

LETTER TO THE EDITOR**TO THE EDITOR****Expression of Yo Antigen in a Prostatic Adenocarcinoma**

Keywords: Anti-Yo paraneoplastic syndrome, Paraneoplastic cerebellar degeneration, Paraneoplastic motor neurone syndrome, Prostatic adenocarcinoma

In some patients with cancer, subacute onset of a cerebellar syndrome can be due to paraneoplastic cerebellar degeneration (PCD). PCD is most commonly associated with ovarian or breast tumours in women seropositive for anti-Yo antibodies.¹ Here we report the case of a male patient with a subacute cerebellar and motor neurone syndrome associated with anti-Yo antibodies related to a prostatic adenocarcinoma.

This 75-year-old man was admitted for a subacute onset of imbalance. On clinical examination, he was dysarthric. There was a nystagmus in the left lateral gaze. Muscular strength was normal in all four limbs, but all deep tendon reflexes were exaggerated with bilateral Babinski sign. He had lower limb fasciculations. There was cerebellar ataxia in all four limbs. There was bilateral finger-to-nose and heel-to-toe ataxia. Gait showed spastic and ataxic features. Biological workup (including vitamins A, E, B1 and B6, viral serologies and CSF analysis) was unremarkable, except for elevated PSA at 9.84 µg/L and positive anti-Yo antibodies on serum in immunoblot (Ravo, Freiburg, Germany). Anti-Yo antibodies were negative by immunofluorescence on monkey cerebrum–cerebellum (Inova Diagnostic Werfen Group, San Diego, California, United States). The positivity of anti-Yo antibodies was confirmed on serum by another immunoblot (Euroimmun, Lubeck, Germany) (Figure 1). Spinal cord MRI was normal. Brain MRI showed mild vermian cerebellar atrophy. Nerve conduction study showed a purely motor axonal neuropathy in the lower limbs with active denervation in electromyography. On the thoracic abdominal–pelvic CT scan, prostate volume was increased, with enlarged pelvic lymph nodes. Prostatic MRI showed, in addition to a prostatic adenoma, a right posterolateral T2 hypointensity. PET scan disclosed hypermetabolic fixation of the right prostatic lobe. Prostatic biopsies were positive for prostatic adenocarcinoma (Gleason score 3+4). Indirect immunofluorescence imaging (IFI) was performed on the patient's biopsies, using a negative control, a positive anti-Yo serum (Inova), the patient's serum and sera from patients with anti-Yo autoantibodies. The reaction was revealed by anti-IgG fluorescein-labelled antibodies. With all the anti-Yo positive sera, IFI showed apical glandular and focal cytoplasmic abnormal fluorescence (Figure 2). The patient was initially treated with intravenous immunoglobulin (IVIg), and once prostatic cancer was diagnosed, he underwent prostatic radiation therapy, with continuation of IVIg. At one year, his neurological condition was slightly improved (partial improvement of his gait) and the prostatic cancer was in remission (PSA 1.06 µg/L).

PCD is almost exclusively reported in women with gynaecological tumours.¹ Even though few cases of PCD associated with other cancers are reported in the literature,^{3–6} it is a very uncommon condition, especially in males. We report here the first case of PCD with anti-Yo antibodies associated with a prostatic

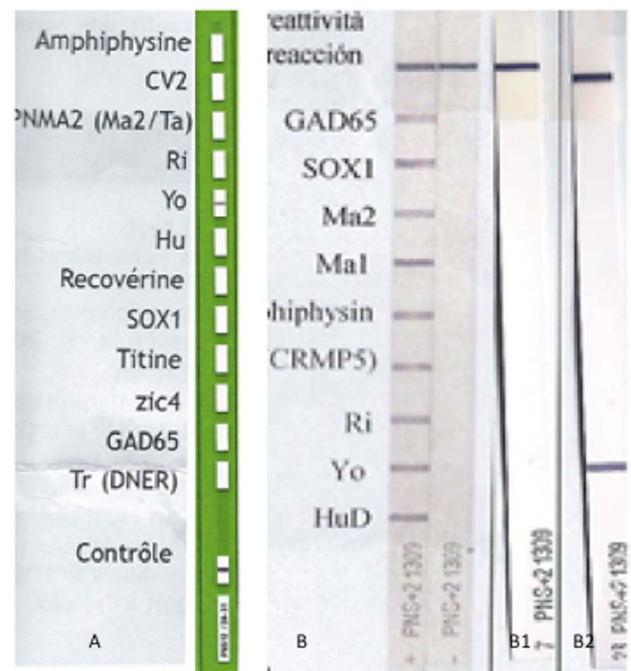


Figure 1: Immunoblot results for Anti-Yo antibodies. (A) Dot (Euroimmun, Lubeck, Germany) results with patient serum (see the black horizontal line at the Yo level). (B) Dot (Ravo, Freiburg, Germany) results (control in B1 and patient in B2).

adenocarcinoma, with Yo Ag expression confirmed on prostatic biopsies performed in a living patient. Our patient's clinical presentation was uncommon because of the association to upper and lower motor neurone disorder.

Paraneoplastic motor neurone syndromes are very uncommon, most cases being reported with anti-Hu antibodies and rarely with anti-Yo or anti-Ri antibodies.⁷ There are only two cases of motor neurone syndrome (either upper or lower) related to anti-Yo antibodies reported in detail in the literature.^{8,9} Both of these patients had no cerebellar symptoms at the time of diagnosis. Paraneoplastic syndromes (PNSs) include a wide range of clinical symptoms associated with cancer. Most of them are distinctly recognized, but some are still difficult to categorise as a result of their overlap. Our case underlies the diversity, complexity and wide spectrum of features in a PNS. Immunochemistry analysis of the tumour tissue allowed us to establish a clear link between neurological symptoms and prostatic adenocarcinoma, which was all the more relevant as it allowed us to adapt our therapeutic strategy. Indeed, due to the rarity of anti-Yo PNS associated with prostatic cancer, in the absence of such a confirmation, we would have recommended annual PET scan followups, looking for another cancer.

Anti-Yo PCD associated with motor neurone syndrome is a very rare condition. This case underscores the importance of broad cancer screening in patients presenting with anti-Yo antibody syndrome, which in males may include PSA and prostatic investigations. Due to the rarity of the association, neurologists should ask for immunochemistry analysis of prostatic biopsies,

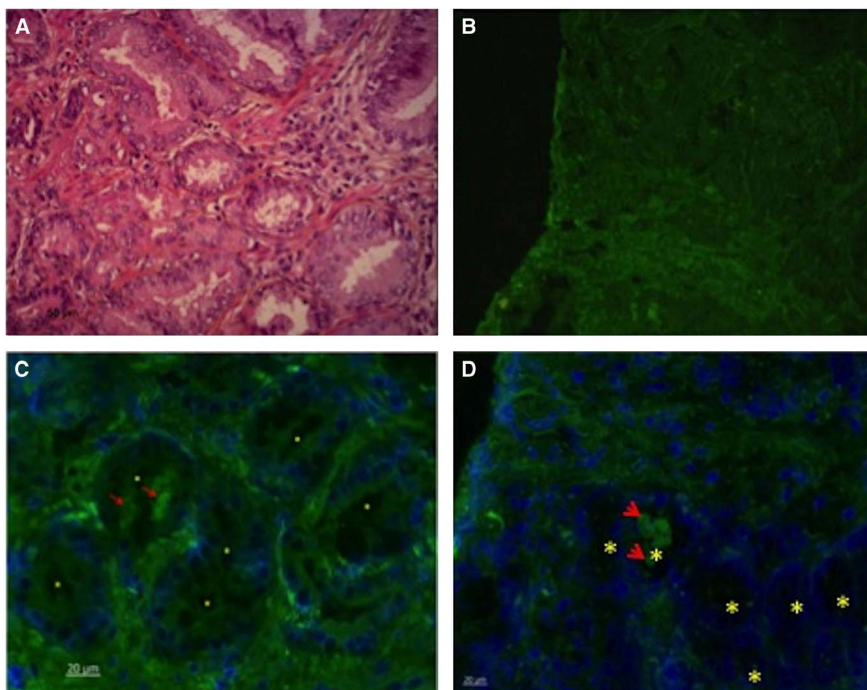


Figure 2: (A) Paraffin embedded slide (20 \times). HES imaging showing prostatic adenocarcinoma cells. (B,C,D) Indirect immunofluorescence on prostatic biopsies: (B) incubated with negative serum (X20) showing no fluorescence; (C) incubated with the serum of a patient highly positive for anti-Yo antibodies; and (D) incubated with anti-Yo positive control serum (Inova Diagnostic Werfen Group, San Diego, California, United States) showing apical glandular and focal cytoplasmic fluorescence. In blue: nuclei (DAPI staining); red arrows: granular deposits; yellow stars: glandular lumen.

in order to ascertain the relationship between prostatic adenocarcinoma and neurological symptoms. Such a confirmation is essential, as cancer treatment is mandatory to treat and at least stabilize paraneoplastic symptoms.

DISCLOSURES

Nicolas Rosine, Pascale Chrétien, Clovis Adam, Guillemette Beaudonnet, Adeline Not, Julien Draï, Katayoun Vahedi, Cécile Cauquil and Marie Theaudin do not have anything to disclose.

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