Brain sonography features in X-linked dystonia-parkinsonism

A. Rocco [1,2], U. Walter [1], C. Klein [3], R. Rosales [4], C. Go [4,5], D. Dressler [6], L.V.Lee [4]

[1] Neurology Section, Department of System Medicine, University of Rome "Tor Vergata", Italy
[2] Department of Neurology, University of Rostock, Germany
[3] Institute of Neurogenetics, University of Lübeck, Lübeck, Germany
[4] XDP Study Group, Philippine Children's Medical Center, Quezon City, Philippines;
[5] Faculty of Neurology and Psychiatry, University of Santo Tomas, Manila, Philippines
[6] Movement Disorders Section, Department of Neurology, Hannover Medical School, Hannover, Germany

Introduction

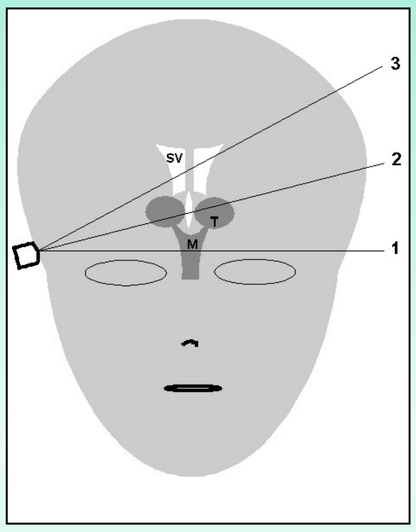
X-linked recessive dystonia-parkinsonism (XDP, Lubag, DYT3) is a rare movement disorder that is highly prevalent in the Philippines. XDP has been associated with different genetic mutations on the X chromosome not yet unequivocally determined and with morphological and functional evidence of an involvement of the dopaminergic nigrostriatal pathway (1, 2). Here, we evaluated the correlation between transcranial brain sonography (TCS) findings and the genetic and clinical state in XDP patients, relatives and controls.

Patients

Altogether, 89 participants (36 female; mean age 45.1±12.9 years) were enrolled. Participants were classified with respect to family history, mutational status, and clinical symptoms of XDP.
40 participants were clinically affected XDP patients with positive genetic status, 20 were clinically unaffected relatives of XDP patients (7 with positive genetic status, 7 with negative genetic status, 6 with unknown genetic status), and 29 served as healthy controls.

Methods

Sonography.
Ultrasound system: Esaote MyLab 25 Gold; 2.5-MHz phased-array transducer.
Investigation: Transtemporally in three axial scans (Fig.). SN size measurements were performed on axial midbrain scan automatically after manually encircling SN's outer circumference. SN sizes < 0.20 cm^2 were classified as normal, sizes ≥ 0.25 cm^2 as markedly hyperechogenic, and sizes in between as moderately hyperechogenic. Echogenicity of the lenticular nuclei (LN) was classified as hyperechogenic when it was more intense than the surrounding white matter (3). SN and LN echogenicity was quantified post-hoc on digitized analysis of anonymized images using Math-Lab based software.
Statistics. Descriptive statistics; chi-square test, Fisher exact test.



3 = *Cella-media axial scan:* Width of the lateral ventricle (cella media) is measured contralaterally.

2 = *Diencephalic axial scan:* Investigation of the contralateral thalamus, lenticular and caudate nuclei, widths of the third ventricle and the contralateral frontal horn of the lateral ventricle.

1= *Mesencephalic axial scan:* Measurement of ipsilateral SN echogenic area, evaluation of nucleus ruber and midbrain raphe.

TCS of brain parenchyma: Transtemporal investigation on three axial scans

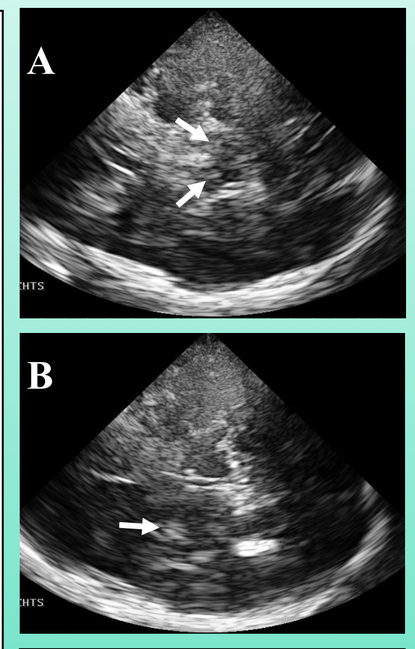
Results

Relationship between TCS findings and clinical status

- 27 (79%) of 34 assessable, clinically affected XDP patients exhibited SN+ but only 9 (53%) of 17 relatives of XDP patients and 9 (38%) of 24 healthy control subjects (p = 0.005).
- 30 (81%) of 37 assessable, clinically affected XDP patients exhibited LN+ but only 4 (25%) of 16 relatives of XDP patients and 7 (28%) of 25 healthy control subjects (p < 0.001).

Relationship between TCS findings and mutational status

- 31 (78%) of 40 assessable patients with XDP mutation exhibited SN+ but only 10 (34%) of 29 subjects without mutation (p < 0.001).
- Considering only the unaffected relatives of XDP patients, 4 (67%) of 6 assessable subjects with XDP mutation exhibited SN+ but only 1 (20%) of 5 subjects without mutation (p < 0.001). By contrast, only 2 (40%) of 5 assessable subjects with XDP mutation exhibited LN+ and 1 (20%) of 5 subjects without mutation (p = 0.50).



A) Bilateral substantia nigra hyperechogenicity (SN+; arrows)
B) Unilateral lenticular nucl. hyperechogenicity (LN+; arrow)

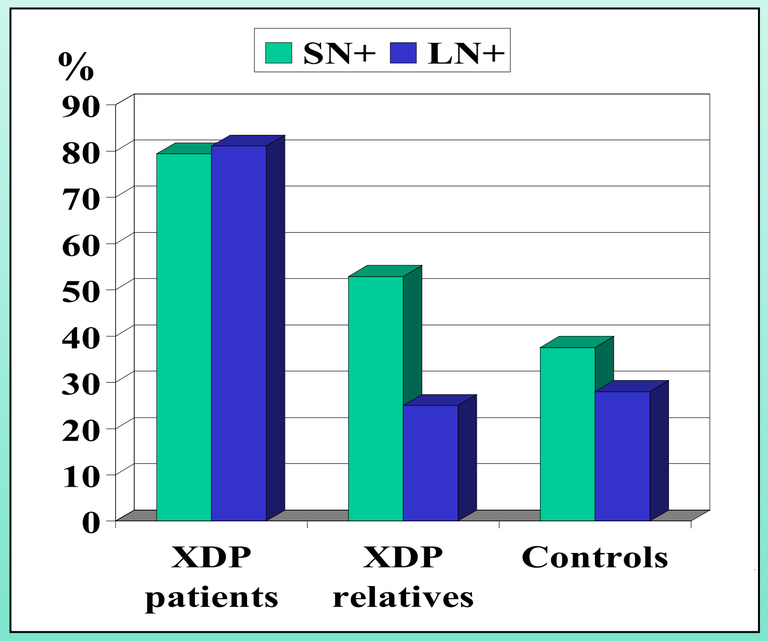


Diagram showing the frequency of abnormal hyperechogenicity of substantia nigra (SN+) and lenticular nucleus (LN+) on digitized image analysis of TCS images in clinically affected XDP patients, affected and unaffected relatives, and healthy controls.

Conclusions

- **SN and LN alteration are frequent sonographic features in XDP.**
- **SN alteration may be a diagnostic marker already in presymptomatic disease stages.**
- **LN is affected predominantly in the symptomatic stages.**

References:

(1) Domingo A et al. *Eur J Hum Genet* 2015 Jan 21. doi: 10.1038/ejhg.2014.292. (2) Tackenberg B et al. *Mov Disord* 2007;22(6):900-902.

(3) Walter U et al. *Ultrasound Med Biol* 2007;33(1):15-25.

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