Published in final edited form as:

Am J Med Genet. 1992 September 01; 44(1): 118–120. doi:10.1002/ajmg.1320440129.

Survey of Mentally Retarded Males for Cutis Verticis Gyrata and Chromosomal Fragile Sites

George A. Dahir,

Department of Orthopedics and Rehabilitation

Lora K. Miller, and

Department of Pediatrics, Division of Genetics, Meharry Medical College, Nashville, Tennessee

Merlin G. Butler

Department of Pediatrics and Pathology, Division of Genetics, Vanderbilt University School of Medicine

To the Editor

We read with interest the paper by Musumeci et al. [1991] on chromosome fragile sites in 3 patients with cutis verticis gyrata (CVG). Two patients had the Xq27.3 folate-deficient fragile site while one patient had a 10q25 fragile site enhanced by the incorporation of BrdU. They proposed that chromosome fragile sites (e.g., Xq27.3 and 10q25) may be associated with CVG.

CVG is a rare skin anomaly characterized by scalp rugae running over the crown and back of the head. CVG develops after puberty [Warkany, 1971] and is associated with mental retardation, microcephaly, seizures, and eye and brain abnormalities [Felding, 1988]. Most cases are sporadic with a prevalence of 1/100,000 males and 2.6/10,000,000 females [Åkesson, 1964]. However, the prevalence in mentally retarded institutionalized males is much higher, 0.21 to 2.2% [MacGillivray, 1967; Palo, 1970]. Scalp rugae may also be observed in patients with brain disruption sequence, but these individuals show severe microcephaly, overlap of skull sutures, and prominence of the occipital bone. In this condition scalp rugae are caused by partial brain destruction during the second or third trimester with resulting decreased intracranial hydrostatic pressure and subsequent skull collapse [Russell et al., 1984]. Scalp rugae in fetal brain disruption sequence are temporary (unlike CVG) and usually disappear by age 6 months [Moore et al., 1990].

In a recent survey of 200 mentally retarded institutionalized males (ranging in age from 8 to 86 years), one individual had CVG. This patient was a nonambulatory 27-year-old mentally retarded white man with short stature, microcephaly, and typical CVG with 4 rugae running in an anteroposterior direction over the vertex. He had no other minor anomalies, no history of seizure activity, and his CVG developed after puberty. The family history was unremarkable. Cytogenetic studies from this patient of 210 metaphases (100 cells grown in

RPMI 1640 medium with bromodeoxyuridine (BrdU) and 110 cells in both Medium 199 and RPMI 1640 medium with fluorodeoxyuridine) for the induction of fragile sites following established protocols [Butler et al., 1990] showed no obvious chromosome anomalies. Specifically, no Xq27.3 or 10q25 fragile sites observed by Musumeci et al. [1991] in their CVG patients were identified in the cells analyzed in our patient. Our survey of mentally retarded institutionalized patients showed 4 males with the fragile X syndrome (Xq27.3), 2 patients with an Xq27.2 fragile site, 5 patients with an Xq26 site, and 2 patients with an X chromosome telomere structural change [Butler et al., 1990]. None of the fragile X syndrome males or males with one cell having a chromosome lesion on the distal long arm of the X chromosome exhibited CVG. In addition, 14 individuals were observed with at least one out of 125 cells examined having a 10q25 fragile site, but none of these males exhibited CVG.

In summary, our clinical and cytogenetic study of a relatively large number of mentally retarded males without a known cause of their retardation did not show an association between CVG and chromosomal fragile sites, particularly the folate-sensitive Xq27.3 site or the 10q25 site induced by the presence of BrdU as previously suggested by Musumeci et al. [1991]. Our study also confirms the presence of CVG in mentally retarded males with an incidence of 0.5%.

References

- Åkesson HO. Cutis verticis gyrata and mental deficiency in Sweden: I) Epidemiologic and clinical aspects. *Acta Med Scan.* 1964; 175:115–127.
- Butler MG, Allen GA, Haynes JL, Clark SJ. Chromosome lesions which could be interpreted as Fragile Sites on the distal end of Xq. *Am J Med Genet.* 1990; 37:250–253. [PubMed: 2248293]
- Felding I, Feingold M. Cutis verticis gyrata. *Am J Dis Child.* 1988; 142:305–306. [PubMed: 3344719]
- MacGillivray RC. Cutis verticis gyrata and mental retardation. *Scot Med J.* 1967; 12:450–454.
- Moore CA, Weaver DD, Bull MJ. Fetal brain disruption sequence. *J Pediatr.* 1990; 16:383–386.
- Musumeci SA, Ferri R, Viglianesi M, Elia M, Ragusa RM, Bergonzi P. Cutis verticis gyrata and chromosomal fragile sites. *Am J Med Genet.* 1991; 38:249–250. [PubMed: 2018067]
- Palo J, Iivanainen M, Blomqvist K, Pesonen S. Aetiological aspects of the cutis verticis gyrata and mental retardation syndrome. *J Ment Defic Res.* 1970; 14:33. [PubMed: 5517962]
- Russell LJ, Weaver DD, Bull MJ, Weinbaum M. In utero brain destruction resulting in collapse of fetal skull, microcephaly, scalp rugae, and neurologic impairment: The fetal brain disruption sequence. *Am J Med Genet.* 1984; 17:509–521. [PubMed: 6702901]
- Warkany, J. *Congenital Malformations: Notes and Comments: Cutis verticis gyrata.* Chicago: Year Book Medical Publishers; 1971. p. 1192-1193.