Acta Neuropsychiatrica
An International Journal of Translational Neuropsychiatry

Acta Neuropsychiatrica 2012

DOI: 10.1111/j.1601-5215.2012.00657.x

ACTA NEUROPSYCHIATRICA

Case Report

Primary and reversible Pisa syndrome in juvenile normal pressure hydrocephalus

Leon-Sarmiento FE, Pradilla G, Zambrano MR. Primary and reversible Pisa syndrome in juvenile normal pressure hydrocephalus.

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-year-old, Colombian, male patient, was referred because he had cognitive abnormalities, gait disturbances and urinary incontinence. This patient also displayed pleurothotonos. Neurofunctional evaluations of sensory and motor integration at peripheral and central nervous system levels were done. Idiopathic normal pressure hydrocephalus (NPH) was diagnosed.
Results: Pisa syndrome disappeared after spinal tap drainage with further gait, balance and behavioural 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.

Fidias E. Leon-Sarmiento[1,2,3,4], Gustavo Pradilla[5], Maria del Rosario Zambrano[6]

[1]Smell and Taste Center, University of Pennsylvania, Philadelphia, PA, USA; [2]Department of Otorhinolaryngology – Head and Neck Surgery, University of Pennsylvania, Philadelphia, PA, USA; [3]Unit of Parkinson and Movement Disorders, Mediciencias Research Group, Unit of Aerospace Medicine, Universidad Nacional, Bogota, Colombia; [4]Human Aerospace Laboratory, Mount Sinai School of Medicine, New York, NY, USA; [5]Department of Internal Medicine, UIS, Unit of Neurology, Bucaramanga, Colombia; and [6]Neurorehabilitation Unit-NeuroSalud, ''Ramon & Cajal'' Panamerican Health Foundation, Bogota, Colombia

Keywords: central nervous system; cerebral cortex; dementia; psychiatric disorders

Dr Fidias E. Leon-Sarmiento, Smell and Taste Center, University of Pennsylvania, 5 Ravdin Pavilion 3400, Spruce Street, Philadelphia, PA 19104, USA.
Tel: +13152458183;
Fax: +13152458183;
E-mail: feleones@gmail.com

Accepted for publication February 10, 2012

Introduction

Pisa syndrome or pleurothotonus, is a delayed axial dystonia characterised 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 and prevalent, albeit potentially reversible, disorder causing dementia in the geriatric population (3). It is characterised by abnormal gait, urinary incontinence and behavioural 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 (PPS), in a young Colombian patient suffering idiopathic normal pressure hydrocephalus (iNPH).

Methods and results

A 26-year-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 were noted. By that time, urinary and fecal incontinence as well as severe insomnia became evident. Five milligrams 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, 3 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. Generalised brisk reflexes, bilateral patellar clonus, positive glabella and billateral 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 (Fig. 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 ms, right N20: 19.8 ms); latencies and amplitudes elicited by left tibial nerve stimulation were also abnormal (Fig. 2); F waves persistence in left median and tibial nerve was 5%; Conventional electroencephalography was unspecific. More importantly, magnetic resonance imaging of the brain displayed generalised cerebral atrophy and ventricles enlargement (Fig. 3); stroke, trauma or infectious diseases were ruled out by neuroimaging as well.

On the basis of 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 was 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.

Twenty-four hours after performing the spinal tap procedure, behavioural 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

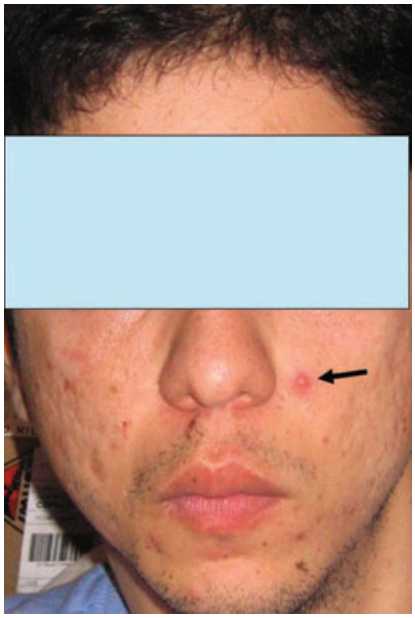

Fig. 1. Granulomatous dermatitis (arrow) present since the beginning of the disease.

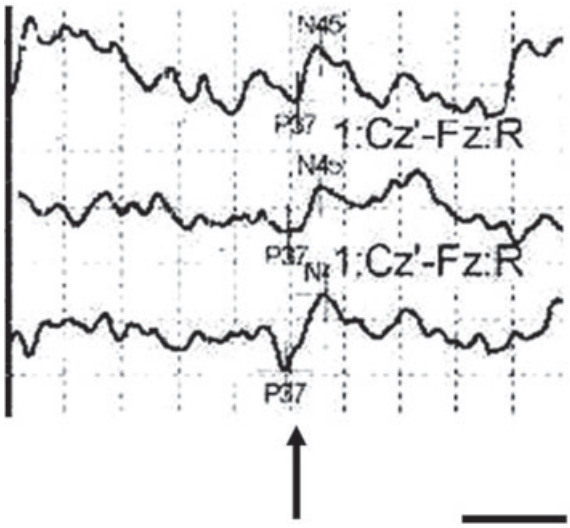

Fig. 2. Somatosensory evoked potentials recorded at somatosensory cortex after stimulating left tibial nerve. The three traces show the reproducibility of the latency prolongation, and low amplitude of the cortical response (P37). Horizontal: 20 ms.

https://doi.org/10.1111/j.1601-5215.2012.00657.x Published online by Cambridge University Press

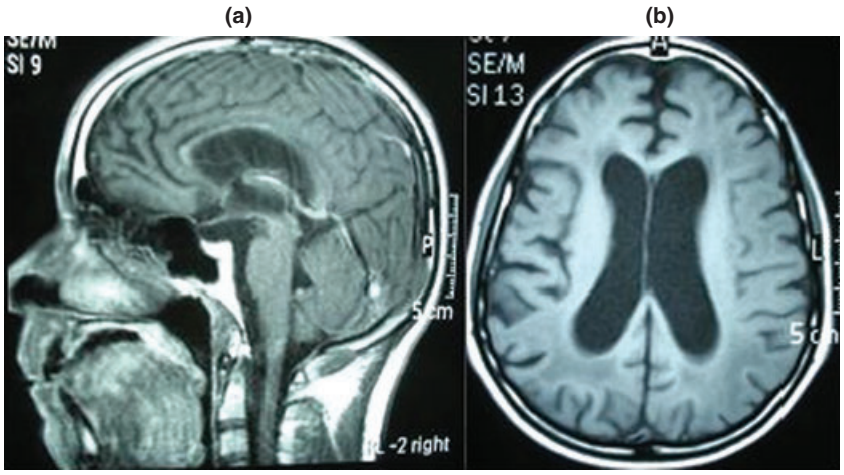

Fig. 3. Sagital (a) and axial (b) T2 magnetic resonance imaging of a patient with chronic (normal pressure) hydrocephalus. Note the corpus callosum atrophy, lateral ventricles enlargement as well as cortical and white matter atrophy. Likewise, it is possible to observe transependymal flow and rounded horns.

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 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 (7,8), downregulating extrapyramidal, cognitive and behavioural 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, 3 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,

https://doi.org/10.1111/j.1601-5215.2012.00657.x Published online by Cambridge University Press

Table 1. Classification of primary (1) and secondary (2) Pisa syndrome

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)

CNS, central nervous system; PNS, peripheral nerve system.
Equal sign means that the probability of having PPS or SPS is similar.

assessed nauromagnetically (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 1).

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.

Acknowledgements

The authors would like to thank Dr Carlos V. Rizzo-Sierra and Dr Richard L. Doty for their help during the preparation of this manuscript. The input gave by Dr Salomon Hakim (deceased) to an earlier version of this manuscript is greatly appreciated. Dr F. E. L-S. was supported by the US National Institutes of Health (RO1DA019055-04) and the Department of Defense (USAMRAA 8100002). The authors declare no conflict of interest. All authors equally contributed to the conception, analysis, preparation and writing of the manuscript; they all have approved the final manuscript.

References

1. Suzuki T, Matsuzaka H. Drug-induced Pisa syndrome (pleurothotonus): epidemiology and management. CNS Drugs 2002;**16**:165–174.
2. Villarejo A, Camacho A, García-Ramos R et al. Cholinergic-dopaminergic imbalance in Pisa syndrome. Clin Neuropharmacol 2003;**26**:119–121.
3. Hakim S, Adams RD. The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. Observations on cerebrospinal fluid hydrodynamics. J Neurol Sci 1965;**2**:307–332.
4. Pereira Damasceno B. Normal pressure hydrocephalus. Diagnostic and predictive evaluation. Dememt Neuropsychol 2009;**3**:8–11.
5. Leon-S FE, Pradilla G, Villamil L, Vesga B, Dallos M. Análisis crítico del minimental en el mundo: 1975–1995. Acta Neurol Col 1999;**15**:135–145.
6. Leon-S FE, Gomez A, Kimura J. Neurofisiologia clinica. In: Toro J, Yepes M, Palacios E, eds. Neurologia, 7th edn. Mexico, DF: Manual Moderno, 2010: 683–701.
7. Leon-S FE, Arimura K, Sonoda Y, Arimura Y, Osame M. Instability of R3 of the blink reflex in patients with HAM/TSP. Funct Neurol 1994;**8**:199–202.
8. Leon-S FE, Pradilla G, Calderon A, Duque JR. Dilación, dilatación e inclinación en hidrocefalia de presión normal. Rev Colomb Psiquiat 2008;**37**:280–286.
9. Relkin N, Marmarou A, Klinge P. Diagnosing idiopathic normal-pressure hydrocephalus. Neurosurgery 2005; **57**(Suppl. 3):4–16.
10. Leon-S FE, Pradilla G, Calderon A. Pleurototonus. Acta Med Colomb 2008;**33**:153.
11. Bret P, Chazal J. Chronic ("normal pressure") hydrocephalus in childhood and adolescence. A review of 16 cases and reappraisal of the syndrome. Childs Nerv Syst 1995;**11**:687–691.
12. Colosimo C. Pisa syndrome in a patient with multiple system atrophy. Mov Disord 1998;**13**:607–609.
13. Patel S, Tariot PN, Hamill RW. Pisa syndrome without neuroleptic exposure in a patient with dementia of the Alzheimer type. J Geriatr Psychiatry Neurol 1991;**4**:48–51.
14. Bhattacharva KF, Giannakikou I, Munroe N, Chaudhuri KR. Primary anticholinergic-responsive Pisa syndrome. Mov Disord 2000;**15**:1285–1287.
15. Lee WK, Shiah IS, Chen CY, Lin TL, Shen LJ. Electroconvulsive therapy-associated Pisa syndrome in clozapine treatment. Psychiatry Clin Neurosci 2008;**62**:753.
16. Kan AE. Striatonigral degeneration. Pathology 1978;**10**: 45–52.
17. Ouchi Y, Nakayama T, Kanno T, Yoshikawa E, Shinke T, Torizuka T. In vivo presynaptic and postsynaptic striatal dopamine functions in idiopathic normal pressure hydrocephalus. J Cereb Blood Flow Metab 2007;**27**: 803–810.
18. Kondziella D, Sonnewald U, Tullberg M, Wikkelso C. Brain metabolism in adult chronic hydrocephalus. J Neurochem 2008;**106**:1515–1524.
19. Krauss JK, Regel JP, Droste DW, Orszagh M, Borremans JJ, Vach W. Movement disorders in adult hydrocephalus. Mov Disord 1997;**12**:53–60.
20. Peiser C, Fisher A. Expression of dopamine receptors in sensory neurons of the rat. Am J Respir Crit Care Med 2001;**163**:A905.
21. Morishita T, Foote KD, Okun MS. INPH and Parkinson disease: differentiation by levodopa response. Nat Rev Neurol 2010;**6**:52–56.
22. Doménech J, Tormos JM, Barrios C, Pascual-Leone A. Motor cortical hyperexcitability in idiopathic scoliosis: could focal dystonia be a subclinical etiological factor? Eur Spine J 2010;**19**:223–230.
23. Bohlhalter S, Leon-S FE, Hallett M. Abnormality of motor cortex excitability in peripherally induced dystonia. Mov Disord 2007;**22**:1186–1189.
24. Bhatia KP, Quinn NP, Marsden CD. Clinical features and natural history of axial predominant adult onset primary dystonia. J Neurol Neurosurg Psychiatry 1997;**63**:788–791.
25. Hawkes CH, Doty RL. The neurology of olfaction. Cambridge: Cambridge University Press, 2009.
26. Kapoor KG. Do patients with idiopathic intracranial hypertension suffer from hyposmia? Med Hypotheses 2008;**71**:816–817.
27. Crowson AN, Magro C. Insterstital granulomalotous dermatitis with arthritis. Hum Pathol 2002;**35**:779–780.

https://doi.org/10.1111/j.1601-5215.2012.00657.x Published online by Cambridge University Press