Prostate cancer-associated polyarteritis nodosa: improvement of clinical manifestations after prostatectomy

Sirs,

Polyarteritis nodosa (PAN) is a systemic necrotising vasculitis of small- and medium-sized muscular arteries (1). This disorder can sometimes be caused by infections, drugs, and malignancies. We experienced a rare case of PAN in a 68-year-old man with prostate cancer, in whom the patient's PAN-related symptoms improved after prostatectomy without immunosuppressive therapy.

In May 2015, the patient was pointed out to have elevated levels of prostate-specific antigen at 9.0 ng/mL (normal limit: <4.0 ng/mL) by an annual prostate cancer screening. Biopsy revealed the prostate adenocarcinoma with a Gleason morphologic grade of 3 + 4. Around the same time, the patient experienced a high fever, arthralgia, myalgia, and livedo reticularis in his lower extremities (Fig. 1A). He was, then, admitted to our hospital for treatment of the prostate cancer and determination of the cause of the symptoms. Blood test determined C-reactive protein level of 13.70 mg/dL and the negative results of auto-antibodies, hepatitis B virus antigen and cryoglobulin. Nerve conduction study proved mononeuritis multiplex in his bilateral sural and left peroneal nerves. Computed tomography imaging and 99mTc-hydroxy-methylene-diphosphonate bone scintigraphy indicated no metastasis or abnormalities of the visceral arteries, such as aneurysms or arterial occlusions. The clinical diagnosis was stage I (cT1cN0M0) prostate cancer, and a total prostatectomy was performed.

Histological analyses of the prostate showed moderately differentiated prostate adenocarcinoma (Gleason morphologic grade 4 + 3, pT2aN0MX, stage I). Meanwhile, fibrinoid necrosis and neutrophilic infiltration were found in small- and medium-sized muscular arteries of the prostate gland, indicating necrotising vasculitis (Fig. 1B). Additionally, a skin biopsy from the livedo reticularis exhibited neutrophilic invasion to the subcutaneous muscular arteries (Fig. 1C). Due to the diagnostic findings and presenting symptoms, the patient was diagnosed with PAN (1).

Within a week post-prostatectomy, the symptoms of a high fever and arthralgia improved without glucocorticoids or immunosuppressive drugs. One month later, all of his manifestations completely disappeared and the C-reactive protein level decreased to within the normal range. To date, the spontaneous remission has been maintained, without recurrence of the prostate cancer or PAN.

The definition of paraneoplastic vasculitis is based on two criteria: (1) the concurrence of both vasculitis and neoplasms within 12 months, and (2) their parallel course (2-4). In this case, the manifestations of PAN appeared around the time of the prostate cancer diagnosis. The disease activity and treatment response for both the prostate cancer and PAN were also concordant. Of course, PAN can heal spontaneously and when exactly the prostate cancer developed is unclear; thus, the disappearance of the PAN symptoms after the prostatectomy might be fortuitous (5). However, in our case, the temporal relationship between both conditions suggested a paraneoplastic origin.

The majority of paraneoplastic vasculitides are cutaneous leukocytoclastic vasculitides secondary to malignant haematological disease. Conversely, PAN caused by solid tumours is rare with the prevalence of 6.7-10.8% (6, 7).

Prostate manifestations of PAN could mimic those of prostate cancer (8). However, the co-existence of both PAN and prostate cancer was determined by histopathological analysis on the prostate gland in our case.

Some hypotheses have been proposed to explain the pathological mechanisms between neoplasms and vasculitis, including: (1) direct invasion of cancer cells, (2) autoimmune reaction against the vessels by immune complexes comprising tumour-associated antigens, (3) impaired clearance of normally produced immune complexes, and (4) influence of tumour-derived substances in the normal tissues (9, 10).

Radical cancer treatment usually leads to improvements in the paraneoplastic vasculitis. However, systemic necrotising vasculitides usually require intensive induction and long-lasting maintenance therapies with immunosuppressive drugs (7, 11, 12). It is difficult to decide whether immunosuppressive treatment is needed for paraneoplastic vasculitis. Regardless, the cancer treatment should be prioritised in the clinical workflow.

In conclusion, this is the first case report describing prostate cancer-associated PAN with clinical remission after prostatectomy. The pathophysiological relationship between malignant diseases and vasculitis should be further investigated.

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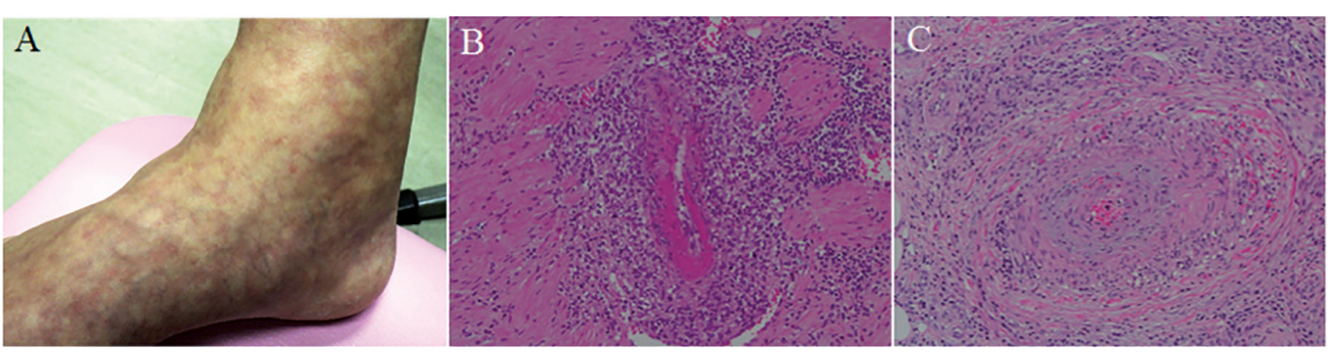

Fig. 1. Macroscopic and microscopic views of (**A**) livedo reticularis on the right lower extremity (**B**) pathological specimen of prostate gland (haematoxylin-eosin staining): fibrinoid necrosis and neutrophilic infiltration of small and medium-sized muscular artery walls in the prostate gland (**C**) pathological specimen of livedo reticularis (haematoxylin-eosin staining): neutrophilic invasion to subcutaneous muscular arteries.

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