ISSN: 2754-4990

Journal of Ophthalmology Research Reviews & Reports

SCIENTIFIC Research and Community

Case Report

Open Access

The Significance of Glaucoma Screening in Children Diagnosed with Singleton-Merten Syndrome

Bayan Mutlaq Almasoudi[1]*, Abeer Alawi[1] and Razan Mutlaq Almasoudi[2]

[1]Paediatric Ophthalmology Department, King Khalid Eye Specialist Hospital, Riyadh, Saudi Arabia

[2]College of Medicine Department, Vision College, Riyadh, Saudi Arabia

***Corresponding author**
Bayan Mutlaq Almasoudi, Paediatric Ophthalmology Department, King Khalid Eye Specialist Hospital, Riyadh, Saudi Arabia.

Received: March 07, 2026; **Accepted:** March 11, 2026; **Published:** March 21, 2026

Introduction

Singleton-Merten Syndrome (SMS) is a rare genetic disorder that is inherited in an autosomal dominant manner and is characterized by the presence of glaucoma, psoriasis, and abnormalities in dental, skeletal, and cardiac structures, as reported in the scientific literature [1-7]. This is attributed to mutations in DDX58 and IFIH1, which produce proteins that are part of the RIG-I- like receptor family and play a role in the type I interferon pathway [1-4]. In this case report, we provide a detailed clinical course of glaucoma in an individual who was found to have a pathogenic variant of the IFIH1 gene, along with symptoms of SMS.

Case Presentation

A 5-year-old boy presented by his parents to the King Khalid Eye Specialist Hospital Emergency Department in Riyadh after visiting a private clinic for eye checkup and found that he had high intraocular pressure and received STAT anti-glaucoma medications without improvement. There were no associated headaches, eye pain, redness, nausea, or vomiting. His past medical history included atopic disease versus psoriasis, followed by a dermatologist, Cryptorchidism. The patient had no history of asthma or chronic kidney disease. His ocular history was unremarkable except for myopia with glasses of - 6.25 D in both eyes, no history of amblyopia, or patching. There was no history of ocular surgery or topical medication use. He was a full-term child and a product of cesarean section due to fetal distress. There was no history of neonatal intensive care admission. The patient had no family history of glaucoma or blindness. He had six healthy sibling. His developmental history was normal with good performance at school.

Our patient was diagnosed with Singleton-Merten syndrome with an IFIH1 gene (interferon induced with helicase C domain 1) missense pathogenic variant NM_022168.3: c.2465G>A (p. Arg822Gln) five months ago in another general hospital. Unfortunately, no ophthalmologist has screened for glaucoma as a genetic disease.

Clinical examination showed a visual acuity of 20/60 in the right eye and 1/300 in the left eye, and Intraocular Pressure (IOP) measurements upon presentation were 40 mmHg and 38 mmHg, respectively. Anterior segment examination was unremarkable. Goniscopy examination was performed and showed an open angle grade four the Shaffer grading system of angle width. Retinoscopy suggested bilateral myopic fundus and optic disc cupping with a cup-to-disc ratio of 0.75 in the right eye and 0.9 in the left eye, flat retina. The decision was made to pursue admission for medical management. Topical anti-glaucoma medications were started: brinzolamide 1% ophthalmic eye drops every 12 hours, latanoprost -0.005%- eye drops once daily at bedtime, Timolol Maleate -0.5% solution- eye drops every 12 hours with Oral Acetazolamide -Diamox- (10 mg/ml solution) 60 mg twice daily. On the first day of follow-up, the intraocular pressure was 43/41 mmHg in the right and left eyes, respectively. The decision was made to proceed with deep sclerectomy with mitomycin C in both the eyes, which was uneventful. The interesting anatomical findings intraoperatively during the second flap creation showed no adequate filtration, and peeling of the schlem canal was attempted, which was far from the anatomical limbus until filtration was started. On the first postoperative day, the intraocular pressure reached 4/3 mmHg in the right and left eyes, respectively. Gentle ocular ultrasound revealed superior shallow choroidal detachment in both eyes. The patient was kept inpatient on prednisolone acetate1% eye drops, moxifloxacine every six hours, and pilocarpine eye drops once daily. On postoperative day five, the shallow choroidal detachment resolved, and the intracoular pressure measured by I care was 7 mmHg in the right eye and 16–22 mmHg in the left eye. Two weeks postoperatively, the Intraocular pressure was high in the left eye (30 mmHg), and the decision was made to proceed with examination under anesthesia plus bleb revision with mitomycin C in the left eye only. Pachymetry was 514/528 in the right and left eyes, respectively. Ultrasound Biomicroscopy showed a 360 °iris touching the lens with the lens pushing the iris anteriorly, causing narrow angles superiorly in both eyes. Ultrasound axial length was 23.75 mm and 25.52 mm in the right and left eye, respectively. In the first follow-up after two weeks of the procedure, the intraocular pressure successfully remained controlled in 9/11 right and left eyes.

Our evaluation of the patient's physical examination revealed normal results for early motor and cognitive development. However, he presented with psoriasiform eczema, which affected the lesions on the hands, feet, and extensor surfaces. These symptoms were identified as the manifestations of psoriasis (Figure 1). In terms

of his facial features, he exhibited a high anterior hairline, broad forehead, smooth philtrum, and thin upper vermilion (Figure 2). He had no history of skeletal abnormalities, and a cardiac workup consisting of echocardiogram and electrocardiogram was within normal limits, especially in the absence of aortic calcification. He continues to be followed up by ophthalmology in our hospital, cardiology, and pediatrics in a general hospital.

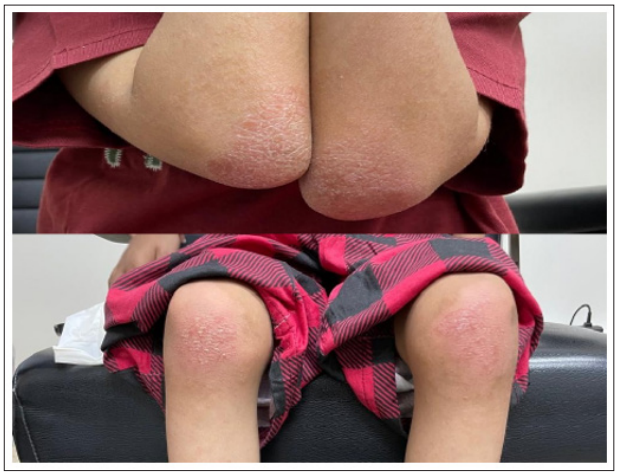

Figure 1: Psoriasiform Skin Rash

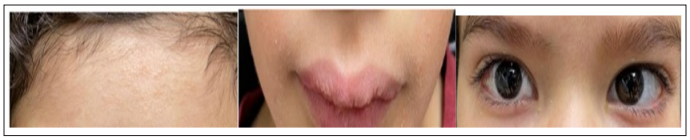

Figure 2: Facial Features: High Anterior Hairline Broad Forehead Smooth Philtrum and thin upper vermilion are the main signs

This case highlights a rare but significant association between SMS and glaucoma, suggesting that Singleton-Merten syndrome may contribute to ocular abnormalities beyond the typical SMS phenotype, and screening for early diagnosis and management of glaucoma in SMS patients is critical to prevent irreversible vision loss.

Discussion

Singleton-Merten syndrome is a rare genetic disorder caused by heterozygous mutations in the IFIH1 gene, leading to autosomal dominant inheritance with variable expression and type I interferonopathy. Characterized by a range of symptoms, including dental dysplasia, aortic calcification, skeletal abnormalities, glaucoma, and psoriasis, our patient presented with normal dentition, suggesting atypical manifestation of the condition.

Owing to its low prevalence (1 < 1,000,000), few cases have been reported. The first missense heterozygous variant of the interferon-induced helicase C domain-containing protein 1 (IFIH1) gene was identified in three families. Subsequently, seven other pathogenic variants were identified in patients with SMS, as reported by [8-13].

Glaucoma occurred in only a few patients, was congenital, and led to severe vision loss in some patients. The pathophysiology of glaucoma in patients with SMS or IFIH1 mutations is not well understood. It is likely multifactorial involving a combination of chronic inflammation, interferonopathy, vascular abnormalities, potential direct genetic effects on ocular tissues, and autoimmune processes affecting the Trabecular meshwork causing fibrosis, scarring and development of glaucomatous damage [12].

Feigenbaum et al. (1988) conducted a comprehensive review of the existing cases of Singleton- Merten Syndrome, both previously and currently published, and found that glaucoma occurred in only a few patients. In his article, he reported the first family with three cases of SMS Family 1 [McLoughlin et al. 1974; Theman et al. In 1979, Feigenbaum, et al. 1988]. The first individual, at the age of 34 years, was determined to have monocular open-angle glaucoma (intraocular pressure, 46 mmHg; goniscopy findings of a ciliary body band but normal disc) treated medically. The second patient from the same family had unilateral glaucoma in early adulthood, which required laser surgery. In Family 2 two patients developed glaucoma [11]. The first patient was diagnosed with bilateral juvenile glaucoma at the age of 2.5 years after she complained of visual problems and underwent corrective surgery at 3 years. The second patient, diagnosed with bilateral glaucoma at the age of 3 years, underwent successful goniotomy and trabeculectomy, similar to his sister. According to a case report published by, a 2-year-old child underwent trabeculotomy [12]. However, the use of anti- glaucoma drops was mentioned in the report for IOP control, and bilateral Baerveldt glaucoma implants were ultimately needed [14].

In addition to the core characteristics of the syndrome, such as aortic calcification, dental anomalies, and distal limb ossification disturbances, we report an unusual presentation and confirm that glaucoma and psoriasis can be part of this entity [15]. From our point of view, it is reasonable to assume that other relatives may also have been affected; however, we do not have sufficient evidence to support this hypothesis.

In summary, our patient had SMS and glaucoma with significant optic nerve damage that was diagnosed five months after the diagnosis of SMS. Early screening for the diagnosis and management of glaucoma in SMS patients is critical to prevent irreversible vision loss and to improve the quality of life of these patients. Ophthalmological evaluations are recommended for all patients with SMS upon diagnosis. Further studies are needed to better understand the relationship between SMS and glaucoma to improve the management strategies for affected individuals [16-19].

References

1. Ferreira CR, Crow YJ, Gahl WA, Tracy A Briggs, Ji Woo Park, et al. (2019) DDX58, and classic Singleton- Merten syndrome. J Clin Immunol 39: 75-80.
2. Jang MA, Kim EK, Now H, Nhung TH Nguyen, Woo-Jong Kim, et al. (2015) Mutations in DDX58, which encodes RIG-I, cause atypical Singleton-Merten syndrome. Am J Hum Genet 96: 266-274.
3. Lu C, MacDougall M (2017) RIG-I-like Receptor signaling in Singleton- Merten syndrome. Front Genet 8: 1-118.
4. Prasov L, Bohnsack BL, El Husny AS, Lam C Tsoi, Bin Guan, et al. (2022) DDX58(RIG-I)-related disease is associated with tissue-specific interferon pathway activation. J Med Genet 59: 294-304.
5. Feigenbaum A, Mu€ller C, Yale C (2013) Singleton-Merten syndrome: an autosomal dominant disorder with variable expression. Am J Med Genet A 161A: 360-370.
6. Ozyuksel A, Ersoy C, Canturk E, Akcevin A (2014) Progressive supra-aortic stenosis in a young adult with the findings of Singleton Merten syn- drome. BMJ Case Rep 5: bcr2014205985.
7. Ghadiam H, Mungee S (2017) Singleton Merten syndrome: a rare cause of early onset aortic stenosis. Case Rep Cardiol 2017: 8197954.

8. Rutsch F, Mary MacDougall, Changming Lu, Insa Buers, Olga Mamaeva, et al. (2015) A Specific IFIH1 Gain-of-Function Mutation Causes Singleton-Merten Syndrome. The American Journal of Human Genetics 96: 275-282.
9. Rivera SS, Boese EA, Dumitrescu A (2023) Glaucoma in a patient with Singleton-Merten syndrome. J AAPOS 27: 367-368.
10. Rutsch F, MacDougall M, Lu C, Buers I, Mamaeva O, et al. (2015) A specific IFIH1 gain-of-function mutation causes Singleton-Merten syndrome. Am J Hum Genet 96: 275-282.
11. Bursztejn AC, Briggs TA, del Toro Duany Y, Anderson BH, O'Sullivan J, et al. (2015) Unusual cutaneous features associated with a heterozygous gain-of-function mutation in IFIH1: Overlap between Aicardi-Goutieres and Singleton-Merten syndromes. British Journal of Dermatology 173: 1505-1513.
12. De Carvalho LM, Ngoumou G, Park JW, Ehmke N, Deigendesch N, et al. (2017) Musculoskeletal disease in MDA5-related type I interferonopathy: A Mendelian mimic of Jaccoud's arthropathy. Arthritis & Rheumatology 69: 2081-2091.
13. Takeichi T, Katayama C, Tanaka T, Okuno Y, Murakami N, et al. (2018) A novel IFIH1 mutation in the pincer domain underlies the clinical features of both Aicardi–Goutières and Singleton–Merten syndromes in a single patient. British Journal of Dermatology 178: e111-e113.
14. Vengoechea J, DiMonda J (2020) A case of Singleton-Merten syndrome without cardiac involvement harboring a novel IFIH1 variant. American journal of medical genetics. Part A 182: 1535-1536.
15. Xiao W, Feng J, Long H, Xiao B, Luo ZH (2021) Case report: aicardi-goutières syndrome and singleton-merten syndrome caused by a gain-of-function mutation in IFIH1. Frontiers in Genetics 12: 660953.
16. Hasegawa K, Tanaka H, Futagawa N, Miyahara H, Higuchi Y, et al. (2022) A novel pathogenic variant p. Asp797Val in IFIH1 in a Japanese boy with overlapping Singleton-Merten syndrome and Aicardi-Goutières syndrome. American Journal of Medical Genetics Part A 188: 249-252.
17. Rivera SS, Boese EA, Dumitrescu A (2023) Glaucoma in a patient with Singleton-Merten syndrome. Journal of American Association for Pediatric Ophthalmology and Strabismus 27: 367-368.
18. Singleton EB, Merten DF (1973) An unusual syndrome of widened medullary cavities of the metacarpals and phalanges, aortic calcification, and abnormal dentition. Pediatric radiology 1: 2-7.
19. Feigenbaum A, Müller C, Yale C, Kleinheinz J, Jezewski P, et al. (2013) Singleton–Merten syndrome: an autosomal dominant disorder with variable expression. American Journal of Medical Genetics Part A 161: 360-370.