ANCA-negative cases have severe underlying CNS involvement [4–6]. This prevalence is high if we consider that only 5–10% of WG patients were shown to have CNS disease in large cohorts [6]. Therefore, ANCA-negative WG may hide remarkable CNS involvement [5].

In our patient, WG initially presented as a systemic disease and C-ANCA (anti-PR3) tested positive using routine IIF and direct-ELISA. At the time WG relapsed with upper airway tract and meningeal involvement, ANCA were negative on routine assays. Surprisingly, PR3-capture ELISA detected strongly positive PR3-ANCA. PR3-capture ELISA uses, as a capturing ligand for PR3, a mouse monoclonal antibody (MoAb 4A3) directed to a PR3 epitope that is rarely targeted by human ANCA. The PR3 epitopes may be more accessible using this assay, which is also thought to better preserve the conformation of PR3 [7]. In the first clinical evaluation of this capture-ELISA, its diagnostic sensitivity was higher compared with C-ANCA by IIF in patients with WG-related renal disease [7]. Recently, a multicentre evaluation of capture-ELISA compared with direct-ELISAs and IIF confirmed the higher sensitivity of capture-ELISA [8]. Moreover, detection of PR3-ANCA by capture-ELISA showed a higher sensitivity than that obtained by direct-ELISA in diagnosing relapse during the follow-up of vasculitis [9]. The superiority of PR3-capture ELISA could be due to analytical reasons or to its ability to detect PR3-ANCA/PR3 immune complexes [10].

Meningitis is a rare and insidious complication of WG and it may be difficult to distinguish from meningeal involvement secondary to neoplasms or infections, particularly in immunosuppressed patients. In such cases, finding positive PR3-ANCA can be useful to steer the diagnosis towards a WG manifestation. This is also why a more sensitive assay, such as PR3-capture ELISA, should be included in the diagnostic armamentarium of apparently ANCA-negative WG cases, particularly when atypical clinical presentations make the diagnosis more challenging. Like in our case, if diagnosed early, WG-related meningitis usually responds to immunosuppressive therapy, whereas if left untreated it can cause severe and life-threatening complications.

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Rheumatology key message

- Look for alternative reasons of deterioration in scleroderma lung function.

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Letters to the Editor

Polyarteritis nodosa and testicular pain: ultrasonography reveals vasculitis of the testicular artery

Sir,

Polyarteritis nodosa (PAN) is a rare disease characterized by necrotizing vasculitis that may present as an aggressive form associated with multiorgan involvement [1]. Vast heterogeneity of initial clinical symptoms of PAN can occur and may lead to delayed diagnosis. We present a patient with testicular pain as one of the initial clinical symptoms where ultrasonography revealed an impressive vasculitis of the testicular artery and report the clinically protracted and complicated course of the disease, which has been fully documented by laboratory parameters, photographs, videos and Doppler/Power ultrasonography.

In 1866, Kussmaul and Maier firstly described an until then unknown disease as ‘Periarteritis nodosi’ [2]. While the American College of Rheumatology classification criteria (1990) do not distinguish between classical PAN and microscopic polyangiitis [3], the Chapel Hill Consensus Conference (1994) resulted in definitions for the nomenclature of systemic vasculitides [4]. The term classical PAN was proposed to be restricted to arteritides of small and medium-sized arteries. Published estimates of the annual incidence of PAN vary from 2 to 9/million, but could be even lower when the Chapel Hill Consensus Conference definitions were exactly followed [5].

A 29-year-old man was admitted to the hospital because of malaise, fever, painful skin lesion in the left calf, sore throat, abdominal pain, painful right forearm and swollen right hand. Chest radiography and abdominal ultrasonography were without pathological findings. The painful skin lesion was initially suggested as being an erythema nodosum. However, the laboratory test showed an elevated erythrocyte sedimentation rate and increased levels of C-reactive protein, WBC-count, creatinine and creatinine kinase. Therapy with NSAIDs and antibiotics was started immediately. Nevertheless the patient showed a rapid worsening of symptoms: new skin lesions emerged and became necrotic (Fig. 1B; Supplementary Data Figs 1 and 2), the whole right forearm became swollen (Fig. 1A), the patient also developed sensomotoric deficits (Supplementary Data Movie 1) and testicular pain on the right. This symptom was clinically diagnosed as epididymitis, and Doppler/Power ultrasonography revealed an enormously enlarged and swollen right epididymis with reduced blood circulation (Supplementary Data Fig. 3). Additionally, an impressive vasculitis of the testicular artery with consecutively reduced arterial flow down to 5 cm/s was verified (Fig. 1C) leading to diminished perfusion of the caudal testicular parenchyma (Supplementary Data Fig. 4). The rapidly increasing neurological deficits were found to be accompanied by pathological findings in EMG/ENG. Neither the presence of hepatitis B reactants nor increased level of ANCA could be detected in serum.

The patient fulfilled 5 out of 10 criteria for diagnosis of PAN, determined by the American Association of Rheumatology (1990) [3]. He showed weight loss greater than 4 kg, testicular pain, myalgias, mononeuropathy/polynuropathy, diastolic blood pressure >90 mmHg and elevated blood serum creatinine levels. The presence of 3 or more of the 10 criteria is associated with a sensitivity of 82.2% and specificity of 86.6% [3]. Immunosuppressive therapy with high dose glucocorticoids was initiated. The rapid progress of the disease necessitated an immediate onset of immunosuppressive therapy so that the sural-nerve and muscle biopsies could have only be taken afterwards. However, the biopsies did not show any necrotizing vasculitis. This could be caused by the segmental character of the vasculitis rather than by the immunosuppressive therapy already initiated. Within 7 days upon immunosuppression, the vasculitis as displayed by the enlarged artery wall and the consequent stenosis of the testicular artery regressed. The arterial flow of the testicular artery ameliorated up to 15 cm/s upon immunosuppression (Fig. 1D).

The inflammatory parameters decreased rapidly and serum creatinine, creatinine kinase and the diastolic blood pressure normalized. The sensomotoric deficits as well as the swelling of the right forearm showed regression, but the haemorrhagic necroses were still present. Oral cyclophosphamide (100 mg/day) was added to the therapeutic scheme. Whenever a dose reduction of i.v. methylprednisolone <100 mg/day was tried, the inflammatory parameters immediately increased and the sensomotoric deficits as well as swelling of the right forearm worsened again. This clinical course prompted us to increase the oral cyclophosphamide...