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May-Hegglin, another Cause of Cataract: Case Report and Review

N. El Mrimar[1, 2*], N. Bouslous[1, 3], A. Raghani[1, 2], L. Oussaih[4], Z. Hidane[4], M. Aghrouch[5]

[1]Faculty of Medicine and Pharmacy of Agadir, Morocco
[2]Hematology Laboratory – CHU – Agadir, Morocco
[3]Ophtalmology Department – CHU Souss Massa – Agadir, Morocco
[4]Atlantic Oncology Center
[5]Av des FAR Medical Laboratory

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***Corresponding author:** N. El Mrimar
Faculty of Medicine and Pharmacy of Agadir, Morocco

Abstract **Case Report**

May-Hegglin anomaly (MHA) is a rare autosomal dominant genetic disorder characterized by the presence of large, abnormally shaped platelets (macrothrombocytes), thrombocytopenia, and distinctive leukocyte inclusions known as Döhle-like bodies. First described by the German physician Heinrich May in 1909 and further characterized by Swiss hematologist Otto Hegglin in 1945, MHA is part of a group of disorders collectively referred to as the MYH9-related diseases, which also include Sebastian syndrome, Fechtner syndrome, and Epstein syndrome. A 41-year-old male presents with a 10-year history of thrombocytopenia and a recent development of bilateral cataracts over the past three years. The patient reports that the thrombocytopenia has been resistant to corticosteroid treatment. He has experienced occasional episodes of mild bleeding, including easy bruising, epistaxis, and petechiae, but no severe hemorrhagic events. He denies any history of significant trauma, surgeries, or other major medical conditions. There is no known family history of similar hematological or ophthalmological issues. One of the primary ophthalmological concerns in MHA is the increased risk of retinal hemorrhages. Thrombocytopenia, a hallmark of MHA, predisposes patients to bleeding complications due to insufficient platelet numbers [3, 4]. The retinal vasculature, being highly sensitive to changes in hemostasis, is particularly vulnerable. Retinal hemorrhages can manifest as dot-blot hemorrhages or more extensive preretinal hemorrhages, potentially leading to vision impairment. Regular ophthalmologic examinations are crucial for early detection and management of these hemorrhages to prevent permanent vision loss. This case underscores the importance of considering MYH9-related disorders in patients presenting with thrombocytopenia resistant to standard treatments and associated with atypical clinical features, such as cataracts and leukocyte inclusions. Comprehensive diagnostic evaluations, including blood smear analysis and genetic testing, are crucial for accurate diagnosis and appropriate management of these rare but significant disorders.

Keywords: May-Hegglin anomaly (MHA), Thrombocytopenia, Macrothrombocytes, Döhle-like bodies, Retinal hemorrhages.

INTRODUCTION

May-Hegglin anomaly (MHA) is a rare autosomal dominant genetic disorder characterized by the presence of large, abnormally shaped platelets (macrothrombocytes), thrombocytopenia, and distinctive leukocyte inclusions known as Döhle-like bodies. First described by the German physician Heinrich May in 1909 and further characterized by Swiss hematologist Otto Hegglin in 1945, MHA is part of a group of disorders collectively referred to as the MYH9-related diseases, which also include Sebastian syndrome, Fechtner syndrome, and Epstein syndrome.

The underlying genetic defect in MHA is a mutation in the MYH9 gene, which encodes non-muscle myosin heavy chain IIA (NMMHC-IIA). This protein plays a crucial role in the cytoskeleton of cells, including platelets and leukocytes, affecting their shape, structure, and function. The mutation results in defective megakaryocyte maturation and platelet formation, leading to the observed thrombocytopenia and macrothrombocytes. Additionally, the MYH9 mutation impacts leukocyte morphology, leading to the characteristic Döhle-like bodies observed in peripheral blood smears.

Clinically, MHA patients may present with mild to moderate bleeding tendencies, such as easy bruising, epistaxis, and menorrhagia, which correlate with the degree of thrombocytopenia. However, many individuals with MHA remain asymptomatic and are diagnosed incidentally during routine blood examinations. The severity of bleeding symptoms does not always correlate directly with platelet counts, as platelet function can be relatively preserved despite thrombocytopenia.

In addition to hematological manifestations, MHA can also present with ophthalmological findings. These may include cataracts, retinal hemorrhages, and other abnormalities that can impact vision. The presence of these ophthalmological symptoms underscores the importance of comprehensive clinical evaluations in patients with MHA.

The diagnosis of MHA is typically based on a combination of clinical findings, blood smear analysis, and genetic testing to identify the MYH9 mutation. Differential diagnoses include other inherited thrombocytopenias and conditions causing similar leukocyte inclusions. Management of MHA focuses on symptomatic treatment of bleeding episodes and preventative measures to minimize bleeding risks. In severe cases, platelet transfusions may be necessary, although this is rarely required.

Understanding the molecular and cellular mechanisms underlying MHA provides insight into broader aspects of platelet biology and cytoskeletal function. Ongoing research aims to elucidate the full spectrum of clinical manifestations associated with MYH9 mutations and to develop targeted therapies that address the specific pathophysiological pathways involved in this and related disorders.

CASE REPORT

A 41-year-old male presents with a 10-year history of thrombocytopenia and a recent development of bilateral cataracts over the past three years. The patient reports that the thrombocytopenia has been resistant to corticosteroid treatment. He has experienced occasional episodes of mild bleeding, including easy bruising, epistaxis, and petechiae, but no severe hemorrhagic events. He denies any history of significant trauma, surgeries, or other major medical conditions. There is no known family history of similar hematological or ophthalmological issues.

On physical examination, the patient appears well-nourished and in no acute distress. Bilateral lens opacities consistent with cataracts are confirmed upon ophthalmological examination, and his visual acuity is significantly reduced (20/200 bilaterally). There are no signs of conjunctival pallor, jaundice, or lymphadenopathy. The abdominal examination reveals no hepatosplenomegaly.

Laboratory investigations reveal persistent thrombocytopenia with a platelet count of 50 x 10^9/L (normal range: 150-450 x 10^9/L). Hemoglobin levels are normal at 14.5 g/dL (normal range: 13.5-17.5 g/dL), and white blood cell counts are within normal limits at 6.8 x 10^9/L (normal range: 4.0-11.0 x 10^9/L). Coagulation profiles, including prothrombin time (PT) and activated partial thromboplastin time (aPTT), are within normal ranges.

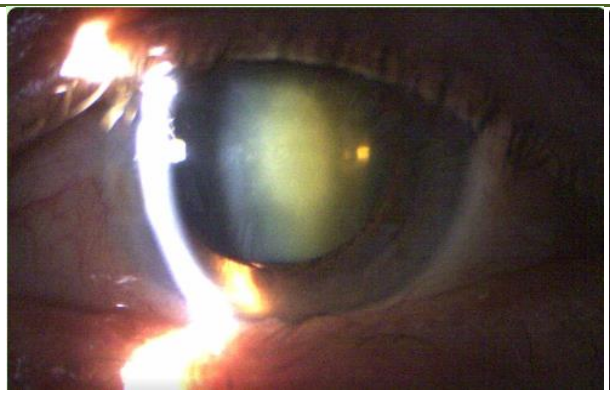
A peripheral blood smear is performed, revealing large, abnormally shaped platelets (macrothrombocytes), measuring up to 6-7 micrometers in diameter. Distinctive leukocyte inclusions, known as Döhle-like bodies, are observed in neutrophils. These findings are indicative of a platelet disorder with accompanying leukocyte inclusions, raising suspicion for a MYH9-related disorder, specifically May-Hegglin anomaly (MHA).

Given the combination of hematological and ophthalmological findings, a diagnosis of MHA is strongly considered. Genetic testing is conducted to confirm the diagnosis, and a heterozygous mutation in the MYH9 gene is identified, confirming MHA.

Further evaluation reveals that the patient's thrombocytopenia has been stable over the past decade, with no progression in severity. He reports that the corticosteroid treatment, initially prescribed to manage presumed idiopathic thrombocytopenic purpura (ITP), was ineffective. Despite the low platelet count, the patient has not experienced severe bleeding episodes, suggesting relatively preserved platelet function.

Management of the patient's condition includes surgical intervention for the cataracts, resulting in improved visual acuity postoperatively. The patient is advised on strategies to minimize bleeding risk, such as avoiding medications that affect platelet function and taking precautions during activities that might result in injury. Regular follow-ups are scheduled to monitor his platelet count, visual acuity, and overall health.

The patient is educated about the genetic nature of his condition, including the autosomal dominant inheritance pattern, and is advised to consider genetic counseling for family planning. He is also informed about the potential for other MYH9-related manifestations, such as hearing loss and renal abnormalities, although he currently shows no signs of these complications.




DISCUSSION

May-Hegglin Anomaly (MHA) is a rare autosomal dominant disorder characterized by thrombocytopenia, giant platelets, and Döhle-like bodies in leukocytes [1]. While the hematological features of MHA are well-documented, its ophthalmological manifestations have garnered less attention, yet they can significantly impact patient quality of life [2].

One of the primary ophthalmological concerns in MHA is the increased risk of retinal hemorrhages. Thrombocytopenia, a hallmark of MHA, predisposes patients to bleeding complications due to insufficient platelet numbers [3, 4]. The retinal vasculature, being highly sensitive to changes in hemostasis, is particularly vulnerable. Retinal hemorrhages can manifest as dot-blot hemorrhages or more extensive preretinal hemorrhages, potentially leading to vision impairment. Regular ophthalmologic examinations are crucial for early detection and management of these hemorrhages to prevent permanent vision loss [5].

In addition to hemorrhagic tendencies, patients with MHA may experience recurrent subconjunctival hemorrhages [6,7]. The conjunctiva, a delicate and highly vascularized tissue, can bleed easily in thrombocytopenic conditions. Although subconjunctival hemorrhages are generally benign and self-limiting, their frequent recurrence can be distressing for patients and may indicate underlying systemic issues related to platelet dysfunction [8].

Moreover, the structural abnormalities of platelets in MHA can contribute to altered ocular hemostasis. Giant platelets, although fewer in number, may exhibit dysfunctional aggregation and adhesion properties [9, 10]. This can complicate surgical procedures involving the eye, such as cataract extraction or vitrectomy, where precise hemostatic control is essential. Preoperative assessment of platelet function and careful perioperative management are vital to mitigate the risk of intraoperative bleeding and ensure successful surgical outcomes [11].

Another significant ophthalmological concern in MHA is the potential for vitreous hemorrhages. The vitreous body, a gel-like structure filling the eye, can be affected by bleeding from retinal vessels, especially in the context of severe thrombocytopenia [12, 13]. Vitreous hemorrhages can lead to sudden vision loss and, if not resolved, may require surgical intervention such as pars plana vitrectomy. The presence of giant platelets may complicate such procedures, necessitating specialized surgical expertise and postoperative care [14].

Beyond hemorrhagic complications, MHA may also be associated with inflammatory ocular conditions. Döhle-like bodies, intracytoplasmic inclusions in leukocytes, may reflect underlying cellular stress and inflammation [15]. This can contribute to the development of uveitis. Uveitis can present with symptoms such as eye pain, redness, and vision changes, and requires prompt diagnosis and management to prevent complications like cataracts and glaucoma [16, 17].

Additionally, MHA has been linked to increased intraocular pressure (IOP) in some patients. While the exact mechanism remains unclear, it is hypothesized that platelet dysfunction and abnormal leukocyte activity may contribute to impaired aqueous humor outflow, leading to elevated IOP. Regular monitoring of IOP in MHA patients is essential to detect and manage potential glaucomatous changes early, preserving optic nerve function and preventing irreversible vision loss [18, 19].

In summary, the ophthalmological manifestations of May-Hegglin Anomaly encompass a spectrum of hemorrhagic and inflammatory conditions that can significantly impact vision and quality of life. Retinal and vitreous hemorrhages, recurrent subconjunctival hemorrhages, uveitis, and increased intraocular pressure are key concerns that require vigilant monitoring and management [20, 21]. A multidisciplinary approach, involving hematologists, ophthalmologists, and surgeons, is crucial for comprehensive care of MHA patients, ensuring both systemic and ocular health are optimally maintained. Further research is needed to elucidate the precise mechanisms linking hematological abnormalities to

ocular manifestations in MHA, paving the way for targeted therapies and improved patient outcomes [22, 23].

In addition to the hemorrhagic and inflammatory complications, May-Hegglin Anomaly (MHA) may also present with other ophthalmological manifestations that warrant attention. One such manifestation is the development of cataracts. Although not directly linked to the primary hematological abnormalities of MHA, recurrent intraocular hemorrhages and chronic inflammation can accelerate cataract formation. This opacification of the lens leads to progressive vision impairment, necessitating timely surgical intervention to restore visual acuity [24, 25].

Moreover, patients with MHA may experience retinal detachment, a serious condition where the retina separates from its underlying supportive tissue [26]. This detachment can be precipitated by vitreous hemorrhages or traction from recurrent intraocular bleeding. Prompt recognition and surgical management are crucial to reattach the retina and preserve vision.

Additionally, MHA can be associated with microvascular abnormalities within the eye, such as telangiectasia and capillary fragility. These changes can further predispose patients to retinal bleeding and edema, complicating the clinical picture. Fluorescein angiography is a valuable diagnostic tool to assess the extent of these microvascular changes and guide treatment strategies [27].

Furthermore, corneal complications, although less common, can occur in MHA. Recurrent subconjunctival hemorrhages and inflammation can extend to involve the cornea, leading to conditions such as keratitis or corneal neovascularization. These conditions can cause significant discomfort and vision problems, requiring targeted therapeutic interventions, including anti-inflammatory medications and, in severe cases, corneal transplantation [28].

Another potential manifestation is optic neuropathy, which may arise secondary to increased intraocular pressure or chronic inflammation. Optic neuropathy can result in progressive vision loss and visual field defects. Regular assessment of optic nerve function through visual field testing and optical coherence tomography (OCT) is essential for early detection and management [29].

Finally, dry eye syndrome is a frequent but often overlooked complication in MHA. Chronic inflammation and ocular surface abnormalities can disrupt tear production and stability, leading to symptoms of dryness, irritation, and fluctuating vision. Management includes artificial tears, anti-inflammatory agents, and punctal plugs to improve tear film stability and patient comfort [30].

The ophthalmological spectrum of May-Hegglin Anomaly extends beyond hemorrhagic and inflammatory conditions to include cataracts, retinal detachment, microvascular abnormalities, corneal complications, optic neuropathy, and dry eye syndrome. These diverse manifestations underscore the need for a comprehensive and multidisciplinary approach to the care of MHA patients, integrating regular ophthalmologic evaluations with tailored therapeutic strategies to preserve vision and enhance quality of life.

CONCLUSION

This case underscores the importance of considering MYH9-related disorders in patients presenting with thrombocytopenia resistant to standard treatments and associated with atypical clinical features, such as cataracts and leukocyte inclusions. Comprehensive diagnostic evaluations, including blood smear analysis and genetic testing, are crucial for accurate diagnosis and appropriate management of these rare but significant disorders.

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