

## Acute dystonia in a patient with 22q11.2 deletion syndrome

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### Abstract

The 22q11.2 deletion syndrome (di George syndrome) is one of the most prevalent genetic disorders. The clinical features of the syndrome are distinct facial appearance, velopharyngeal insufficiency, conotruncal heart disease, parathyroid and immune dysfunction; however, little is known about possible neurodegenerative diseases. We describe the case of an 18-year old patient suffering from 22q11.2 deletion syndrome. Since adolescence, he presented with behavioral disorders, recommended treatment with 2 mg aloperidin and he presented cervical dystonia and emergence of torticollis and trunk dystonia. Antipsychotic medications either accelerate or reveal dystonic symptoms.

### Introduction

The 22q11.2 deletion syndrome is one of the most prevalent genetic disorders and has been found to be one of the most common causes of learning disability and mild mental retardation.<sup>1</sup> It is caused by micro deletion in the long arm of chromosome 22 and its clinical characteristics include congenital heart disease; palatal abnormalities; hypocalcaemia and T-cell immunodeficiency; and abnormal faces that include a bulbous nasal tip and prominent nasal root, narrow and with flat cheeks, narrow palpebral fissures, small mouth, receding chin and small cupped ears.<sup>2</sup> Children with 22q11.2 deletion syndrome have been found to have a substantially greater risk for the development of schizophrenia and bipolar disorder with approximately 25-30% presenting psychotic symptoms in adolescence.<sup>3</sup>

### Case Report

We describe the case of an 18-year old patient suffering from 22q11.2 deletion syndrome. Since adolescence, he manifested with behavioral disorders, aggression, verbal abuse and sleep disorders. Diagnosis of 22q11.2 was confirmed at the age of 3 with a special chromosomal detector (D22 s75, ONCOR). His performance at school was poor. After a heated argument with his parents, he presented intense anger, started breaking and throwing things and was verbally aggressive. His parents contacted the treating physician, who recommended treatment with 2 mg aloperidin. The patient received treatment dissolved in water. The treatment calmed him down, but a few hours later, he presented with cervical dystonia and emergence of torticollis and trunk dystonia with continuous twisting movements of the trunk and limbs, as well as accompanying dysarthria and pain. The patient visited the emergency outpatient clinic of the hospital, where he was given 1 amp Biperiden i.m. His acute dystonia was considered a side effect of aloperidin administration and he was subsequently subjected to full laboratory testing to investigate the risk factors associated with acute dystonia. The brain magnetic resonance imaging (MRI) revealed no abnormal findings and he was then subjected to a DATscan to investigate a possible dysfunction of the basal ganglia, which proved negative. After two weeks the patient was hospitalized in a psychiatric clinic and was administered quetiapine 200 mg, p.o. This particular treatment improved his clinical picture, without manifesting the usually induced side effects evoked by haloperidol.

### Discussion

A literature search was conducted using the Medline computer database. It focused on all studies concerning 22q11.2 deletion syndrome and dystonia. The keywords were selected from titles, abstract and keywords and they were the following: *Dystonia parkinsonism* and *di George syndrome*. Butcher *et al.*<sup>4</sup> suggest that 22q11.2 deletions represent a novel genetic risk factor for early-onset of Parkinson disease (PD) with variable neuropathological presentation reminiscent of LRRK2-associated PD neuropathology. Shulman *et al.*<sup>5</sup> emphasize that the 22q11.2DS-associated microdeletion affects approximately 30 genes, including several intriguing candidates with potential links to PD pathophysiology. Among the genes in this region is *COMT*, encoding a key enzyme involved in dopamine catabolism and an established therapeutic target in PD. Zaleski *et al.*<sup>6</sup>

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suggest that the genetic of PD is complex. An increased risk to first degree relatives, even in apparently sporadic cases, suggests multifactorial causation of PD. Hereditary forms account for only about 1-3% of all PD cases and tend to have younger age at onset. Mutations in parkin, *PINK1* and *DJI* are known to cause autosomal recessive early onset PD and mutations in alpha synuclein, ubiquitin C terminal hydrolase and *LRRK2* can cause autosomal dominant PD with variable age of onset. Pinquier *et al.*<sup>7</sup> report a case of 22q11 deletion in a 17-year-old girl that was initially diagnosed as paranoid schizophrenia. In the case describe, transitory hypocalcemia induced dystonic symptoms that were believed to be cataleptic symptoms or neuroleptic secondary effects. Verri *et al.*<sup>8</sup> describe a new male patient, 33-year-old, with 10p partial deletion affected by hypocalcemia, basal ganglia calcifications and a severe autistic syndrome associated with mental retardation. The patient presented with dysmorphic features and at neurological evaluation, bilateral complete cataract, hypotonia, symptoms have been observed in 14% to 28% of children with di George syndrome and the receipt of antipsychotic treatment increase the risk of dystonic symptoms.<sup>9</sup> Dystonia induced by aloperidin may arise from an imbalance between dopaminergic and mus-

carinic receptors activity in nigrostriatum in the brain.<sup>10</sup> The possible side effects of antipsychotic medications – either accelerating or reveal dystonic symptoms – merit further study.

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## Conclusions

Studies of di George syndrome add to the global understanding of the pathophysiology of the neurological symptoms of this common neurodegenerative disease.

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## References

1. Lajiness-O'Neil R, Beaulieu I, Asamoah A, et al. The neuropsychological phenotype of velocardiofacial syndrome (VCFS): relationship to psychopathology. *Arch Clin Neuropsychol* 2006;21:175-84.
2. Gothelf D, Lombroso PJ. Genetics of childhood disorders: XXV. Velocardiofacial syndrome. *J Am Acad Child Adolesc Psychiatry* 2001;40:489-91.
3. Eliez S, Antonarakis SE, Morris MA, et al. Prenatal origin of the deletion 22q11.2 and brain development in velocardiofacial syndrome. *Arch Gen Psychiatry* 2001;58:64-8.
4. Butcher NJ, Kiehl TR, Hazrati LN, et al. Association between early-onset Parkinson disease and 22q11.2 deletion syndrome: identification of a novel form of Parkinson disease and its clinical implications. *JAMA Neurol* 2013;1:1359-66.
5. Shulman JM. Structural variation and the expanding genomic architecture of Parkinson disease. *JAMA Neurol* 2013; 70:1355-6.
6. Zaleski C, Bassett AS, Tam K, et al. The co-occurrence of early onset Parkinson disease and 22q1.2 deletion syndrome. *Am J Med Genet A* 2009;149:525-8
7. Piquier C, Héron D, de Carvalho W, et al. Microdeletion 22q11: apropos of case of schizophrenia in an adolescent. *Encephale* 2001;27:45-50.
8. Verri A, Maraschio P, Devriendt K, et al. Chromosome 10p deletion in a patient with hypoparathyroidism, severe mental retardation, autism and basal ganglia calcifications. *Ann Genet* 2004;47:281-7.
9. Jolin EM, Weller RA, Weller EB. Psychosis in children with velocardiofacial syndrome (22q11.2 deletion syndrome). *Curr Psychiatry Rep* 2009;11:99-105.
10. Matsui-Sakata A, Ohtani H, Sawada Y. Pharmacokinetic-pharmacodynamic analysis of antipsychotics-induced extrapyramidal symptoms based on receptor occupancy theory incorporating endogenous dopamine release. *Drug Metab Pharmacokinet* 2005;20:187-99.