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(CASE REPORT)

Familial dominant drusen (Malattia leventinese / Doyne honeycomb retinal dystrophy)

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Abstract

Familial dominant drusen is an autosomal dominant, progressive retinal disorder characterized by central retinal drusen which often coalesce to form a honeycomb pattern. It is usually bilateral and occurs in early adulthood. Early diagnosis and follow up is essential as occurrence of choroidal neovascularisation is a possibility. Currently there is no effective treatment for this condition. Genetic counselling and molecular diagnosis are recommended.

Keywords: Familial dominant drusen; Choroidal neovascularization; Malattia Leventinese; Doyne honeycomb retinal dystrophy; EFEMP1; Drusen

1. Introduction

Doyne honeycomb retinal dystrophy is a familial autosomal dominant macular dystrophy which was first described by Doyne in the United Kingdom in 1899 and a similar condition known as Malattia Leventinese was recognized by Vogt in patients residing in the Leventine Valley of southern Switzerland, in 1925[1]. In 1999, Stone and coworkers showed that Doyne's honeycomb retinal dystrophy and Malattia Leventinese were infact one disorder caused by a single point mutation (Arg345Trp) in the EFENP1 gene [1]. EFEMP1 encodes the epidermal growth factor containing fibrillin like extracellular matrix protein [2]. It is characterized by the accumulation of macular and peripapillary yellow white deposits (drusen) between retinal pigment epithelium and bruchs membrane [3]. Visual acuity is preserved until central atrophy; pigment proliferation or choroidal neovascularization develops [4,5]. Genetic counselling and molecular diagnosis are recommended for these individuals to differentiate from age related macular degeneration [4,6].

2. Case report

A 29-year-old male presented with complaints of gradually progressive painless loss of vision in both eyes since childhood. He gave family history of similar findings in his father and sister. There was no history of consanguineous

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marriage. The visual acuity was 6/60 in both eyes with best corrected visual acuity of 6/18 in both eyes. Anterior segment was normal in both the eyes. Pupillary reaction was normal in both eyes with abnormal colour vision and distorted lines on amsler's grid examination. Fundus examination showed bilateral multiple small to medium drusen distributed in radial pattern involving more in the posterior pole of both eyes. Optical coherence tomography showed multiple irregular hyper-reflective nodules between retinal pigment epithelium and bruchs membrane. The features were suggestive of familial dominant drusen also known as Malattia Leventinese or Doyne honeycomb retinal dystrophy. The patient was managed conservatively and was adviced to come for routine follow up. Genetic counselling was done.

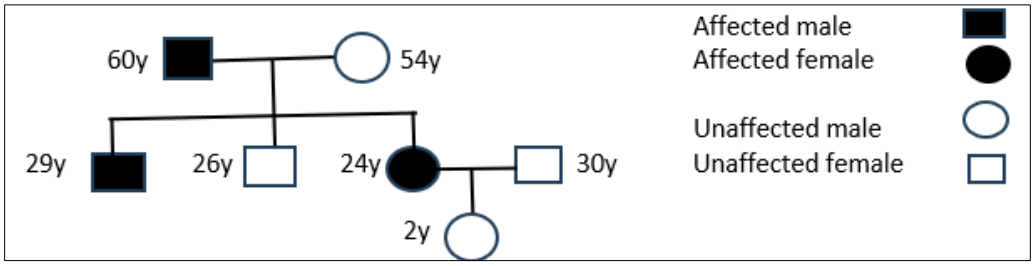

Figure 1 Pedigree chart

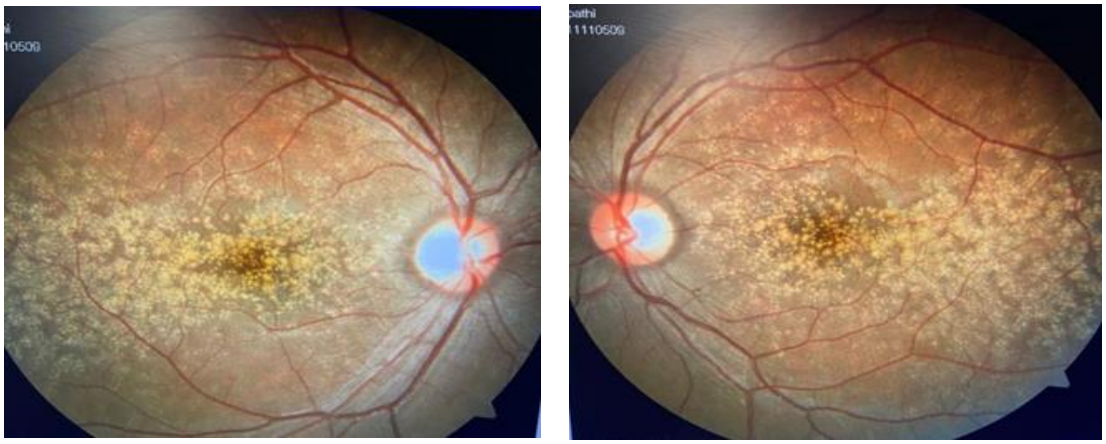

Figure 2a) Right eye and 2b) Left eye showing multiple small to medium drusen involving the posterior pole, vascular arcades and peripapillary area

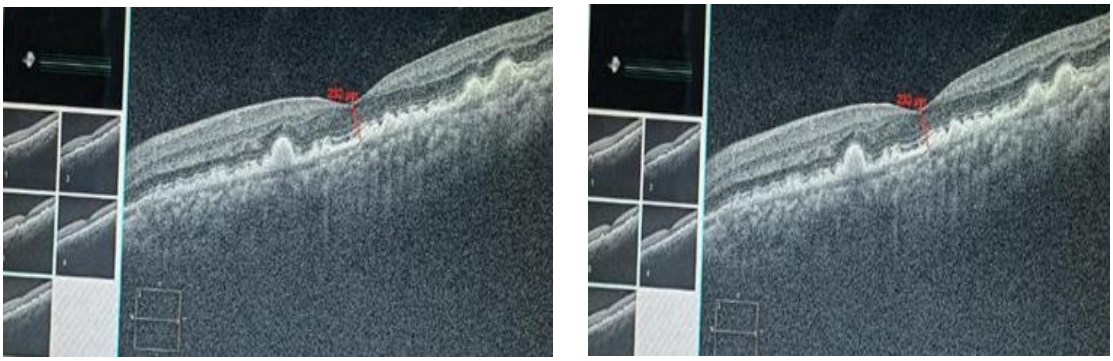

Figure 3 a) Right eye and 3b)Left eye showing multiple irregular hyper reflective nodules between the retinal pigment epithelium and bruchs membrane Figure 3 a) Right eye and 3b)Left eye showing multiple irregular hyper reflective nodules between the retinal pigment epithelium and bruchs membrane

3. Discussion

Doyne Honeycomb Retinal Dystrophy (DHRD) was first described by Doyne in four sisters of England in 1899. He found that each had an early onset retinal dystrophy involving the macula and peripapillary area which he termed as "Honeycomb" pattern [7]. In 1925, Vogt described a similar phenotypic picture in a cluster of individuals in the Leventine Valley of Switzerland and termed as Malattia Leventinese (MLVT) [8]. In 1999, Stone et al. discovered that a single mutation in the EFEMP1 gene on chromosome 2 in both DHRD and MLVT confirmed that the two represented slight phenotypic variances of the same disease [9]. Hence, it is now considered to be the same clinical entity. It is characterized by an autosomal dominant mutation in the EFEMP1 gene, specifically a single missense Arg345Trp (R345W) mutation in exon 10. EFEMP1 stands for EGF-containing fibulin-like extracellular matrix protein 1, and the gene coding for it lies on chromosome 2p16[10].

The disease is typically characterized by early adult onset drusenoid deposits presenting at the posterior pole, peripapillary area and along vascular arcades. It is described as multiple radially distributed drusen with honeycomb appearance. In its initial phases, small to medium drusen's are observed and in the later stages of the disease, large drusen's with pigmentary changes are seen [11]. Visual acuity is preserved until retinal pigment epithelial proliferation, geographic atrophy or choroidal neovascularization develops [11].

Spectral domain optical coherence tomography imaging can reveal focal dome-shaped or diffuse hyper reflective deposits with elevation between the RPE and bruch's membrane, usually becoming more confluent over time. The full field ERG is usually normal, but the pattern ERG is abnormal in most eyes [12].

Currently, there are no genetic or targeted therapies to correct the underlying genetic mutation in DHRD. Typically, patients with Doyne honeycomb retinal dystrophy are managed conservatively with observation, unless a choroidal neovascularisation develops [13].

Choroidal neovascularisation in DHRD is typically treated with a series of intravitreal anti-VEGF injections. Anti-VEGF injections such as Bevacizumab have been shown to improve vision and resolve subretinal fluid. Subthreshold retinal laser and photodynamic therapy are other alternatives [14].

4. Conclusion

Doyne honeycomb macular dystrophy is a rare autosomal dominant disorder and is usually seen in the second decade. Visual acuity is preserved in the early stages of the disease but gradually decreases as the age progresses. Long term followup is recommended to see for the development of choroidal neovasccularisation that may have to be treated using intravitreal anti VEGF or photodynamic therapy.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Ethical approval has been obtained from the institutional ethics committee.

Statement of informed consent

Informed consent was obtained from the participant included in the study.

References

[1] Srinivas R. Sadda,Andrew sachachat,Charles Wilkinson,David Sarraf,K Brailey Freud et al. Retinal degenerations and dystrophy, Ryan's retina 7thedition (2022) ; 910-913.

[2] Anusha pawar,Sonal Bangwal,Piyush Bajaj,Tripti Choudhary.familial dominant drusen with Cnvm : Cnvm :a case report,JMSR, 2017 ,vol 5; issue 8 ;26300-26302.

[3] Sheyanth IN, Lolas IB, Okkels H, Kiruparajan LP, Abildgaard SK, Petersen MB. First reported case of Doyne honeycomb retinal dystrophy (Malattia Leventinese/autosomal dominant drusen) in Scandinavia. Mol Genet Genomic Med. 2021 Apr;9(4): e1652. doi: 10.1002/mgg3.1652. Epub 2021 Mar 10. PMID: 33689237; PMCID: PMC8123724.

[4] Thomas NR,Mohankumar A, Rajan M . Malattia Leventinese.Indian journal of ophthalmology Case report 2023;3:959.

[5] Gelvez N, Hurtado-Villa P, Flórez S, Brieke Rodríguez F, Bertolotto AM, et al. Diagnostic definition of malattia leventinese in a family from Colombia. Biomedica 2021; 41:388-95.

[6] Hulleman JD. Malattia leventinese/doyne honeycomb retinal dystrophy: Similarities to age-related macular degeneration and potential therapies. Adv Exp Med Biol 2016; 854:153-8.

[7] Doyne, R.W. Peculiar condition of choroiditis occurring in several members of the same family. Trans. Ophthalmol. Soc*. UK* 19, 71 –71 (1899).

[8] Vogt, A. in Handbuch der gesammten Augenheilkunde. Untersuchungsmethoden (eds Graefe, A. & Saemisch, T.) 1–118 (Verlag von Wilhelm Engelman, Berlin, 1925).

[9] Stone, Edwin M., et al. "A single EFEMP1 mutation associated with both Malattia Leventinese and Doyne honeycomb retinal dystrophy." Nature genetics 22.2 (1999): 199-202.

[10] Fu, Li, et al. "The R345W mutation in EFEMP1 is pathogenic and causes AMD-like deposits in mice." Human molecular genetics 16.20 (2007): 2411-2422.

[11] ZECH, JEAN-CHRISTOPHE, et al. "Macular dystrophy of malattia leventinese. A 25 year follow up." British journal of ophthalmology 83.10 (1999): 1194-1194.

[12] Querques, Giuseppe, et al. "Multimodal morphological and functional characterization of Malattia Leventinese." Graefe's Archive for Clinical and Experimental Ophthalmology 251.3 (2013): 705-714.

[13] Sohn, Elliott H., et al. "Responsiveness of Choroidal Neovascular Membranes in Patients with R345W Mutation in Fibulin 3 (Doyne Honeycomb Retinal Dystrophy) to Anti–Vascular Endothelial Growth Factor Therapy." Archives of ophthalmology 129.12 (2011): 1626-1628.

[14] Parameswarappa, D. C., & Rani, P. K. (2021). Utility of pattern recognition and multimodal imaging in the diagnosis and management of doyne honeycomb retinal dystrophy complicated with type one choroidal neovascular membrane. BMJ Case Reports CP, 14(2), e237635.