Microscopic polyangiitis (MPA) is a rare systemic vasculitis with an incidence of about 1–3/100,000/year [1]. MPA is defined as a necrotizing vasculitis, with few or no immune deposits, primarily affecting small vessels including capillaries, venules or arterioles [2]. MPA mainly affects kidneys and lungs, nevertheless cutaneous vasculitis, musculoskeletal symptoms, gastrointestinal involvement and peripheral neuropathy also occur [3]. Circulating antineutrophil cytoplasm antibodies (ANCA) are present in about 74.5% of patients with MPA, mainly perinuclear ANCA with specificity for myeloperoxidase (p-ANCA) [4], more rarely, in about 40% of the cases, cytoplasmic ANCA with specificity to proteinase-3 (c-ANCA) are present [5]. Depending on the extent of systemic vascular involvement, clinical findings can be quite variable; nevertheless, sexual and reproductive system involvement in patients with MPA has not previously been reported.

Case report

We report the case of a male with MPA involving the lungs, kidneys, peripheral nervous system, musculoskeletal apparatus and the reproductive system. The patient, a 53-year-old man, was hospitalized in another institution because of malaise, slight temperature, myalgia and arthralgia, which had begun 2 months earlier; these symptoms were relieved by a steroid therapy. Systolic and diastolic blood pressure values were 130/80 mmHg, and heart rate was 75/min. Laboratory tests showed leucocytosis (WBC:11,000 U/l) with neutrophilia (79%), microhematuria (5–10 RBC for microscopical field) and high values of erythrocite sedimentation rate (ESR 51 mm/h) and C-reactive protein (CRP 49 mg/L), whereas the remaining tests, including glycemia (86 mg/dL), total cholesterol (156 mg/dL), triglycerides (80 mg/dL) and high-density lipoprotein (52 mg/dL), were within the normal range. Moreover, c-ANCA were highly positive. The ear, throat and nose examination showed no abnormalities. A computed tomography scan of the thorax showed several opacities in the inferior pulmonary lobe, bilaterally, with no evidence of nodular or cavitary images. Seriate blood cultures, Mantoux intradermal reaction (5U reading 48 and 72 h), Widal-Wright and Weil Felix serodiagnosis as well as tumor markers were negative, thus ruling out infectious diseases and malignancies. An electrophysiology scan of the thorax showed several opacities in the inferior pulmonary lobe, bilaterally, with no evidence of nodular or cavitary images. Seriate blood cultures, Mantoux intradermal reaction (5U reading 48 and 72 h), Widal-Wright and Weil Felix serodiagnosis as well as tumor markers were negative, thus ruling out infectious diseases and malignancies. An electrophysiology scan of the thorax showed several opacities in the inferior pulmonary lobe, bilaterally, with no evidence of nodular or cavitary images.
features was observed in the contralateral testis. A testicular biopsy was then carried out, which showed an ischemic testicular necrosis.

Hence the final diagnosis was MPA with ischemic testicular necrosis. The patient underwent cyclic treatments with cyclophosphamide and was admitted to our day hospital.

In the course of an interview during his hospitalization, the patient reported an erectile dysfunction (ED): he did not achieve normal rigidity, and he complained in particular of difficulty in maintaining his erections. Sexual desire was referred as moderate, and ejaculatory control as normal. The sexual health inventory for men (SHIM) questionnaire showed a score of 6, which was highly suggestive for ED [6]. His past medical history was negative for drugs, smoking habit or other pathologies causing ED such as hypertension, diabetes or cardiovascular disease. The patient underwent also a specialized psychodiagnostic evaluation, which ruled out psychogenic components. The ED, therefore, was correlated with the vasculitis. An anesthesiological examination, as well as an additional ultrasound, showed only a slight bilateral decrease in testicular volume (14 and 15 mL right and left testis, respectively). Moreover, the presence of hypoechoic areas, primarily in the right testis, was confirmed by the ultrasound.

Total testosterone level was 3.26 ng/mL, with a free fraction of 7.2 pg/mL measured by RIA and 44.6 pg/mL calculated by Vermeulen formula [7], thus suggesting hypogonadism. A dynamic Doppler sonography of the penile vessels with 10 µg prostaglandin E1 (PGE1) repeated after 15 min, since a suboptimal clinical response was attained, was performed showing systolic peak velocities of 45.43 (right) and 47.63 cm/s (left; normal values >30 cm/s), diastolic peak velocities of 9.9 (right) and 8.4 (left; nv < 4.5 cm/s), and resistive indices of 0.78 (right) and 0.82 (left; nv > 0.85%), which suggested increased venous drainage [8]. Patient refused both cavernosography and corpora cavernosa biopsy.

Table 1 shows clinical, laboratory and instrumental findings.

| Medical history | Unremarkable: no hypertension, diabetes, cardiovascular disease, smoking habits or drugs causing ED |
| Clinical features | Lung and kidney vasculitis, arthritis and myalgias, mononeuropathy, testicular pain and tenderness, erectile dysfunction |
| Biochemical results | High acute phase reactant protein levels, microhaematuria, c-ANCA positive |
| Instrumental results | Thorax CT scan: opacities in the inferior pulmonary lobe, bilaterally. Electroneurography: bilateral peripheral neuropathy of the deep peroneal nerve. Testicular ultrasound: hypoechoic internal areas primarily in the right testis. PDU: right and left systolic peak velocities 45.43 and 47.63 cm/s, right and left, respectively; diastolic peak velocities 9.9 and 8.4, right and left, respectively. Resistive indices 0.78 (right) and 0.82 (left) |

Discussion

This case seems particularly interesting since there is, to our knowledge, no report in the literature of any case of testicular necrosis and ED in a patient with MPA. In our case, pulmonary involvement addressed the diagnosis towards an ANCA-associated small vessel vasculitis, thus ruling out polyarteritis nodosa (PAN), which typically affects medium and small-sized arteries except of the lungs [9]. Necrotizing small vessels vasculitides include MPA, Wegener’s granulomatosis (WG) and Churg-Strauss syndrome (CSS). WG is defined as granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting small to medium-sized vessels, such as capillaries, venules and arterioles [10], whereas CSS is classified as eosinophil-rich granulomatous inflammation involving the respiratory tract, necrotizing vasculitis affecting small to medium-sized vessels, and associated with asthma and eosinophilia [11]. The absence either of upper/lower respiratory tract granulomatous lesions or asthma/eosinophilia allowed us to perform the diagnosis of MPA, despite positive cANCA being mainly associated with WG.

The involvement of the reproductive system is rarely investigated in vasculitides, except in polyarteritis nodosa (PAN), in which testicular pain or tenderness is one of the diagnostic criteria [12]. Kitauchi et al. [13] were the only authors to report the case of a man with PAN complaining of ED, although in this patient diagnostic tests had revealed the presence of arterial ED: angiography of the internal pudendal arteries had shown multiple arterial microaneurysms, which are typical features of PAN.

In our case, testicular vessel vasculitis and consequent necrosis may be considered responsible for the ischemic lesions documented by both testicular ultrasound and biopsy. In MPA, in fact, biopsy results are not specific, mostly showing necrotic tissues with few or no immune deposits [14]. In addition, vasculitides, independent of their classification criteria, may involve several organs, thus generating overlapping syndromes and heterogeneous
clinical features that may also include unusual targets such as testis. Testicular necrosis, which caused hypogonadism, likely contributed to venogenic ED [15]; nevertheless, it could be an intriguing hypothesis that ED may also partially depend on the involvement of venules of the corpora cavernosa. It was not possible to confirm such a hypothesis either by a cavernosography, which is considered the reference diagnostic standard for venogenic ED, or by a cavernosal biopsy. In conclusion, in our case, necrotizing vasculitis involving testicular vascular walls may explain the impairment of male reproductive health and functioning, thus suggesting a new possible target.

References