Don’t Fall In The Pit

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Introduction

- Alport syndrome (AS) is a rare inherited disease affecting genes coding for collagen IV.
- It affects approximately 1–5:50,000
  - 85% of patients present an X-linked inheritance with COL4A5 gene mutation
  - 15% show autosomal recessive inheritance with biallelic mutations in the COL4A3 and COL4A4 genes[1-3].
- In AS, the assembly of the collagen triple helix is impaired and more susceptible to proteolytic processes
- The main susceptible site is the kidney due to the high content of collagen IV in the glomerular basement membrane[4].
- However ocular involvement is seen with corneal, lens and retinal susceptibility.
  - Posterior polymorphous corneal dystrophy and anterior lenticonus are well-described ocular findings in AS patients due to the affected basement membranes of the corneal endothelium and lens epithelium[5-7].
  - Retinal findings have included neuroretinal thinning of the temporal macula, macular holes, dull foveal reflex, dot and fleck retinopathy and bull’s eye maculopathy[5,6,8-10].
- More recently authors have described foveal hypoplasia and a staircase foveopathy in patients with AS; with irregular depletion of inner retinal layers in the central macular region, resulting in a broadly thinned retina and stair-like appearance with indiscernible foveal pit.

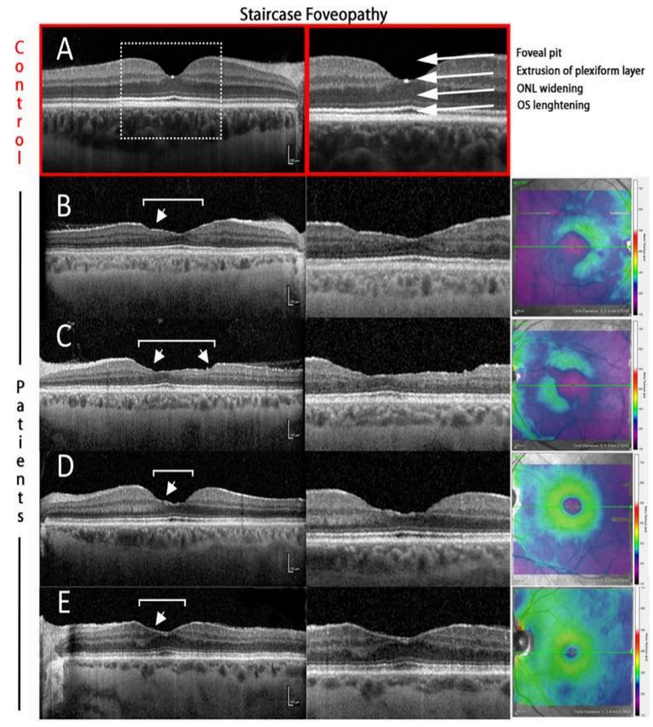


Figure 1

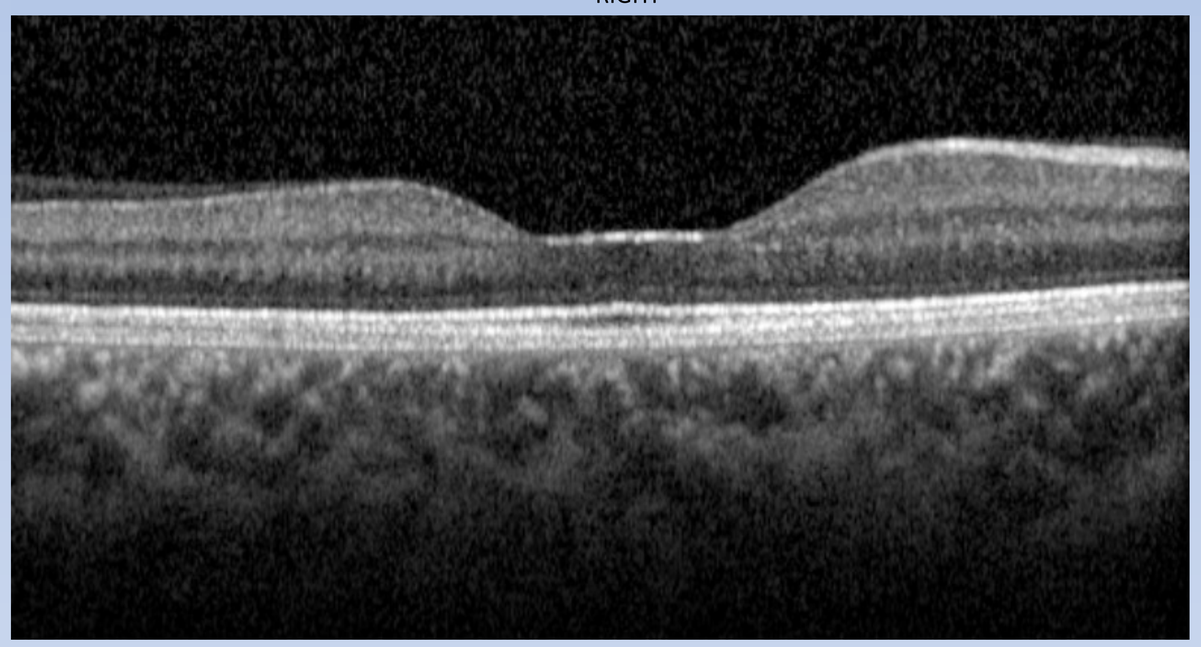
Phenotypic spectrum of “staircase-foveopathy” in Alport syndrome. A normal foveal configuration as shown in the upper panel (**A**), whereas the exemplary patients show irregular depletion of the inner retinal layers, beginning in parafoveal areas nasally and temporally. The thinning is not homogenous but in a “staircase”-like manner (white arrows). Despite this broadly allocated thinning, the outer retina is preserved in all cases. The (apparently) higher reflectivity of the choroid in patients compared to controls is related to the enhanced depth imaging mode used in patients, which visualizes the thinner choroids in patients more clearly than the regular OCT mode.

Hess K, Pfau M, Wintergerst MWM, Loeffler KU, Holz FG, Herrmann P. Phenotypic Spectrum of the Foveal Configuration and Foveal Avascular Zone in Patients With Alport Syndrome. Invest Ophthalmol Vis Sci. 2020

Case

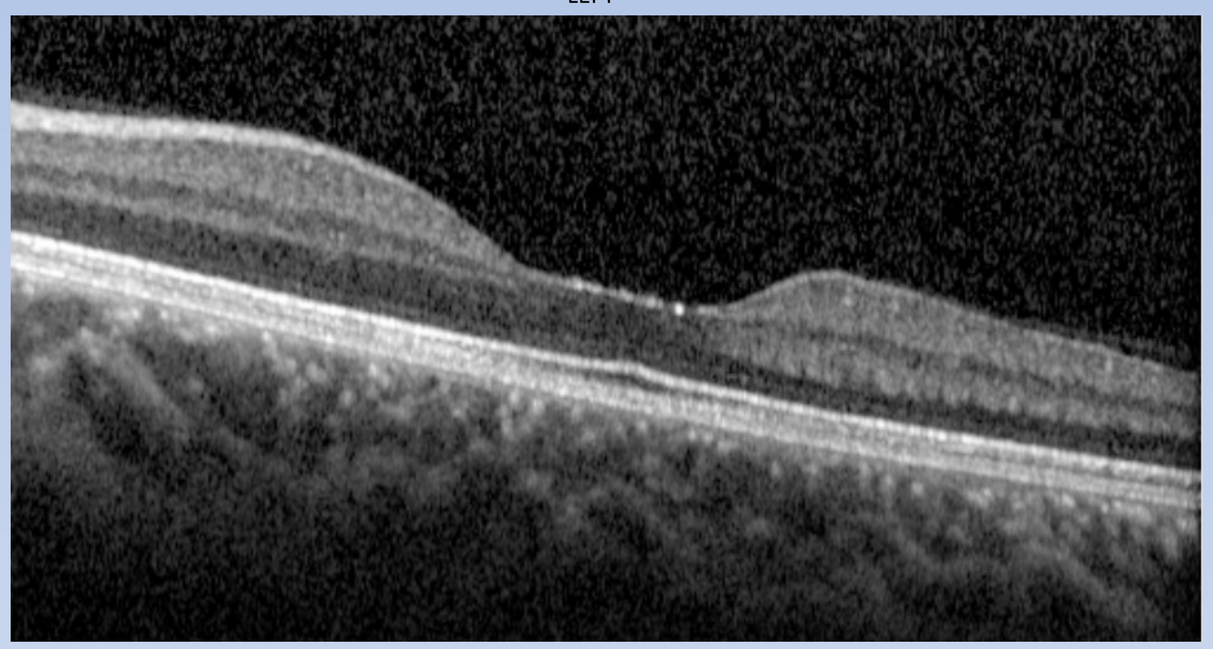
We present a 14 year old male who initially presented aged 4 with haematuria. worked up and found to have autosomal recessive AS .
RVA: 0.08 LogMar, LVA: 0.04 LogMar. Prominent foveal reflexes noted on examination.

RIGHT

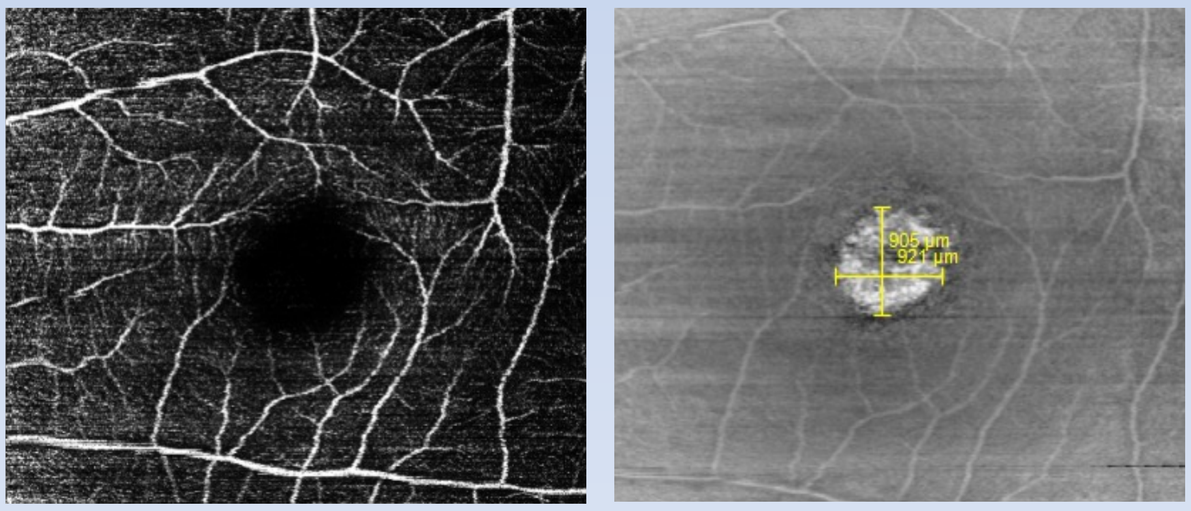


OCT of right eye showing wide but uniform foveal pit measuring 957microns (Heidelberg Eye Explorer)

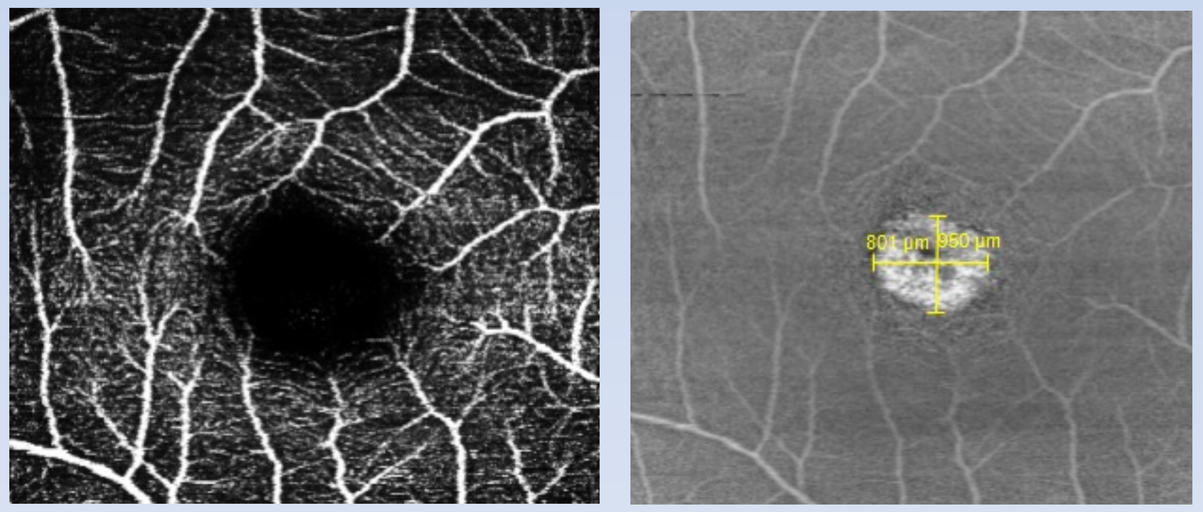
LEFT



OCT of left eye showing wide but uniform foveal pit measuring 867 microns (Heidelberg Eye Explorer)



OCT- Angio of the right eye. En-face OCT-A of superficial vascular plexus (left) and extracted FAZ (right), measuring 905 x 921 microns.



OCT- Angio of the left eye. En-face OCT-A of superficial vascular plexus (left) and extracted FAZ (right), measuring 801 x 950 microns.

Discussion & Conclusion

- Staircase foveopathy, defined as irregular loss of inner retinal layers in the central macular region, leading to a broadly thinned retina with a stair-like appearance, can be visualized using OCT imaging
- Foveal hypoplasia and staircase foveopathy have been described in AS; with irregular depletion of inner retinal layers, resulting in a broadly thinned retina and stair-like appearance with indiscernible foveal pit.
- These structural changes were observed in adults but not children, which may suggest a progressive, degenerative process rather than a stationary observation. This is supported by mouse models showing the absence of collagen IV has only limited impact on basement membrane development, since laminin is sufficient to form the basic matrix but cannot act as an equivalent long-term scaffold
- Of those with AS assessed, optical coherence tomography angiography (OCT-A) revealed a scattered vasculature around an enlarged foveal avascular zone (FAZ) compared to carriers.
- The foveal phenotypic spectrum in AS ranges from foveal hypoplasia and absence of a FAZ to staircase foveopathy with an enlarged FAZ. Because the development of the FAZ and the foveal pit are closely related, these findings suggest an important role for collagen type IV in foveal development and maturation.
- Our case was that of an adolescent with symmetrical inner retinal depletion giving a discernible but broad-based foveal pit; clinically and optically detectable. This corresponded to an enlarged foveal avascular zone bilaterally.
- This structural change did not appear to be causing visual disturbance, in this case but may do so in the future.
- It is important to appreciate the variance in foveal morphology in patients with AS to avoid unnecessary investigation and also educate patients on prognosis.

References

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