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Primary and Reversible Pisa Syndrome in Juvenile Normal Pressure Hydrocephalus

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Abstract

Objective—To report a case of Pisa syndrome in a patient with idiopathic normal pressure hydrocephalus, who had never been exposed to psychotropic medications.

Methods—A 26 years-old, Colombian, male patient, was referred because he had cognitive abnormalities, gait disturbances and urinary incontinence. This patient also displayed pleurothotonos. Neurofunctional evaluation of sensory and motor integration at peripheral and central nervous system levels were done.

Results—Pisa syndrome disappeared after spinal tap drainage with further gait, balance and behavioral improvement. A brainstem-thalamocortical deregulation of the central sensory and motor programming, due to the chaotic enlargement of brain ventricles was thought to be the pathophysiological mechanism underlying this case.

Conclusion—NPH must not be longer considered as an exclusive geriatric disorder. Further, uncommon movement disorders may appear with this disorder, which should be carefully approached to avoid iatrogenic and deleterious pharmacological interventions.

Introduction

Pisa syndrome or pleurothotonos, is a delayed axial dystonia characterized by trunk rotation, lateral flexion and the head to one side (1). It has usually been thought to be due to medications, mostly antipsychotics; for this reason it is named secondary Pisa syndrome (SPS) (1). Female gender, old age, and organic brain disorders are considered its most common risk factors (2). Normal pressure hydrocephalus, on the other hand, is a complex

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and prevalent, albeit potentially reversible, disorder causing dementia in the geriatric population (3). It is characterized by abnormal gait, urinary incontinence, and behavioral disturbances, described by the Colombian physician Salomon Hakim, in 1965 (3). The annual incidence found in recent surveys performed in Germany and Norway was in between 1.8/100,000 and 5.5/100,000 inhabitants, and the prevalence was 22/100,000 (4). We report a case of reversible sporadic truncal dystonia, with typical findings of primary Pisa syndrome, in a young Colombian patient suffering idiopathic NPH (iNPH).

Methods and Results

A 26 years-old, male patient, without past medical history of cerebrovascular, infectious or traumatic disease, presented labile mood, short-term memory disorders, personality changes which turned to be compulsive, hyperarousal, isolation and no fear at age 23. Depression was initially diagnosed, and then paranoid schizophrenia was considered by some family physicians that took care of him elsewhere. In the following year, the patient developed gait and balance disturbances and a lean to the right while standing; then, left arm dystonia, distal tremor in upper limbs and loss of balance was noted. By that time, urinary and fecal incontinence as well as severe insomnia became evident. Five mg of olanzapine was prescribed by private clinical neurologist, confirmed by general psychiatrics, with no improvement of clinical symptoms at all. Rehabilitation was never considered by clinicians.

Neurological exam performed by our group, three years after disease starting revealed ideomotor apraxia, and the mini-mental state examination validated for spanish-speaking countries (5) was 17/30; attention and calculation, orientation to place and complex demands were impaired. Likewise, the patient reported anosmia since the beginning of the disorder. He had decreased pin-prick and facial palsy in left hemiface, stage II in the House Brackmann scale, cogwheel rigidity in upper limbs and left leg, left laterocolis and postural tremor in hands. Generalized brisk reflexes, bilateral patellar clonus, positive glabella and bilateral marinesco signs were also present; fundoscopia was normal. In addition, Pisa syndrome and “magnetic gait” was observed. Sequels or current brain trauma, stroke, infectious disease or any other parenchymal cerebral lesion were ruled out by medical history, neuroimaging and at clinical exam.

Since the beginning of these medical complaints the patient developed papules and plaques in face, trunk and limbs histologically reported as granulomatous dermatitis (Figure 1).

Functional neurological studies were performed following methodologies explained elsewhere (6). Briefly, electrically elicited blink reflexes at supraorbital nerves and recorded in the orbiculari oculi muscles bilaterally were performed with patient's eyes open; they showed instability of late responses (R3) as well as an early contralateral left R1 response (7); left to right difference of somatosensory cortical N20 latencies, obtained by left and right median nerve stimulation was found (left N20: 22,9 msc, right N20: 19,8 msc); latencies and amplitudes elicited by left tibial nerve stimulation were also abnormal (Figure 2); F waves persistence in left median and tibial nerve was 5%; Conventional EEG was unspecific. More importantly, magnetic resonance imaging (MRI) of the brain displayed generalized cerebral atrophy and ventricles enlargement (Figure 3); stroke, trauma or infectious diseases were ruled out by neuroimaging as well.

Based on the aforementioned clinical and laboratory findings idiopathic NPH was diagnosed (8,9). Therefore, a cerebral spinal fluid (CSF) tap drainage test was performed, and 40 mL of CSF were drained. The opening pressure was 110 mm Hg; protein was 23 mg/dL, glucose was 54 mg/dL (blood sugar was 98 mg/dL), cell counts showed two lymphocytes/HFS.

Twenty four hours after performing the spinal tap procedure, behavioral and sleep disturbances improved, as commented elsewhere (8); mini-mental state examination score also improved to 23/30 (in orientation to place and complex demands items). A significant decrease of “magnetic” gait was noted, balance and left laterocollis improved, and Pisa syndrome disappeared completely. After this, the patient was sent to the neurorehabilitation unit under specific protocol, but he was lost in the follow-up. A wider description and pathophysiological explanation of clinical and laboratory findings including focal cranial nerve involvement and long tract neurological findings were reported elsewhere, in Spanish (8,10).

Discussion

Pisa syndrome with no previous exposure to neuroleptics or primary Pisa syndrome (PPS) and its improvement following spinal tap drainage, an interventional measure used in iNPH, has never been reported in young people. If we were to follow the commonly proposed criteria in older people suffering iNPH(8,9), the age of the patient would be against iNPH diagnosis. However, since several years ago, this disorder has indeed been diagnosed in people younger than 20 years-old (11). Being unaware of these facts could confuse local practitioners elsewhere, who wrongly prescribed olanzapine, which triggers PPS (1), and worsened the primary axial dystonia this patient had as a consequence of presenting iNPH.

Germane to this report, PPS has also been reported in multiple system atrophy (12), Alzheimer disease (13), as a possible consequence of peripheral nerve injury (14), and after receiving electroconvulsive therapy (15). This indicates that PPS is a separate clinical entity that was indeed present in our patient. Due to the limited amount of publications on PPS, its pathophysiology is still uncertain and probably more complex than thought; however, some considerations can be advanced from the mechanisms proposed in SPS.

Brain cortical atrophy, ventricular dilatation (1), striatonigral degeneration (16), or asymmetric distribution of dopaminergic receptors (17) reported in SPS could account, at some extent, for the clinically established PPS as well. Moreover, brain asymmetry in iNPH affects neurotransmitters function (18), downregulating D2 receptors in the striatum due to nigrostriatal dopaminergic pathways alteration (19). Thus, it is conceivable that the uneven enlargement and structural deformities found in the brain of our young patient originated a widespread brainstem-thalamocortical dysfunction (7,98), downregulating extrapyramidal, cognitive and behavioral circuits and its corresponding neurotransmitters leading to the myriad of signs and symptoms reported here. Further, the abnormal clinical motor output reflected as axial dystonia in our patient, was very likely perpetuated by dopamine dysfunction at sensory pathways level that made defective the afferent signal-noise ratio (20), leading to display the instability of the brainstem responses. However, more work has to be done in PPS to better understand this new clinical entity.

Although the axial dystonia found in this unique case seemed to be due to central nervous system alterations, other movement disorders (e.g., parkinsonism), found very often in iNPH, when brain asymmetry is detected (21), present scoliosis, which is another type of focal dystonia thought to be part of abnormal movements associated with afferent sensory system injuries (22,23). Interestingly, three out of 18 patients with axial primary dystonia and an unexpected higher prevalence of previous peripheral trauma had scoliosis-like symptoms resembling PPS (24). And, blepharospasm, another focal dystonia with chronic afferent sensory dysfunction, also preceded PPS (13). These facts, along with the novel abnormalities found by us in patients with primary focal dystonia-associated peripheral nerve injury, assessed neuromagnetically (23), support the contention that peripheral trauma may precede PPS as well (14). Therefore, a new classification on Pisa syndrome emerges

here that will help in offering better neuromodulatory approaches to improve the quality of life of these patients (Table).

Other less understood abnormalities present in iNPH involve altered serotonin, noradrenalin, and acetylcholine neural transmission (1), which modulate smell function (25). Of remark, olfactory nerves have the greatest contribution to cerebrospinal drainage; if affected, as in iNPH, it would alter smell function (26). Although we did not quantify the patient's olfactory dysfunction, we anticipate that smell testing might be a very sensitive predictor and useful follow-up tool in iNPH. Incidentally, the dermatological abnormality appearing at the beginning of the disorder has been associated to rheumatologic problems (27). Its significance in iNPH is unknown.

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Figure 1.
Granulomatous dermatitis (arrow) present since the beginning of the disease.

Figure 2. Somatosensory evoked potentials recorded at somatosensory cortex after stimulating left tibial nerve. The three traces show the reproducibility of the latency prolongation, and low amplitude of the cortical response (P 37). Horizontal: 10 msc

Figure 3. Sagittal (A) and axial (B) T2 MRI of a patient with chronic (normal pressure) hydrocephalus. Note the corpus callosum atrophy, lateral ventricles enlargement as well as cortical and white matter atrophy. Likewise, it is possible to observe transependymal flow and rounded horns.

Table

Classification of primary (1) and secondary (2) Pisa syndrome. PNS: peripheral nerve system; CNS: central nervous system. Equal sign means that the probability of having PPS or SPS is similar.

Prior medication	Yes	(2)	No	(1)
Clinical presentation	Acute	(1=2)	Chronic	(1=2)
Anticholinergic response	Yes	(2)	No	(1)
Type of injury	PNS	(1=2)	CNS	(1=2)