Retinal café-au-lait macules: A rare retinal finding in a patient with neurofibromatosis type 1

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We report the retinal and choroidal manifestations using multimodal imaging in a patient with Neurofibromatosis type 1 (NF-1). In this report, we describe the occurrence of a new retinal finding which we label as retinal café-au-lait macules. Also, we describe the superiority of multicolour imaging in comparison to colour fundus photography for identifying the retinal manifestations in NF-1.

Key words: Café-au-lait spots, colour fundus photography, multicolour imaging, neurofibromatosis

Neurofibromatosis type 1 (NF-1), also known as Von Recklinghausen disease, is a genetic disease caused by the mutation of the *NF1* gene located to chromosome 17q11.2.[1] NF-1 commonly affects the skin and eye. The dermatological manifestations for the diagnosis of NF-1 are the presence of café-au-lait spots, plexiform neurofibromas and axillary or inguinal freckles.[2] Ophthalmic manifestations in NF-1 include the presence of Lisch nodules, plexiform neurofibromas, prominent corneal nerves, choroidal hamartomas, retinal tumours and optic nerve glioma.[2,3] The fundal lesions mainly the choroidal hamartomas are poorly visible on clinical examination and conventional colour fundus photography (CFP). Multicolour scanning laser imaging (MCI) is a newly introduced innovative, non-invasive, imaging modality developed for Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany). It has been widely used to describe the findings in various retinal and choroidal pathologies.[4] In MCI, three reflectance images of the retina are simultaneously acquired using three individual lasers thereby allowing analysis of changes at various levels within the retina and choroid. The information from these three images are integrated to form a composite multicolour image.[5] Newer imaging modalities like the swept-source optical coherence tomography angiography imaging have been used to describe the choroidal nodules seen in NF-1.[6] In this report, we identify new fundus lesions on the macula, not commonly seen with NF-1 and label them as the retinal café-au-lait macules. In addition, we describe the MCI features of other ophthalmic manifestations seen in NF-1.

Case Report

A 31-year-old man, diagnosed with NF-1 since many years, was referred for ophthalmic examination. Best-corrected visual acuity was 20/20 in both eyes. The left eye upper lid showed a plexiform neurofibroma. Intraocular pressure was within normal limits in both eyes. Anterior segment examination was normal other than the presence of Lisch nodules [Fig. 1]. Dilated fundus examination of the left eye was apparently normal while right eye fundus showed multiple, well-defined, light brown flat lesions temporal to the fovea of variable sizes and pigmentation. The pigmentation was noted at the margin in a few lesions and within the lesion in the rest. The remaining fundus appeared normal. Conventional CFP, fundus autofluoroscence (AF) images and MCI using the 30° scanning protocol was done and macula-centered images were taken. The right eye macular lesions showed increased reflectance and appeared white on blue (BR), green (GR) and infrared (IR) reflectance images and dark on fundus AF. In addition, both eyes IR images showed multiple areas of hyper reflectance located deep underneath the retina and retinal pigment epithelium within the choroid suggestive of choroidal hamartomas. The left eye BR, GR and IR images showed an area of increased reflectance temporal to the fovea suggestive of a small retinal astrocytic hamartoma. Enhanced depth optical coherence tomography imaging (EDI-OCT) was done through the choroidal hamartoma and retinal astrocytoma lesions confirming their presence [Figs. 2 and 3].

Discussion

NF-1 is caused by the mutations in the *NF1* gene which encodes for the tumour suppressor protein, neurofibromin. *NF1* gene and neurofibromin have intriguing functions in keratinocytes and melanocytes.[7] Neurofibromin regulates melanin synthesis and keratinocyte differentiation in a currently unknown manner.

Mutation in the *NF1* gene causes downregulation of neurofibromin and activation of the Ras-signalling pathway

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leading to the development of various dermatological and ophthalmic features of NF-1, including café-au-lait spots in the skin.

The lesions seen in the right eye macula are pale, flat and light brown in colour resembling the clinical description of café-au-lait spots noted in the skin in patients with NF-1. Similar looking macular conditions like torpedo maculopathy and amelanotic choroidal nevus were considered as well. However, the clinical features in our case did not correspond with the features described in literature.[8]

Histologically, café-au-lait spots contain increased melanin within the basal keratinocytes without melanocyte proliferation.[9] Increased reflectance seen on BR, GR and IR images and hypo AF seen on fundus AF image corresponding to the lesions seen on CFP and compared to the surrounding retina clearly suggests the increased melanin content within the lesion; similar to what has been described with café-au-lait spots seen in the skin. Hence, we label these lesions as retinal café-au-lait macules. Cotlier reported two cases of NF with mild pigmentary changes in the fundus and described them as café-au-lait spots.[10] In one case, associated retinal hamartomas were present as well. In addition, the orange red lesions seen on multicolour images corroborated well with the white lesions seen on IR images. These lesions were identified as choroidal hamartomas and further confirmed on OCT. Similar findings on MCI in a patient with NF-1 was reported by Kumar *et al*.[6] A small focus of hyper reflectance on MCI noted in the left eye temporal to the fovea could suggest the presence of abnormal astrocytic cells within the retinal layers. This is identified on the OCT image as well. Both the retinal and choroidal hamartomas, not seen on conventional CFP, were picked up better on MCI.

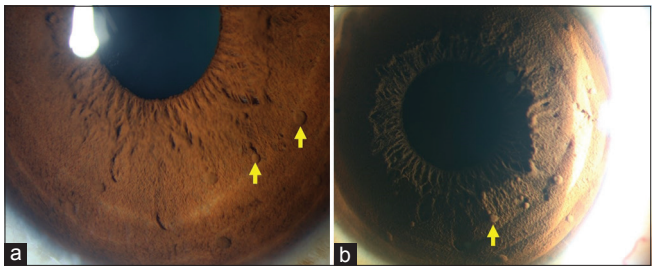

Figure 1: Lisch nodules on iris in a patient with NF-1. (a and b) Anterior segment photograph showing the classical Lisch nodules (yellow block arrow) in NF-1 on diffuse and slit illumination

Conclusion

Thus, with this report, we find MCI to be a superior imaging modality to conventional CFP in identifying the ophthalmic manifestations of NF-1. Also, we describe a relatively new and uncommon entity called retinal café-au-lait macules in this report.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

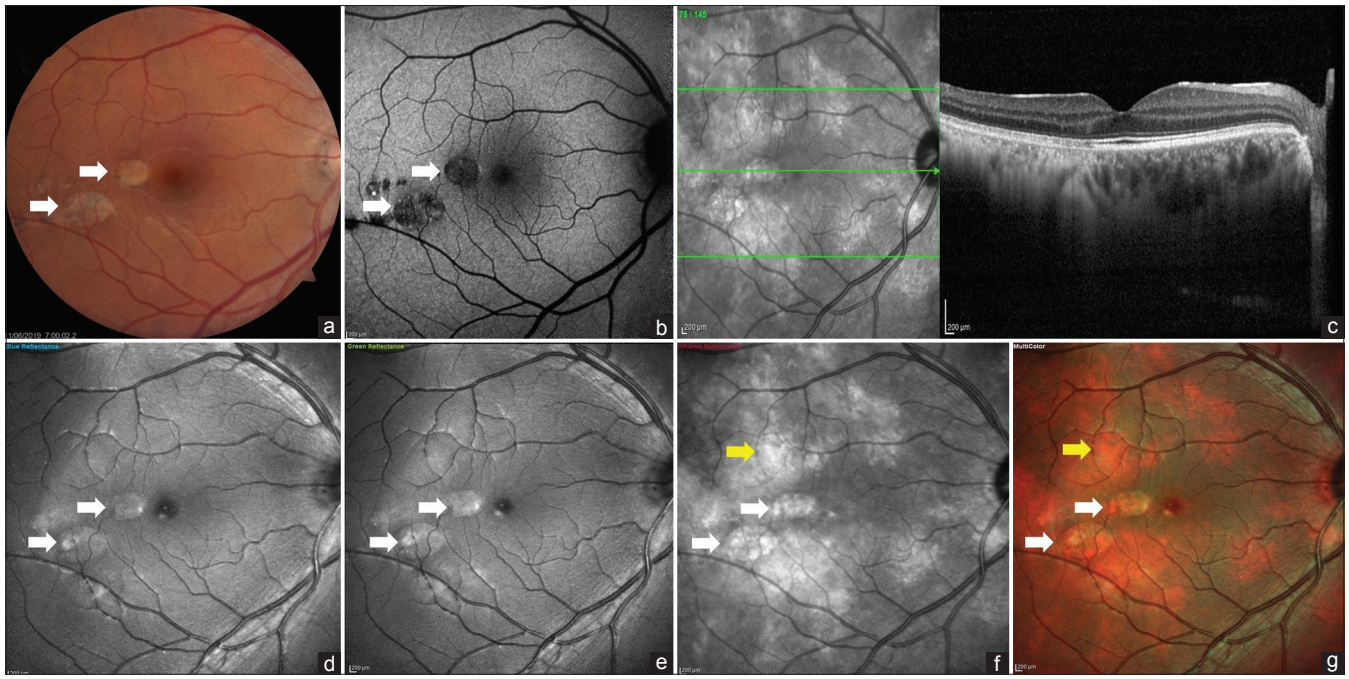

Figure 2: Retinal café-au-lait macules in NF-1. (a-c) Colour fundus photograph of the RE showing multiple pale, brown coloured flat lesions temporal to macula (white arrows). These lesions are seen as hypo autofluoroscent lesions on fundus AF. (d-g) These lesions are seen as areas of hyper reflectance on the blue, green and infrared reflectance images. The high melanin content in the lesion is responsible for this high reflectance pattern. These lesions are labelled as retinal café-au-lait macules

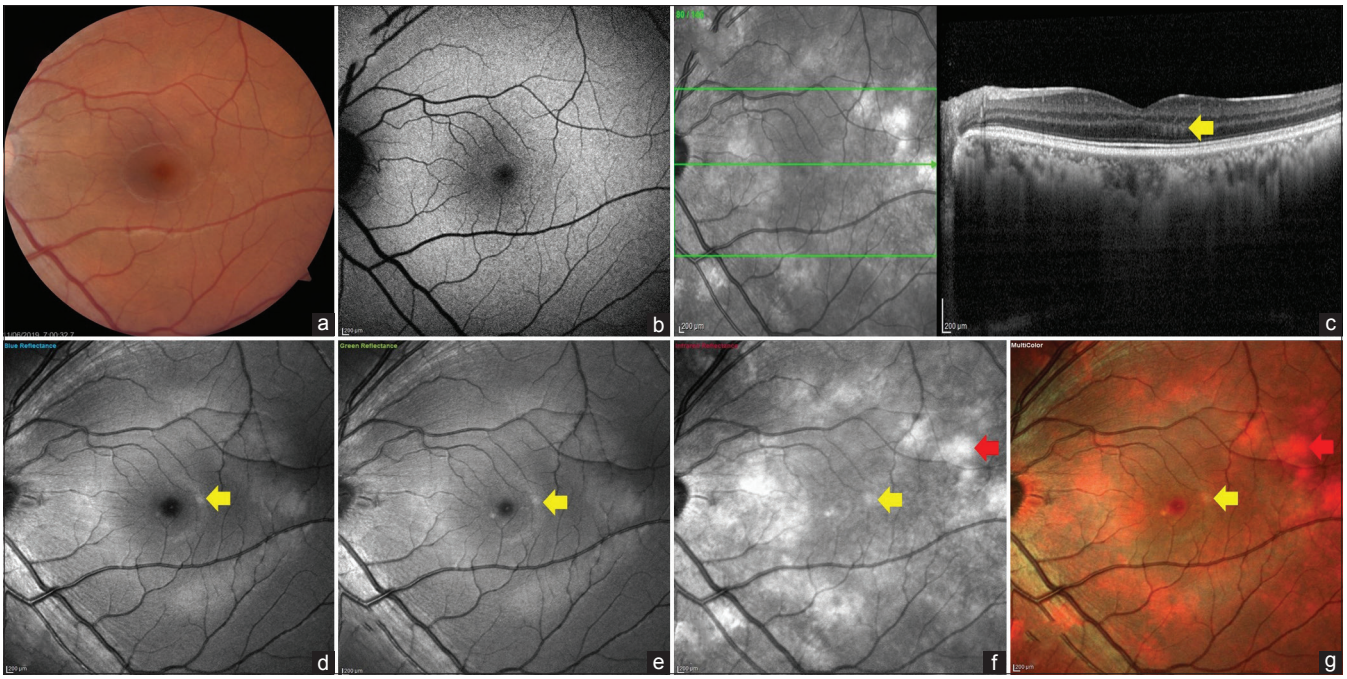

Figure 3: Retinal and choroidal hamartomas in NF-1. (a-g) Left eye colour fundus photograph and fundus autofluoroscence image looking relatively normal. Areas of hyper reflectance are seen on IR image and as orange coloured lesions on multicolour image. These lesions are not seen on the BR and GR images. These lesions are labelled as choroidal hamartomas (red arrows). EDI-OCT through the choroidal hamartomas shows areas of hyper reflectivity corresponding to the lesions seen on MCI. A focal hyperreflective spot is also noted in the left eye, temporal to fovea suggestive of a small retinal astrocytic hamartoma (yellow arrow)

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Barker D, Wright E, Nguyen K, Cannon L, Fain P, Goldgar D, *et al*. Gene for von Recklinghausen neurofibromatosis is in the pericentromeric region of chromosome 17. Science 1987;236:1100-2.
2. Chernoff KA, Schaffer JV. Cutaneous and ocular manifestations of neurocutaneous syndromes. Clin Dermatol 2016;34:183-204.
3. Abdolrahimzadeh S, Plateroti AM, Recupero SM, Lambiase A. An update on the ophthalmologic features in the phakomatoses. J Ophthalmol 2016;2016:3043026.
4. Feng HL, Sharma S, Stinnett S, Asrani S, Mruthyunjaya P. Identification of posterior segment pathology with EN face retinal imaging using multicolor confocal scanning laser ophthalmoscopy. Retina Phila Pa 2019;39:972-9.
5. Tan ACS, Fleckenstein M, Schmitz-Valckenberg S, Holz FG. Clinical application of multicolor imaging technology. Ophthalmol J Int Ophtalmol Int J Ophthalmol Z Augenheilkd 2016;236:8-18.
6. Kumar V, Singh S. Multimodal imaging of choroidal nodules in neurofibromatosis type-1. Indian J Ophthalmol 2018;66:586-8.
7. Peltonen S, Kallionpää RA, Peltonen J. Neurofibromatosis type 1 (NF1) gene: Beyond café au lait spots and dermal neurofibromas. Exp Dermatol 2017;26:645-8.
8. Venkatesh R, Bavaharan B, Yadav NK. Multicolor imaging findings in torpedo maculopathy. Indian J Ophthalmol 2019;67:295-7.
9. Takahasi M. Studies on café au lait spots in neurofibromatosis and pigmented macules of nevus spilus. Tohoku J Exp Med 1976;118:255-73.
10. Cotlier E. Cafe-au-Lait spots of the fundus in neurofibromatosis. Arch Ophthalmol 1977;95:1990-2.