Visual Impairment Due to Macular Disciform Scars in a 20-Year-Old Man With Smith-Magenis Syndrome: Another Ophthalmologic Complication

Dusica Babovic-Vuksanovic,1 Syed M. Jalal,2 James A. Garrity,3 Dennis M. Robertson,3 and Noralane M. Lindor1*

1Department of Medical Genetics, Mayo Clinic, Rochester, Minnesota
2Cytogenetic Laboratory, Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota
3Department of Ophthalmology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

We describe a 20-year-old man with Smith-Magenis syndrome and a 46,XY,del(17)- (p11.2p11.2) karyotype. The interstitial deletion was confirmed by metaphase analysis using the fluorescent in situ hybridization probe (D17S29) for the Smith-Magenis region. The patient had hypertelorism, exotropia, and high myopia. Examination under anesthesia showed a lacquer crack near the right macula and a disciform scar of the left macula. Six months later, the patient presented with subacute visual loss. Examination demonstrated end-stage macular degeneration with bilateral disciform scars. There was no evidence of retinal detachment. Prior reports of Smith-Magenis syndrome mention telecanthus, ptosis, strabismus, iris anomalies, cataract, microcornea, optic nerve hypoplasia, myopia, retinal detachment, and lattice retinal degeneration. Bilateral macular degeneration has not been reported previously, and it may be an additional ophthalmologic manifestation of Smith-Magenis syndrome, either as a primary manifestation or as a direct consequence of high myopia. Am. J. Med. Genet. 80:373–376, 1998. © 1998 Wiley-Liss, Inc.

INTRODUCTION

Smith-Magenis syndrome (SMS) comprises multiple congenital anomalies and mental retardation due to an interstitial deletion of chromosome 17p11.2.

*Correspondence to: Noralane M. Lindor, M.D., Department of Medical Genetics, Mayo Clinic, 200 First Street SW, Rochester MN 55905.

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deletion size ranges from ~9–10 Mb to below 2 Mb and correlates with some, but not all, manifestations of SMS [Trask et al., 1996].

Most SMS cases had an interstitial deletion of 17p11.2, and random parental origin of deletion suggested that genomic imprinting does not have a role in the expression of the SMS phenotype [Greenberg et al., 1991]. Mosaicism for del(17)(p11.2p11.2) has been proven using molecular techniques in at least two cases [Juyal et al., 1996; Zori et al., 1993], one of which was an apparently unaffected mother, diagnosed retrospectively after having a child with SMS [Zori et al., 1993].

Most reported cases of SMS have been sporadic, but there are a few reports of familial transmission of chromosome 17 deletion [Friedman et al., 1992]. Recurrence risk for sporadic cases of SMS is estimated to be <5%, which may reflect germinal mosaicism [de Rijk-van Andel et al., 1991].

Ocular Manifestations in SMS

A variety of ophthalmic findings have been reported in SMS (Table I). Epicanthal folds, upward slant of palpebral fissures, telecanthus, Brushfield spots, and strabismus were included in initial description of the SMS phenotype [Smith et al., 1986]. Other ophthalmic anomalies seen in SMS patients are cataract, iris anomalies, pupillary asymmetry, optic nerve hypoplasia, microcornea, and myopia [Barnicoat et al., 1996; Chen et al., 1996; Finucane et al., 1993]. Bilateral macular degeneration has not been described previously.

**Clinical Report**

We evaluated a 20-year-old man for mental retardation and aggressive outbursts. After an uncomplicated pregnancy, the patient was born at term with a birth weight of 2.5 kg. Early neonatal adaptation was complicated by breathing and feeding problems and neonatal jaundice. His development was globally delayed. He walked at age 2 years, talked at age 3, and required special education throughout his schooling.

During childhood, the patient had a repair of inguinal hernia and recurrent otitis media, which prompted adenoidectomy, tonsillectomy, and placement of 10 sets of myringotomy tubes. His family history was noncontributory.

On examination he was found to have brachycephaly, prominent supraorbital ridges, short and broad nose, midface hypoplasia, prognathism, synophrys, and overfolded helices (Fig. 1). His hands were broad with short fingers. The rest of his examination showed normal findings.

**Ophthalmologic Examination**

On initial examination, the patient was found to have myopia of −10 OS and −11 OD. There was a disciform scar in the left macula with sensory exotropia and a linear area of chorioretinal atrophy (lacquer crack) on the right macula (examples on Fig. 2). Six months later, the patient was reevaluated because of subacute visual loss in the right eye. Examination showed white elevated disciform scars in each macula.

**Chromosomal Analysis**

The GTL-banded (G bands by trypsin using Leishman stain) karyotype from stimulated blood culture was 46,XY,del(17)(p11.2p11.2). The interstitial deletion was present in each of the 20 analyzed cells. The deletion was large (~4 Mb), since almost the entire 17p11.2 band appeared lost at the 400 band stage. However, remnants of the 17p11.2 band can be seen at higher resolution (Fig. 3). The deletion was confirmed to include the SMS region by metaphase in situ hybridization of fluorescent DNA probe (D17S29) specific for this region (Fig. 3). The SMS region probe along with the control probe at 17q12 was available commercially from OncorMed (Gaithersburg, MD).

**Discussion**

Disciform degeneration of the macula often follows subretinal neovascularization. Age-related macular degeneration is the most common precursor of disciform degeneration, but other pathological conditions, including high myopia, can precipitate a disciform process. Our patient was myopic and had a lacquer crack at the right macula on the initial evaluation, which was attributed to high myopia. Subsequently, development of bilateral disciform scars was probably due to the same cause.

Finucane et al. [1993] found myopia in eight out of 10 institutionalized SMS patients. The mean age of those patients was 23 years; four developed retinal detachment, thought to be due to trauma in two patients. A common association of myopia is a type of peripheral chorioretinal degeneration known as "lattice degeneration," which can predispose retinal detachment. One of Finucane's patients [1993] had signs of myopic retinal degeneration before detachment, but it is not clear whether this patient had any abnormalities in the macula.
Chen et al. [1996] did not find retinal detachment or retinal degeneration in any of their 28 SMS subjects, but the mean age of their study cohort was only 8.5 years. They postulated that self-injurious behavior may be more prevalent in an institutionalized population described by Finucane et al. [1993] and might place these myopic individuals at risk for retinal detachment. More patients should be analyzed for more definitive conclusions regarding natural history and ocular complications in SMS [Finucane and Jaeger, 1997]. We describe another patient with SMS with high myopia and visual loss from bilateral disciform scars. Ocular manifestations in SMS may be related to the central areolar choroidal dystrophy (CACD) gene,
which is located on 17p, close to the SMS region, but is still not identified. Close proximity of the SMS and CACD loci could explain ocular findings in some SMS patients as a part of a contiguous gene syndrome. Furthermore, our report supports strong correlation of SMS and severe ocular complications, suggesting the need for regular ophthalmologic evaluations, perhaps annually.

Our patient had aggressive, but not severe self-injurious behavior, and there was no known history of ocular trauma preceding the development of the disciform scars. The findings in our patient most likely represent complication from high myopia.

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REFERENCES


