Interesting case report ECARUCA (2013-09)

Sporadic male patients with intellectual disability: Contribution of X-chromosome copy number variants

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http://www.sciencedirect.com/science/article/pii/S1769721212001553

Abstract:
Genome-wide array comparative genome hybridization has become the first in line diagnostic tool in the clinical work-up of patients presenting with intellectual disability. As a result, chromosome X-copy number variations are frequently being detected in routine diagnostics. We retrospectively reviewed genome wide array-CGH data in order to determine the frequency and nature of chromosome X-copy number variations (X-CNV) in a cohort of 2222 sporadic male patients with intellectual disability (ID) referred to us for diagnosis. In this cohort, 68 males were found to have at least one X-CNV (3.1%). However, correct interpretation of causality remains a challenging task, and is essential for proper counseling, especially when the CNV is inherited. On the basis of these data, earlier experience and literature data we designed and propose an algorithm that can be used to evaluate the clinical relevance of X-CNVs detected in sporadic male ID patients. Applied to our cohort, 19 male ID patients (0.85%) were found to carry a (likely) pathogenic X-CNV.

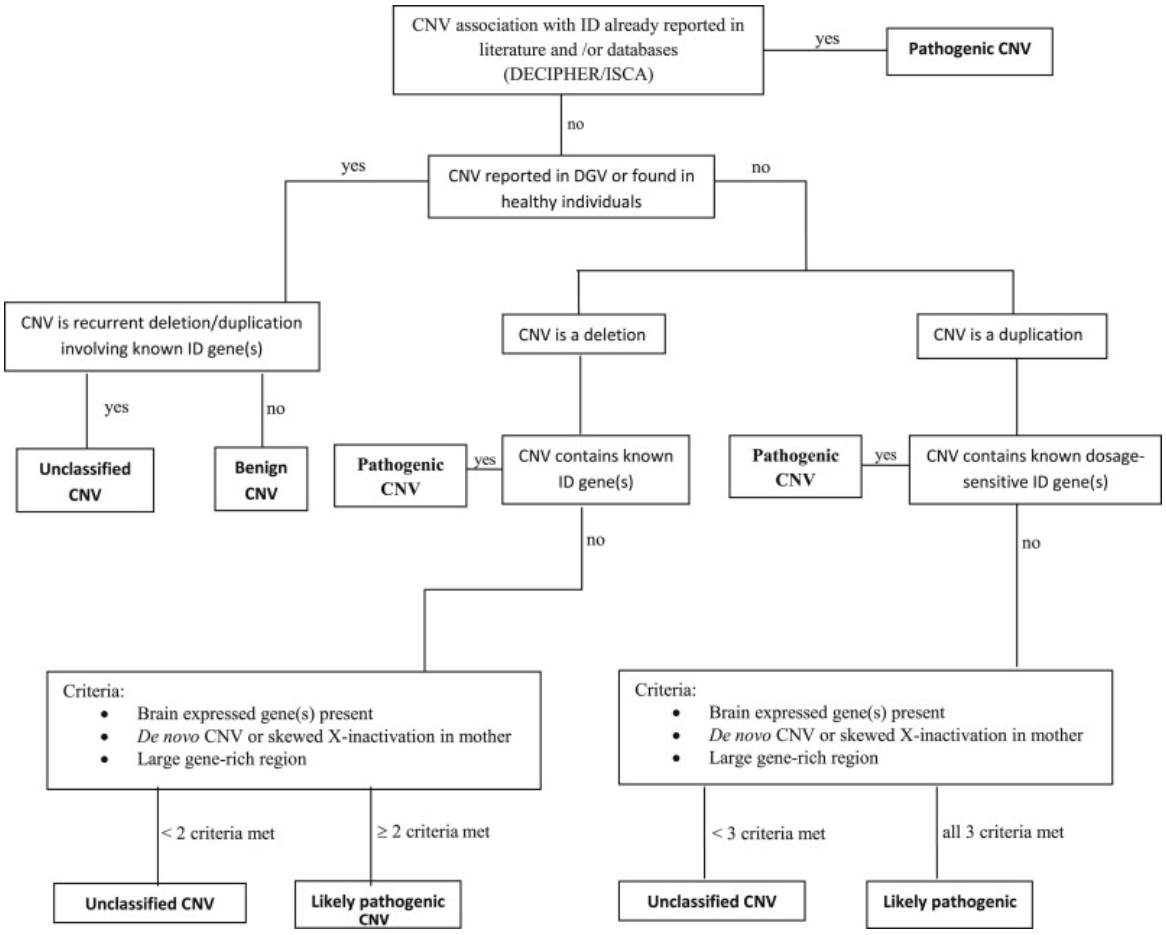

Fig. 1. Proposed decision tree for classification of gene-containing sporadic X-CNVs in males.

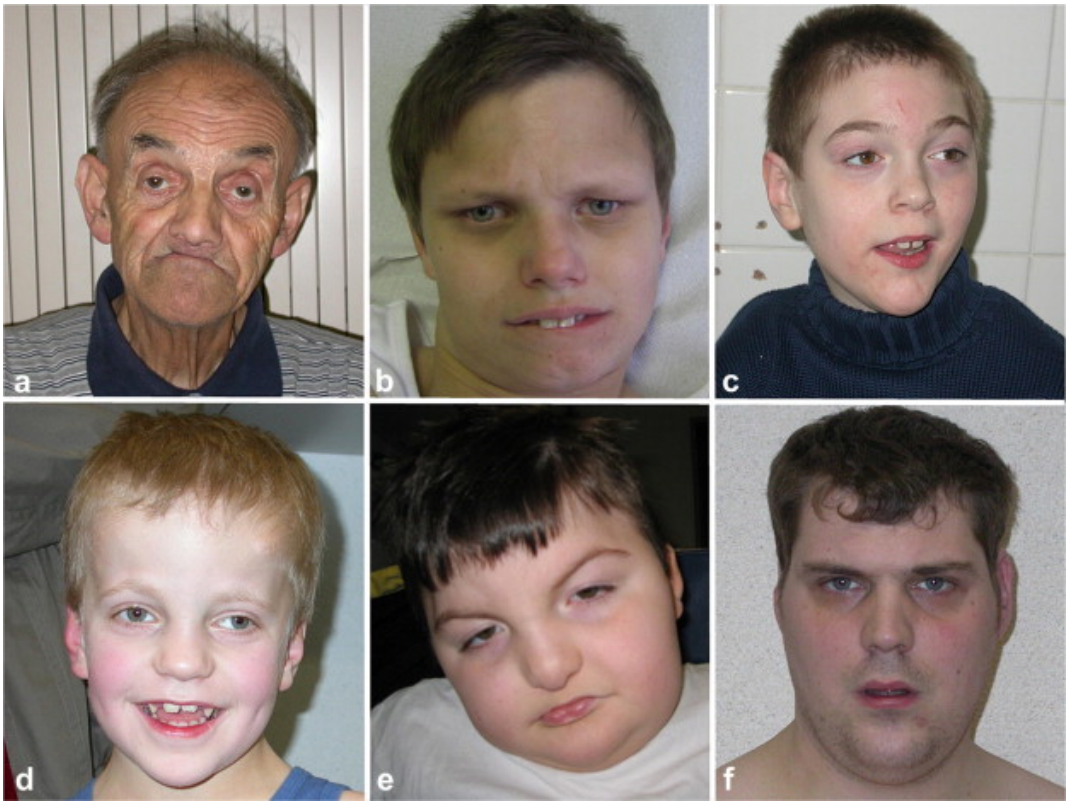

Fig. 2. Facial appearance of patients with (likely) pathogenic CNVs. (a) Patient 9; (b) Patient 10: note deep-set eyes, high front and sparse eyebrows; (c) Patient 13: note flat philtrum, thin upper lip, diasthema and pointed chin; (d) Patient 14: note relative macrocephaly, frontal bossing and strabismus; (e) Patient 16: note hypertelorism, downslanting palpebral fissures, arched eyebrows, broad nose with prominent columella and retrognathia; (f) Patient 18: Note long face, bi-temporal narrowing, straight eyebrows and prominent philtrum.