Abstract: Microphthalmia with linear skin defects (MLS) is a rare X-linked dominant male-lethal syndrome with traits similar to several other disorders. Determination of a correct diagnosis, management and treatment plan is essential for proper visual development and rehabilitation.

Case Report: A four year old Caucasian female presented at the William Feinbloom Center for a low vision reevaluation. She had last been seen at age two. Her systemic history was positive for Microphthalmia, Dermal Aplasia, Sclerocornea (MIDAS) Syndrome also known as Microphthalmia with Linear Skin Defects (MLS) Syndrome. No evidence of sclerocornea had been noted at her previous visit. Systemic history was also significant for intrauterine growth restriction and spina bifida, for which she had undergone surgery two days post gestation. Aided acuities measured with EDTRS were 20/120 Snellen Equivalent OD, 20/500 Snellen Equivalent OS and 20/120 Snellen Equivalent OU. OS acuity was reduced from the 20/270 Teller force choice preferential looking acuity measured at her initial examination. With a 4x hand held telescope, she was able to achieve 20/80 Snellen equivalent OD. Pupils were round, equal and reactant to light. Eye movements were full and unrestricted to all positions of gaze. Cover test revealed a constant left exotropia. External evaluation of both eyes revealed a mild microphthalmia OS. Corneal edema was present along the nasal region OS. Iris adhesion to endothelium was present in nasal region OS. All other external findings OD and OS were within normal limits. Dilated fundus examination revealed clear media OU, small, possibly hypoplastic optic nerves OU, and a mottled retinal appearance consisting of patchy hypopigmented areas throughout the posterior pole and midperipheral retinal regions OU. All other fundus findings were unremarkable. A mosaic pattern of retinal pigmentation has only been noted in two other patients documented with MLS Syndrome. Recent studies, however, indicate there is strong genetic relationship between MLS Syndrome and ocular albinism, as well as with both Aicardi and Gotz Syndromes. From a clinical point of view, the most reliable sign of a carrier of ocular albinism is the mosaic pattern of retinal pigmentation. The patient, as well as her family, was educated about the possibility of being a carrier for ocular albinism and the implications of the condition. In addition, patching was recommended in order to strengthen the visual acuity of the OS.
Discussion: Lyonization is a process by which one of the two copies of the X chromosome present in female mammals is inactivated; this is necessary so that females do not have twice as many X chromosome gene products than males. The contribution of maternal or paternal active X chromosomes to the typical process of random X inactivation follows a bell-shaped distribution curve; the tissues of normal women have, on average, 50% maternally derived and 50% paternally derived active X chromosomes. In some women, however, this ratio is substantially different, which can lead to an unbalanced proportion of maternally to paternally derived chromosomal expression. If such an instance occurs, and a mutation exists on the active X chromosome, it will be present in an overwhelming proportion of cells. This has a number of important biological and medical implications, particularly with regard to X-linked genetic diseases. MLS is an X-linked dominant male-lethal disorder that is classically characterized by unilateral or bilateral microphthalmia (reported in 92% of affected individuals), linear skin defects (present in 89% of individuals) that are limited to face and neck, agenesis of the corpus callosum, sclerocornea, chorioretinal abnormalities, infantile seizures, congenital heart defects, mental retardation, and short stature. However, high clinical variability has been noted with some patients showing no ocular manifestation present and other patients with only eye abnormalities and no dermal lesions present. The cause of MLS is a chromosomal aberration that results either in segmental monosomy of the Xp22 chromosomal region or a mutation of HCCS gene. Incidentally, the genetic locus for X-linked ocular albinism 1 involves the Xp22.3 region, and is therefore closely situated to the chromosomal region affected in MLS. Aicardi and Goltz Syndromes are also X-linked dominant disorders whose genes are hypothesized to be located at the Xp22 chromosomal region; both share common signs and symptoms with ocular albinism 1 and MLS Syndrome. Patchy, striated fundus appearances with light/translucent irides are both strongly associated with carriers of X-linked ocular albinism. Carrier females of ocular albinism are usually asymptomatic, but because of random X inactivation, the majority of them show some signs of ocular albinism including pigment changes in the fundus, iris translucency, and macromelanosomes in skin biopsy. Because of the large similarities between X-linked syndromes and their variability in both systemic and ocular manifestation, it is crucial for optometrists to develop a comprehensive differential diagnosis, in order to determine the optimal management plan for their patients.

Bibliography

1. Phenotypic variation in ophthalmic manifestations of MIDAS syndrome


10. Corneal pathology in microphthalmia with linear skin defects syndrome.