weekly over 3 months for poor response). Leflunomide (20 mg daily) was added in the fourth month she had achieved a good clinical response (DAS28 = 2.6). One month later she started to have upper-abdomen pain, weakness and weight loss. Two weeks later, she developed recurrent vomiting, not associated with other gastrointestinal symptoms or fever, and severe low backache. On examination, she had only mild synovitis; however, there was marked tenderness in the region of the thoracic spine. Chest examination revealed stony dullness to percussion and decreased air entry in the left infrascapular region. The abdomen was soft without any guarding.

A chest radiograph (Fig. 1A) revealed what appeared, at first glance, to be a double left heart border. Careful review suggested a large hemispherical radio-opaque shadow with its outer contour extending beyond the cardiac shadow and cutting across the left hemidiaphragm (a routine chest radiograph obtained at the start of therapy was totally normal). MRI was obtained, whose images (Fig. 1B) showed a large left-sided paravertebral abscess extending along almost the entire thoracic spine, with erosions and partial collapse of D8–D12 vertebrae. The radiological features were consistent with a diagnosis of 'Potts spine' with a large paraspinal abscess [3]. A pigtail catheter was inserted into the paraspinal abscess, and 500 ml of pus was drained. Smear examination did not demonstrate bacteria, mycobacterium and fungi, and cultures were sterile. The patient was started on anti-TB therapy, and at 2 months follow-up, there was significant clinical improvement.

The second patient, a 36-yr old lady had seropositive and erosive RA for the past 12 yrs. Previously, she had received multiple DMARDs (methotrexate, sulfasalazine, hydroxychloroquine and myocrisin) with poor response. She was switched to monotherapy with leflunomide 20 mg once daily, to which she responded partially. Five months after starting leflunomide she presented with pain and swelling in left forearm (4 × 3 cm) and right calf (10 × 5 cm) with overlying bullous lesions. There was no fever or any other constitutional symptoms. A clinical diagnosis of pyomyositis was suspected and confirmed by ultrasound examination. Around 500 ml of pus was drained from calf muscles and 50 ml was drained from lesion in the forearm. Streptococcus pneumoniae was cultured from the pus. Leflunomide was discontinued, and pyomyositis responded to a prolonged course of antibiotics.

Infectious complications come as a part and parcel of immunosuppressive therapy. Reactivation of tuberculosis including spinal TB in patients receiving DMARDs is well described [4–6]. In the first patient, the size of paravertebral abscess and the rapidity with which it developed were unusual. Immunosuppression is a known risk factor for pyomyositis [7]. The severe and multi-focal presentation of pyomyositis in the second patient was also striking. Aggressive DMARD therapy aimed at achieving remission is fast becoming the norm in management of RA, and increased rates of infectious complications are expected. It is difficult to ascertain the relative contribution of immunomodulatory effects of leflunomide in the first case, but in the second one, evidence was more direct. This report underscores the importance of carefully assessing patients on any immunosuppressive (and not just anti-tumour necrosis factor-α drugs) for infectious complications, especially for TB, in areas of high prevalence. Clinical presentations may be unusual, and extensive lesions may appear in a short time.

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![Fig. 1. Extensive Potts spine with paraspinal abscess. (A) Chest radiograph—note the large retrocardiac soft tissue density traversing the diaphragm. (B) MRI reveals the density to be a large paraspinal abscess with erosions and collapse of D8 to D12 vertebrae classical of Potts spine.](image-url)
Use of intravenous cyclophosphamide in the prevention of corneal melt: justified or not?

Sir, We read with interest the article by Clewes et al. about the prophylactic use of intravenous cyclophosphamide in the management of the ocular conditions of two rheumatoid arthritis patients. The authors used the term ‘peripheral ulcerative keratitis’ or PUK in describing the ocular conditions. However, from the clinical information provided, this blinding ocular condition occurred as a complication after ophthalmic surgery [1]. We believe that instead of PUK, the authors were actually reporting cases of surgically induced necrotizing sclerokeratitis (SINS), which is an ocular condition with totally different manifestation, pathogenesis, treatment strategy and prognosis [2–5].

Clinically, PUK refers to a peripheral corneal lesion located in the vicinity of, or straddling across, the corneal–sclera junction, whereas SINS represents a frank scleral inflammation sparing the cornea [2, 3, 5]. SINS usually does not invade the limbus until an advanced stage of disease [2]. Pathogenetically speaking, surgical manipulation or trauma is the sine qua non for the development of SINS as surgical exposure of formerly immune-privileged tissue antigens to the immune system is thought to be the mechanism [2, 3]. Connective tissue disease is not a prerequisite for SINS because only 63% of SINS patients have underlying medical conditions [2]. Moreover, SINS shows no relationship with the activity of the systemic connective tissue disease [2]. Conversely, PUK occurs as a result of vasculitic involvement of the limbal or corneal–scleral junction vessels [5]. This is usually part of the manifestation of underlying systemic vasculitis and may herald a potentially lethal flare-up [5]. Therefore, the onset of PUK in the course of connective tissue disease carries a grave prognosis, not only for the eye but also for general well-being [5]. It necessitates prompt immunosuppressive therapy with corticosteroids and cytotoxic agents in order to save life [5]. On the other hand, concerning the management of SINS, there is an array of treatment plans, including non-steroidal anti-inflammatory agents, immunosuppressive treatment and the local surgical replacement of damaged ocular tissue [2]. Irrespective of the form of therapy, the goal of treatment in SINS, unlike that of PUK, is to control ocular tissue destruction, salvage vision and maintain the integrity of the globe [2].

The interchangeable use of PUK and SINS is extremely unusual and may suffer from the pitfall of inaccuracy.

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