Geographic atrophy

Geographic atrophy is thought to be the natural end stage of the atrophic AMD process when CNV does not appear.

GA occurs in areas where the RPE is dead and the outer neurosensory retina and choriocapillaris disappeared(42, 43).

Due to the loss of RPE and LF, the atrophic area appears dark in FAF imaging (35).

High contrast between the atrophic and the non atrophic retina defines the area of GA more precisely than colour fundus photographs, permitting a clearer and more specific study of GA, as well as its natural development and evolution $\frac{(38,44)}{(Fig. 10 and 11)}$.

The GA patches usually become larger and coalesce as AMD progresses (45,46).

An excessive accumulation of LF, and therefore an increased FAF in the junction are highly suggestive of the appearance or progression of pre-existing GA (Fig. 12).

Preliminary observations suggest that different phenotypes may appear associated with junction FAF changes $\frac{(47)}{2}$.

Recently, a new classification for junction FAF patterns has been proposed in GA patients (48) (Fig. 13).

-Focal increased autofluorescence is defined by single or multiple spots of focal markedly increased FAF localized at the border of the atrophic patch.

-Band pattern of increased autofluorescence is characterized by a continuous stippled band of increased FAF surrounding the entire atrophic area.

-Patchy increased autofluorescence are large patches of increased FAF outside the GA area.

FAF tends to be less intense than that in the focal pattern described above. -Diffuse increase autofluorescence is the most frequent pattern of incresed FAF in eyes with GA.

FAF changes are not limited to the border of the atrophic area and may show inter individual differences that have been further classified into four subtypes.

-Reticular pattern, characterised by several lines of increased FAF usually following a radial pattern.

-Branching pattern shows a diffusely increased FAF with a fine branching pattern of increased FAF.

-Fine granular pattern, is defined by a large area of increased FAF with a granular appearance surrounding the GA area and a clear border between the granular increased FAF and the surrounding normal background FAF.

-Fine granular with peripheral punctate spots pattern is characterised by diffuse FAF changes surrounding the atrophic area with elongated small lesions and increased FAF.

Refined phenotypes help to identify the prognosis and seem to be a prerequisite to determine specific genetic factors in a complex, multifactorial disease such as AMD.

A recent analysis of the follow-up of junction FAF patterns in GA and the rate of progression of atrophic lesions revealed that variation in GA growth rates are dependent on the specific phenotype of FAF at baseline(49).

Atrophy enlargement was slowest in eyes with normal FAF pattern (median, 0.38 mm2/year), followed by focal FAF pattern (median, 0.81 mm2/year), diffuse FAF pattern (median, 1.77 mm2/year), and banded FAF pattern (median, 1.81 mm2/year).

The rate of progression of GA in eyes with patchy FAF pattern were not included in this analysis because of their low frequency, insufficient for statistical analysis.

The rate of progression of "banded" and "diffuse" FAF patterns were significantly higher compared to eyes without FAF abnormalities and "focal" FAF pattern.

Another interesting finding of this study was the identification of eyes with extremely rapid progression of the atrophy, showing distinct FAF features of atrophy that had not been previously reported.

The authors introduced the term "diffuse trickling" for a pattern associated with a significantly faster enlargement of atrophy.

Areas with increased FAF and consequently higher concentrations of RPE LF precede the development of new areas of GA or the enlargement of the pre existing atrophic areas.

The phenotypic features of FAF abnormalities may play a stronger influence on the progression of atrophy than any other previously reported risk factors such as smoking, arterial hypertension or diabetes.

The different rates of enlargement of atrophy may be related to heterogeneity at a cellular and molecular level in the disease.

The high degree of symmetry in GA suggests that genetic determinants may be involved, rather than nonspecific aging changes.

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