

# Sphincter abnormality in polytransfused patient due to paroxysmal nocturnal hemoglobinuria (PNH)

Initial manifestation of tropical spastic paraparesis/  
HTLV-1 associated myelopathy (TSP/HAM)

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Paroxysmal nocturnal hemoglobinuria (PNH) is a clinical entity resulting from specific change to pluripotent hematopoietic cells and subsequent clonal proliferation, with the capacity to affect the entire line<sup>1</sup>. The erythrocytic membrane has greater sensitivity to lathic action of the complement, for CD59 deficiency<sup>2</sup>. Allogenic bone marrow transplantation is the only support treatment available. According to the clinical manifestations of the disease, folic acid and iron, corticosteroids in low doses, androgens, immunosuppressants and blood component transfusion may be administered<sup>1</sup>.

In 1993, HTLV investigation in blood donor banks was officially regulated in Brazil<sup>3</sup>. It is believed that there are around 750,000 HTLV carriers in the country. However, only 5% of them will become symptomatic after years, or even decades. The immunobiological characteristics of the disease that are responsible for this remain unclear<sup>4</sup>. Individuals who develop symptoms will present insidious and gradually increasing muscle weakness in the lower limbs with spasticity, and this is associated with bladder and sensory dysfunction to varying degrees<sup>5</sup>.

The case presented here draws physicians' attention to patients with similar antecedents and unclassified neurological disease, in order to search for a retrovirus as the causal agent. We describe the association between PNH and tropical spastic paraparesis/HTLV-1 associated myelopathy (TSP/HAM), with regard to its diagnosis, management and rehabilitation.

## CASE

The patient was a 48-year-old Caucasian man. For six years, he had presented signs of micturition urgency, incontinence, hesitation and sensation of incomplete bladder voiding. Two years before the current presentation, he started to show a picture of occasional fecal incontinence, erectile dysfunction, paresthesia and sensory reduction in the distal parts of the lower limbs, along with balance impairment. He had been diagnosed with PNH three decades earlier, with confirmation from specific tests (Ham, sucrase and flow cytometry tests). He underwent several blood transfusions at that time.

In the physical examination, hypoaesthesia and abnormal sensitivity to vibrations were detected in the lower limbs. His

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## ALTERAÇÃO ESFINCTERIANA EM PACIENTE POLITRANSFUNDIDO DEVIDO À HEMOGLOBINÚRIA PAROXÍSTICA NOTURNA (HPN): MANIFESTAÇÃO INICIAL DE PARAPARESIA ESPÁSTICA TROPICAL/MIELOPATIA ASSOCIADA AO HTLV-1 (PET/MAH)

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muscle strength was normal. His osteotendinous reflexes were increased in the lower limbs, with bilateral Babinski signs. His muscle tonus was preserved and he was able to walk within the community, although needing support because of his balance dysfunction.

Serological tests for HTLV in blood and cerebrospinal fluid (CSF) were positive (ELISA and Western blot). He tested positive for hepatitis C, but negative for HIV. Laboratory tests showed anemia (hemoglobin: 10 g/dl; hematocrit: 31%), diminished platelet count (51,000 platelets), anisocytosis index of 21.2%, normal serum iron and moderately increased total bilirubin and fractions. Analysis on nervous conduction showed modified somatosensory evoked potential (SSEP) for the lower limbs, with normal motor and visual evoked potentials and normal electromyography. Bone marrow aspiration showed erythroid hyperplasia with slight maturation change. Imaging examinations showed signs of neurogenic bladder, presence of calculous cholecystopathy and slight atrophy of the thoracic spinal cord (Fig 1A and 1B). Urodynamic assessment showed detrusor hyperactivity (detrusor pressure of 55 cmH<sub>2</sub>O), with urine loss. Moreover, it showed micturition with detrusor pressure of 49 cmH<sub>2</sub>O and maximum urinary flow of 2.1 ml/s. The micturition volume was 62 ml, with elevated residual volume (Fig 2).

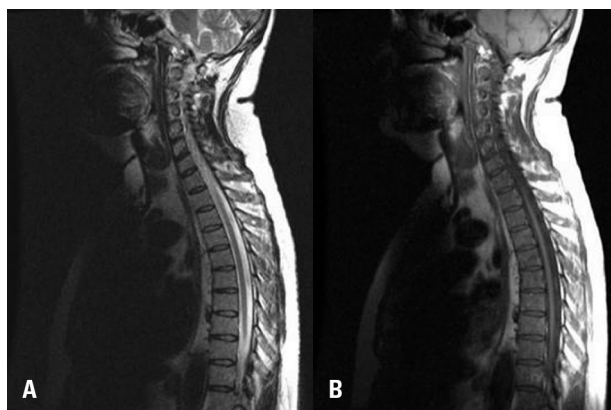
The patient took part in a rehabilitation program with the main objective of training for intermittent bladder catheterization, associated with anticholinergic medication. A physical-functional evaluation was carried out, with indication for walking support and follow-up by an interdisciplinary team. The patient signed an informed consent statement permitting this publication of his case.

## DISCUSSION

PNH is characterized by chronic intravascular hemolysis, thrombotic phenomena and inefficient hematopoiesis, with frequent pancytopenia. It results from somatic mutation of a gene located in chromosome X that codes for a PIG-A protein (phosphatidylinositol glycan protein A) that is essential for the formation of glyceryl phosphatidylinositol (GPI). All the PNH phenotypic mutations obey the PIG-A gene mutations. GPI deficiency bound to the CD59 protein explains PNH intravascular hemolysis<sup>6</sup>.

The first human retrovirus was discovered in the United States in 1980, by Poiesz et al.<sup>7</sup>, in a patient with cutaneous T-cell lymphoma. Adult T-cell leukemia/lymphoma and TSP/HAM are the main pathological conditions associated with HTLV-1.

TSP/HAM is a chronic, debilitating inflammatory disease of the central nervous system, characterized by axonal damage and demyelination, which is mainly present in the thoracic spinal cord. Diagnostic criteria were proposed by Osame in 1990 and confirmatory diagnostic cri-



**Fig 1.** [A and B] Nuclear magnetic resonance on the cervical-thoracic spine: fast spin echo (FSE) sagittal slices with T2 weighting (TR/TE: 3500/123 ms) and T1 weighting (TR/TE: 650/11 ms), demonstrating slight atrophy of the thoracic spinal cord and signal changes in the vertebral bodies.



**Fig 2.** Complete urodynamic evaluation: sustained bladder contraction during the filling phase, with detrusor pressure of 55 cmH<sub>2</sub>O (in 1), followed by urinary loss (in 2). Micturition with flow of 2.1 ml/s (in 3) and detrusor pressure of 49 cmH<sub>2</sub>O (in 4). Micturition volume of 62 ml and elevated residual volume.

teria by De Castro-Costa et al.<sup>5</sup> in 2006. These have been used as a guide for clinical and laboratory definition of cases. In addition to the serological and molecular tests, laboratory tests such as CSF, SSEP and nuclear magnetic resonance have been used for confirmation and differential diagnosis of this disease<sup>8</sup>.

The viral transmission occurs vertically (from mother to child during breastfeeding) and horizontally (sexual intercourse, blood transfusion or use of injectable drugs).

TSP/HAM was firstly described in Brazil in 1989<sup>8</sup>. A nationwide analysis involving all five geographical regions of the country showed that the majority of the cases came from the northeastern and southeastern regions (93.2%). The most common risk factors among these patients were sexual diseases (30.6%) and blood transfusions (21.6%)<sup>9</sup>.

Infected individuals, with or without neurological disease, presented bladder hyperreflexia as the main finding from the urodynamic evaluation. However, other types of bladder conditions have been observed, thus indicating the complexity of this disease and the need for special care regarding the upper urinary system. Urodynamic and micturition abnormalities precede the neurological findings in up to 20% of the cases. Erectile dysfunction associated with bladder dysfunction is an important marker of disease onset, with constipation occurring later<sup>10</sup>.

Irritative and obstructive urinary symptoms may be reported by patients with HTLV-associated myelopathy. The most common urodynamic findings are detrusor hyperactivity, bladder sphincter dyssynergy and presence of elevated residual volume. In some cases, this is a consequence of detrusor hypocontractility and/or incomplete bladder neck opening<sup>10</sup>. With the diagnosis of neurogenic bladder, measures promoting reductions in the number of episodes of urinary tract infection are necessary, among which bladder voiding.

Myelodysplastic syndrome occurs in 8% of the cases. Leukemia may develop in 3 to 5% of individuals with the disease. Myelogram and/or bone biopsy may become necessary<sup>11</sup>.

Rigorous control over blood donor banks through serological screening for HTLV, guidance for seropositive individuals and their relatives and clinical-laboratory follow-up are preventive measures that make it possible to avoid contamination and, consequently, to avoid development of associated diseases, as the most efficient therapy.

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