

## Clinical Observations Concerning Choroidal Folds in Chinese Patients

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**Abstract:** The objective is to evaluate the clinic characteristics of patients with choroidal folds. A retrospective study of 39 patients (68 eyes) with choroidal folds. All the subjects underwent Fluorescence Angiography (FA), however only parts of them underwent Indocyanine Green Angiography (ICGA) and Optical Coherence Tomography (OCT). There were 24 patients with uveitis, of which 12 were Vogt-Koyanagi-Harada disease (VKH). Choroidal folds appeared as alternating light and dark streaks in the pole. On FA examination, the folds showed almost parallel bands of either hypofluorescence or hyperfluorescence. The remarkable thing is that two types of choroidal folds-coarse folds and wrinkles were observed on FA. On ICGA examination, choroidal folds showed either normal or hypofluorescent at early stages and showed either hyperfluorescent or hypofluorescent at late stages. OCT can directly display morphological characteristics of choroidal folds in some patients and the folds involve the Retinal Pigment Epithelium (RPE) and choroidal layer. Uveitis, especially VKH, researchers suspect is the main cause of choroidal folds in Chinese patients. The two types of choroidal folds were noted on FA which are coarse folds and wrinkles.

**Key words:** Choroidal folds, indocyanine green angiography, optical coherence tomography, fluorescein angiography, China

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### INTRODUCTION

Choroidal folds are wave-like formations at the level of Bruch's membrane, the Retinal Pigment Epithelium (RPE) and the choriocapillaries. The folds can be idiopathic or can be seen in association with such diseases like orbital diseases, choroidal tumor, papilledema, hypotony, uveitis, blunt trauma and hyperopia (Cassidy and Sanders, 1999; Uceda-Montanes *et al.*, 2000; Murdoch and Merriman, 2002; Fardeau *et al.*, 2007; Lavinsky *et al.*, 2007; Valmaggia *et al.*, 2007; Wu *et al.*, 2007; Zhao *et al.*, 2009; Tanigawa *et al.*, 2012).

Fluorescence Angiography (FA) showed alternating hyperfluorescence and hypofluorescence bands (Doi *et al.*, 2000). This specific examination helps to differentiate choroidal folds from retinal folds in many cases (Wise, 1975). Cassidy and Sanders (1999), reported that choroidal folds exist in two distinctive forms coarse folds and wrinkles. Wu *et al.* (2007) and Fardeau *et al.* (2007) described the features of choroidal folds of FA, Indocyanine Green Angiography (ICGA) and Optical Coherence Tomography (OCT) in Vogt-Koyanagi-Harada disease (VKH) in 2007. Giuffre and Distefano (2007) concluded that scanning by OCT can differentiate

chorioretinal folds from choroidal folds. Most of the papers reported on a single disease, such as papilledema, hypotony, choroidal tumor and VKH which is associated with choroidal folds (Cassidy and Sanders, 1999; Uceda-Montanes *et al.*, 2000; Fardeau *et al.*, 2007; Wu *et al.*, 2007). However, this report is a pioneer research on the understanding of the composition of choroidal folds and the proportion of coarse folds and wrinkles.

### MATERIALS AND METHODS

Examination of 39 Chinese patients with choroidal folds on FA was done in ophthalmic center of Renmin Hospital of Wuhan University between January, 2004 and June, 2013. The procedure was done with respect to the country laws and followed the tenets of the declaration of Helsinki. Informed consents were gained from all the patients. The average age of the subjects was 38±14 years (range 11-67 years). They included 20 men and 19 women. The subjects were diagnosed with certain diseases like uveitis, papilloedema, hypotony, choroidal tumor, graves disease, blunt trauma and uveal effusion syndrome. Each patient went through complete ocular examinations that included best-corrected visual

acuity, slit-lamp examination, funduscopy and FA. Also, 9 patients underwent ICGA and 14 underwent OCT in addition to these exams. Details of the angiographic and optical coherence tomographic procedures have been described previously (Wen *et al.*, 2004).

There were 24 patients with uveitis of which 12 were VKH (Tabbara, 1995). The diagnosis was based on the revised diagnostic criteria for VKH disease proposed by American Uveitis Society (Read *et al.*, 2001).

### RESULTS

Summary patient data are presented in Table 1. There were 39 patients (68 eyes) with choroidal folds, including 24 cases (46 eyes) of uveitis, 6 cases (10 eyes) of papilloedema, 3 cases (5 eyes) of hypotony, 2 cases (2 eyes) of choroidal tumor, 2 cases (3 eyes) of graves disease, 1 case (1 eye) of blunt trauma, 1 case (1 eye) of uveal effusion syndrome.

Ophthalmoscopically, choroidal folds took the form of light and dark streaks and were usually confined to the posterior pole, rarely extending beyond the equator. The folds occurred commonly on the temporal side and less commonly on the nasal side. They were typically oriented horizontally and radiating from the optic nerve and the macular region.

However, FA demonstrated far more severe fundus changes than ophthalmoscopy. Most of the subjects produced a pattern of numbers of dark lines on FA (Fig. 1) and some had the presence of alternating hyperfluorescence and hypofluorescence bands. The folds varied in number from 8 or 10-21 or more (Fig. 1). In the early stages, the folds were narrow but gradually became wider. There were 2 types of folds the first was coarse folds (Fig. 1) which consisted of wide bands of hypofluorescence. The other was wrinkles (Fig. 1) which manifested as fine bands of hypofluorescence. The folds were seen in the form of wrinkles in 45.59% (31/68) of the

Table 1: Patient data summary

Patients	Sex	Age (years)	Eye	Visual acuity (right, left)	Diagnosis	Examinations	Type of folds
1	F	50	R+L	5/25, 5/50	Uveitis (VKH)	FA	Coarse folds and wrinkles
2	F	43	R+L	5/10, 5/8	Uveitis	FA	Coarse folds and wrinkles
3	F	20	R+L	5/50, 5/50	Uveitis (VKH)	FA, ICGA	Wrinkles
4	F	58	L	5/50	Choroidal tumor	FA, ICGA	Coarse folds
5	F	40	R+L	FC/50 cm, 5/5	Papilledema	FA	Wrinkles
6	M	45	R+L	5/13, 5/5	Papilledema	FA	Wrinkles
7	M	51	R+L	5/5, 5/5	Graves disease	FA, ICGA, OCT	Wrinkles
8	M	24	R+L	5/25, 5/50	Uveitis	FA	Wrinkles
9	M	46	R+L	5/16, 5/10	Hypotony	FA	Coarse folds and wrinkles
10	M	35	R+L	5/50, 5/50	Uveitis	FA, ICGA	Coarse folds and wrinkles
11	F	41	R+L	5/25, 5/16	Uveitis (VKH)	FA	Wrinkles
12	M	38	L	5/4	Uveal effusion syndrome	FA	Coarse folds
13	F	28	R+L	5/16, 5/50	Uveitis (VKH)	FA, ICGA	Wrinkles
14	F	19	R+L	5/50, 5/10	Papilledema	FA	Coarse folds and wrinkles
15	F	11	L	5/6	Choroidal angioma	FA	Coarse folds
16	F	38	R+L	5/5, 5/5	Papilledema(idiopathic)	FA	Wrinkles
17	M	44	R+L	5/16, 5/16	Uveitis (VKH)	FA	Coarse folds
18	M	28	R+L	5/25, 5/25	Uveitis (VKH)	FA, OCT	Coarse folds and wrinkles
19	M	23	L	5/10	Papilledema	FA	Wrinkles
20	M	25	R+L	5/16, 5/16	Uveitis	FA	Wrinkles
21	M	26	R+L	FC/1 m, 5/5	Uveitis	FA, OCT	Wrinkles
22	M	40	R+L	5/50, 5/50	Uveitis (VKH)	FA, OCT	Coarse folds and wrinkles
23	F	50	R+L	5/50, 5/13	Uveitis	FA	Coarse folds and wrinkles
24	M	40	R+L	5/25, 5/50	Uveitis (VKH)	FA, OCT	Wrinkles
25	M	45	R+L	5/13, 5/13	Uveitis	FA, ICGA, OCT	Wrinkles
26	F	67	R+L	5/50, 5/13	Uveitis	FA, OCT	Coarse folds and wrinkles
27	F	16	R+L	5/16, 5/4	Uveitis (Bechet's)	FA, ICGA, OCT	Wrinkles
28	M	20	L	5/50	Blunt trauma	FA	Coarse folds
29	F	38	R+L	5/13, 5/13	Uveitis (VKH)	FA	Coarse folds and wrinkles
30	F	55	R+L	5/13, 5/5	Uveitis (VKH)	FA	Coarse folds
31	F	64	R+L	5/50, HM	Uveitis	FA, ICGA, OCT	Coarse folds
32	M	42	L	5/50	Uveitis	FFA	Wrinkles
33	F	52	R+L	5/16, 5/16	Hypotony	FFA, ICGA, OCT	Coarse folds and wrinkles
34	F	31	R+L	5/4, 5/50	Uveitis	FFA	Coarse folds
35	M	29	R+L	5/10, 5/13	Uveitis (VKH)	FA, OCT	Coarse folds
36	M	33	R	HM	Hypotony	FA	Wrinkles
37	M	58	R	5/10	Graves disease	FA, OCT	Wrinkles
38	F	53	L	5/10	Uveitis (VKH)	FA, OCT	Coarse folds and wrinkles
39	M	54	R	5/50	Papilledema	FA, OCT	Wrinkles

R+L = Right and left eye; L = Left eye; FC = Finger Count; HM = Hand Move; FA = Fluorescein Angiography; ICGA = Indocyanine Green Angiography; OCT = Optical Coherence Tomography

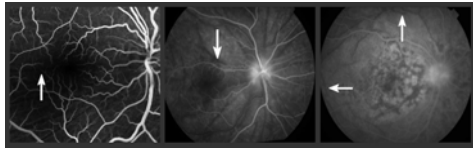


Fig. 1: Left; Fluorescein Angiographic (FA) image of a 51 years old patient with graves disease (patient 7). It shows a large number of horizontal or oblique choroidal folds taking the form of hypofluorescent bands (arrow). Middle: FA image of a 44 years old patient with Vogt-Koyanagi-Harada (patient 17). The image shows about 13 hypofluorescent bands (arrow) radiate from the optic disk to the periphery. Right: FA image of a 52 years old patient with hypotony (patient 33). It shows two types of folds: Coarse folds (vertically arrow) and wrinkles (horizontal arrow)

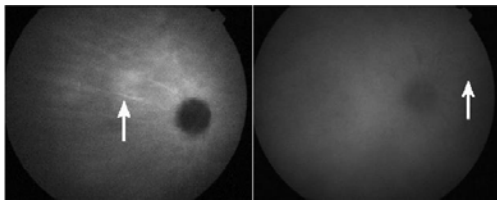


Fig. 2: Left; Indocyanine Green Angiography (ICGA) image of the same patient with the left of Fig 1. Choroidal folds show hypofluorescence at the early stage (arrow). Right: ICGA image of the same patient with the left of Fig 1. Choroidal folds showed hyperfluorescence at the late stage (arrow)

subjects and in the form of coarse folds in 20.59% (14/68) of the subjects. The total of 33.82% (23/68) of the subjects presented with both forms. Folds were particularly prominent in the phase of arterio-venous. The pattern faded, as the angiogram progressed and no leakage of dye occurred at the late phase.

On ICGA examination, choroidal folds showed either hypofluorescent (Fig. 2) or normal fluorescent at the early stages and showed either hyperfluorescent (Fig. 2) or hypofluorescent at the late stages. The streaks corresponded with the lines on FA examination, however the number was less.

The OCT pattern was a concern because it showed choroidal folds involvement in the choroid and retina layer (Fig. 3). Choriorretinal folds displayed a wavy appearance with retinal and RPE lines of apparently normal thickness. Choroidal folds involved the choroid and RPE layers. The folds were seen in the form of choriorretinal folds in 23.08% (3/13) of the subjects and in

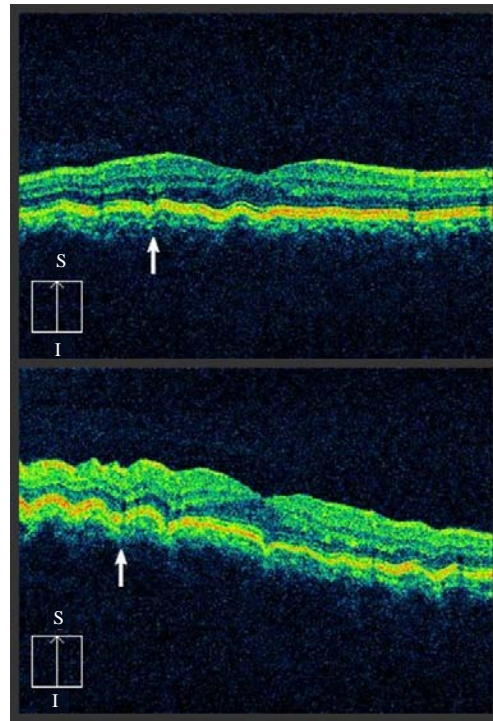


Fig. 3: Up; OCT image of a 51 years old patient with graves disease (patient 7 left eye). OCT reveals the wavy appearance of the RPE, as well as the underlying choroid (arrow). Down: OCT image of a 51 years old patient with graves disease (patient 7 right eye). The scan shows multifocal folds of the whole retino-choroidal complex (arrow)

the form of choroidal folds in 30.77% (4/13) of the subjects. There is no significant change in the remaining 46.15% (6/13) of the subjects.

It was surprisingly evident that those VKH patients who showed relief of edema which also showed gradually disappearance of the folds after the examination. The reductions of folds were also found in relation with elevated of intraocular pressure in patients with hypotony.

## DISCUSSION

In this study, the majority of subjects (61.54%) were uveitis, 45.83% had VKH. This implied that uveitis, especially VKH was the key reason of choroidal folds in Chinese patients. Wu *et al.* (2007) presumed that the folds were secondary to the marked congestion and thickness of choroid to adapt the unchanged intraocular volume. The observation suggested 6 (15.38%) were caused by papilloedema. The raised pressure in the optic nerve sheaths transformed this structure into a rigid tube which indented the posterior globe, producing choroidal

folds (Cassidy and Sanders, 1999). Researchers diagnosed 3 (7.69%) patients with hypotony. All patients underwent trabeculectomies. The folds may either be caused by the reduction in aqueous humor production or the increase in intraocular fluid outflow through uveascleral pathways or both (Morse *et al.*, 1990; Schubert, 1996). Researchers suggest the reason for the folding varies in different diseases.

Choroidal folds are characterized by horizontal, oblique, vertical or irregular grooves or striae in the posterior pole. The folds were almost parallel and tend to vary in both length and width. In this study, the folds mainly (45.59%) presented as small strips of hypofluorescence on FA and some demonstrating the presence of alternating hyperfluorescence and hypofluorescence bands. It may be a possibility that most of subjects are patients with uveitis, choroidal folds were confined to the choroid and RPE layer. On ICGA examination, choroidal folds demonstrated a pattern of either hypofluorescence or normal fluorescence at the early stages and a pattern of either hyperfluorescence or hypofluorescence at the late stages. Wen *et al.* (2004) found the folds turned hyperfluorescent at the late stages of ICGA, concluded that the indocyanine green dye assembled in the troughs and showed hyperfluorescent. Researchers believe the hypofluorescent streaks occurred due to the decreased transmittance of fluorescence through the denser and more compressed RPE.

In this through research, it showed that 43 patients were diagnosed as VKH, 12 (27.9%) had choroidal folds. Wu *et al.* (2007) and Fardeau *et al.* (2007), also reported 12 and 62% patients of VKH showed choroidal folds. Researchers speculated that the different incidence may be due to different periods of disease. At the same occurrence, researchers found that the number of folds remarkably reduced with the relief of edema in VKH patients and elevation of intraocular pressure in hypotony. Cassidy and Sanders (1999) found the folds persisted even after resolution of papilloedema. His hypothesis was that the folds exist for a long time due to the permanent changes of the RPE. This shows that the choroidal folds of different stages have different performance.

The 2 types of folds which includes coarse folds and wrinkles were observed in the study. Coarse folds were seen mainly in choroidal tumors while wrinkles mainly in graves disease. VKH showed not only coarse folds but also wrinkles. Coarse folds may result from folding of the full thickness of the choroid (Cassidy and Sanders, 1999). Choroidal wrinkles were confined to the retinal pigment epithelium and Bruch's membrane (Cassidy and Sanders, 1999). In choroidal and orbital tumors, evidence proved that external mechanical compression and/or shrinkage of the eye wall induces coarse folds (Del Priore, 2006). In

VKH, the folds were secondary to the marked congestion and thickness of choroid to the adaption of unchanged intraocular volume (Wu *et al.*, 2007). The mechanical factors which determine the type of choroidal folds are unknown.

Wu *et al.* (2007) and Giuffre and Distefano (2007), reported the presence of choroidal folds on OCT, Giuffre and Distefano (2007) also used OCT to differentiate chorioretinal fold from choroidal fold. In this study, some patients showed folds on FA, however they showed no apparent changes and no obvious change between coarse folds and wrinkles on OCT. Researchers feel that this research, may need to accumulate more cases to describe the characteristics of choroidal folds on OCT.

## CONCLUSION

The choroidal folds are common clinical sign. Researchers speculate uveitis especially VKH is the main cause of choroidal folds of the Chinese patients. The characteristics of the folds showed distinctive changes with the primary diseases.

Researchers clearly recognize this as a single retrospective study done in one hospital. Further studies with large samples and multi-center are necessary to investigate the constitution of choroidal folds and additional studies with long term follow-up and SD-OCT are needed to detect the mechanism of folds (Spaide *et al.*, 2008; Maruko *et al.*, 2010, 2011).

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