Miliary microaneurysms: An angiographic biomarker of leukemic retinopathy?

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A 16-year-old girl was referred as retinitis and vasculitis post-typhoid fever. Fundus examination revealed bilateral pseudo-sheathing, scattered hemorrhages with retinal infiltrates. Wide-field fundus fluorescein angiography (FFA) showed peripheral vascular hyperfluorescence; 55° FFA images showed a “firecracker-like” peripheral vasculature, but a closer look revealed miliary microaneurysms (MAs). Peribulbar smear examination clinched the diagnosis of chronic myeloid leukemia. MAs on FFA in leukemic retinopathy have been frequently described in the literature. Our report emphasizes its presence, miliary nature, and need for closer inspection of FFA images. We believe that this angiographic sign has potential to become one of the imaging biomarkers of leukemic retinopathy.

Key words: CML, fluorescein angiography, leukemia, leukemic retinopathy, miliary microaneurysm

Leukemic retinopathy is one of the important differential diagnoses of masquerade syndromes in uveitis. Roth’s spots, retinal infiltrates, dispersed hemorrhages, and pseudo-sheathing of retinal vessels are well-known features of leukemic retinopathy. Fundus fluorescence angiography (FFA) is a frequently used modality to differentiate vasculitis from pseudo-sheathing. With advent of wide-field imaging, one can evaluate far peripheral retinal vasculature with great ease, but lack of magnification is a

Conflicts of interest

There are no conflicts of interest.

Declaration of patient consent

According to the Indian Council of Medical Research (ICMR), patient consent forms. In the form the patient(s) has/have indicated that they are willing to participate in this study. The authors certify that they have obtained all appropriate patient consent forms.

Access to patient records

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have indicated that they are willing to participate in this study.

Ethical approval

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Cite this article as: Kawali A, Mahendradas P, Srinivasan S, Shetty R. Miliary microaneurysms: An angiographic biomarker of leukemic retinopathy? Indian J Ophthalmol 2020;68:2017-9.
major drawback. Careful, closer observation of magnified images of FFA is important to detect microaneurysms (MAs) in peripheral retinal vasculature. Presence of such MAs in leukemic retinopathy has been described in few case reports and case series.[1-5]

We report a case of miliary MAs, seen on magnified images of FFA in leukemic retinopathy.

Case Report

A 16-year-old Indian girl, known case of right eye anisometropic amblyopia, came for annual checkup. She had no fresh ocular complaints but gave a history of recent typhoid fever. No laboratory investigations were available at the presentation. Patient was referred as a case of post-fever retinitis with vasculitis. Her best-corrected visual acuity was counting fingers at 2 m in the amblyopic right eye (OD) and 6/6 in left eye (OS).

Intraocular pressure was normal in both the eyes. Anterior segment examination was within normal limits in both the eyes. Fundus examination revealed 1+ vitritis, normal discs and macula, dilated tortuous vessels with pseudo-sheathing, scattered retinal hemorrhages along with retinal infiltrates in both the eyes [Fig. 1a]. Wide-field angiography showed blocked fluorescence due to retinal infiltrates with hemorrhages, peripheral vascular hyperfluorescence, and capillary non-perfusion (CNP) areas [Fig. 1b, e, f]. 55° FFA images showed peripheral CNP areas and a firecracker-like peripheral vasculature [Fig. 1c], but a closer look revealed multiple MAs [Fig. 1d]. A simple laboratory investigation such as total blood counts and peripheral smear examination clinched the diagnosis of chronic myeloid leukemia (CML), which showed markedly increased white blood cells, neutrophils, and myeloid left shift with promyelocytes and blast cells (1%). Patient was referred to hemat-oncologists and thereafter she was lost to follow up.

Discussion

Recently few authors published FFA and optical Coherence Tomography Angiography (OCTA) findings in leukemic retinopathy. Presence of multiple microaneurysms in those cases as well as in previous reports draws one’s attention.[3,4] Jampol et al.[3] have described these findings back in 1975 in a series of 25 patients with CML and chronic lymphocytic leukemia. They noted presence of microaneurysm in 6 out of 17 patients of CML. They did not perform FFA in all of their patients and they were not fortunate to have wide-field angiography during their time. This probably limited their observation by detecting only few patients with microaneurysms. We add yet another case with similar findings to emphasize on this peculiar finding repeatedly seen in published literature and highlight that those MAs can be subtle as in our case and well appreciated on magnified images.

Our case was suspected for post-fever retinitis and vasculitis but was proven to be a masquerade syndrome. Retinal infiltrates as seen in our patient can occur in certain uveitic conditions such as Behçet’s disease, sarcoidosis, candida endogenous endophthalmitis, and masquerade syndromes. Retinitis lesions in post-fever retinitis or so-called epidemic retinitis are located mainly at the posterior pole; they are larger in size and mimic cotton-wool spots.[6] Although there was yellowish discoloration mimicking vasculitic sheathing in temporal vessels [Fig. 1a], other retinal vasculatures showed an altered luster not typical of vasculitis. Angiography was carried out to rule out vasculitic leakage in our case. Peripheral vascular hyperfluorescence seen on wide field FFA in our case could have been mistaken for vasculitis [Fig. 1b], but a closer inspection of 55° images clearly showed miliary MAs. Unfortunately, our patient was lost to follow up with us, and hence posttreatment reversibility of MAs remained unassessed.

At least six reports including ours have now described the sign of MAs in leukemic retinopathy detected on FFA. The case described by Priya et al.[1] also had overlapping diabetic retinopathy changes, which perhaps resulted in formation of larger MAs, whereas in our case MAs were smaller in size, clustered closely to give a firecracker-like appearance of the peripheral vasculature and were evident on closer inspection of FFA images. OCTA studies can also be a useful noninvasive...
imaging modality in documentation of this finding,[3] but low blood flow due to high viscosity in leukemia cases may miss those tiny MAs. Our case highlights the importance of 55° FFA over wide-field FFA in detection of MAs and emphasizes occurrence of military MAs in leukemic retinopathy. Presence of such military MAs with the background fundus picture of vascular sheathing/pseudo-sheathing, retinal infiltrates, hemorrhages, in the absence of history of diabetes, and hypertension can differentiate a variety of other ocular conditions such as Behçet’s disease, Sarcoidosis, or post-fever retinitis/epidemic retinitis (as noted in our case), where miliary MA’s is not a typical finding.

**Conclusion**

We are of opinion that MAs as an angiographic sign has potential to be one of the imaging biomarkers of leukemic retinopathy. Larger angiographic studies are recommended to confirm our observation in leukemic retinopathy.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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