OCT in Toxic and Nutritional Optic Neuropathies

18

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18.1 OCT and Toxic Optic Neuropathies

The anterior visual pathways are susceptible to damage from numerous toxic agents [1]. Toxic optic neuropathies can classically be caused by ingestion of numerous substances, including alcohol (methanol, ethylene glycol), antitubercular drugs (ethambutol, isoniazid), antibiotics (linezolid, sulphonamides, chloramphenicol), antimalarials (chloroquine, quinine), anti-cancer drugs (vincristine, methotrexate), antiarrhythmic (digitalis, amiodarone). Although this list of potentially toxic agents for the optic nerves is constantly increasing, due to the current exponential development of new therapies, only few drugs exhibit a firm evidence of causal relationship.

Toxic optic neuropathies, which are clinically often undistinguishable from nutritional optic neuropathies, typically present as painless, progressive, symmetric and bilateral visual impairment due to central or centrocecal scotoma, dyschromatopsia often being the initial symptom. The site of the primary injury can be very variable, including the retina, retinal ganglion cells, intraocular nerve fibre axons, or chiasm. The majority of clinical findings are caused by selective damage to the papillomacular bundle, which fibres are most susceptible due to their long unmyelinated part in the retina and their relatively small calibre. Preferential involvement of the papillomacular bundle is a common feature to many acquired and genetic optic neuropathies. On the cellular level they also share the similar pathophysiology

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mechanism based on disruption of oxidative phosphorylation in mitochondria, esp. in retinal ganglion cells, and this is the reason to name them mitochondrial optic neuropathies. Drugs shown to cause mitochondrial optic neuropathy by blocking oxidative phosphorylation include ethambutol, chloramphenicol, linezolid, erythromycin, streptomycin, and antiretroviral drugs [2].

Other drugs provoking optic neuropathy, less strongly related to mitochondrial dysfunction include amiodarone, infliximab, quinine, dapsone, pheniprazine, suramin, and isoniazid [2].

It was suggested that since axonal transport is highly energy dependent and mitochondria need to be transported from the neuron body to the distal synaptic terminals, retinal ganglion cells (RGC) with their long axons are particularly vulnerable [2]. In early drug toxicity mitochondria accumulate within RGC axons, and this is detectable as axonal swelling by OCT [3]. In subacute and chronic stages of mitochondrial optic neuropathies OCT demonstrates RNFL thinning of the papillomacular bundle, esp. in the inferotemporal sector. In the later stages, OCT reveals thinning of RNFL in all layers [2]. Early diagnosis is crucial for intervention, i.e. discontinuation of the drug, which may allow clinical recovery. However, early clinical diagnosis may be difficult, due to the normal ophthalmoscopic appearance of the optic disc pallor. Only at later stages is optic disc pallor or atrophy is clinically visible. For this reason, optical coherence tomography (OCT), has been initially considered as a potential method for early diagnosis and possibly monitoring drug toxicity affecting the retina, the retinal ganglion cells complex or the retinal nerve fiber layer (RNFL). Indeed, beyond its extensive use in glaucoma [4], OCT is now commonly used for the evaluation of various optic neuropathies including optic neuritis, ischemic optic neuropathies, papilledema, traumatic optic neuropathy [5–7]. However, interestingly, the number of OCT studies dedicated to toxic optic neuropathies remains relatively small and no OCT guidelines exist to monitor optic nerve drug toxicities.

18.1.1 Ethambutol

Ethambutol hydrochloride is a bacteriostatic antitubercular agent and probably the most common therapy implicated in toxic optic neuropathy. Ethambutol and its metabolite ethylenediaminodibutyric acid chelates several metal-containing enzyme systems like copper and zinc in the nucleic acid structures of mycobacteria leading to decreased levels of metalloproteins [8, 9]. Similar disruption is seen within the cytochromes of the human mitochondria, leading to apoptosis of retinal ganglion cells [8, 9] and subsequent optic neuropathy [10]. Early animal experiments have also demonstrated ethambutol toxicity affecting the retinal ganglion cells, the optic nerve, chiasm and optic tracts [11, 12].

Ethambutol induced optic neuropathy, which may become clinically patent at any time from 2 to 12 months after the initial treatment, is often reversible, if the condition is early recognized, However, permanent damage may occur at toxic or even standard doses (15–25 mg/kg/day), especially in debilitated patients, i.e. with associated renal failure. The ethambutol induced optic neuropathy has a

predilection for the papillo-macular bundle of the retinal nerve fibre layer. Therefore, ophthalmoscopic changes of the optic nerve head are often subtle at the early stages, making OCT a good candidate for early ethambutol optic nerve toxicity detection.

The most common OCT finding in advanced optic nerve ethambutol toxicity is thinning of the retinal nerve fibre layer, especially in the infero-temporal quadrant, corresponding to the papillo-macular bundle [9, 12, 13]. Patients with thinner temporal quadrants display lower visual acuity and significantly reduced colour vision. These OCT findings may also correspond well with the visual field defects on Humphrey visual field analysis. Limited case series have suggested that at early stages, the ethambutol induced optic neuropathy might be associated with increased RNFL thickness [14]. In addition, after cessation of ethambutol, reversible RNFL changes, detectable by OCT may occur [14]. Apart from RML, significant decreases in retinal have been observed at various levels including ganglion cell layer and inner plexiform layer [15, 16].

The up-to-date study, included a group of 21 patients (42 eyes) treated with ethambutol for 2–12 months, showed that early ethambutol-induced optic neuropathy was associated with edema and thickening of peripapillary retinal nerve fiber layer (pRNFL) which persisted for up to 3 months after the onset of symptoms [17]. Also, an initial decrease in the ganglion cell layer plus inner plexus layer (GCIPL) was observed, more remarkable in inner locations (inner ring) than in outer locations. On follow-up OCT, conducted after 6 months, mean thickness of the pRNFL at the temporal, nasal and inferior locations, mean thickness of the inner GCIPL at the temporal, nasal and inferior locations, and mean thickness of the outer GCIPL at the superior and inferior locations were significantly lower than during the baseline examination. The relative decrease in the thickness of the analyzed layers between the first and the second OCT turned out to be markedly more evident for pRNFL than for GCIPL.

The analysis of correlation between the GCIPL thickness and vision recovery after the withdrawal of ethambutol demonstrated a significant positive association between the thickness of the temporal inner GCIPL and the degree of visual acuity improvement within 12 months of the agent discontinuation. A 10-μm loss in the inner GCIPL thickness turned out to be associated with a 0.5 decrease in the amount of logMAR visual acuity recovery at 12 months. No similar relationships were observed at 1, 3 and 6 months after the ethambutol withdrawal, except the temporal inner GCIPL, the thickness of which showed a significant correlation with visual recovery [17]. Taken altogether, these findings imply that temporal GCIPL may serve as an anatomic marker to predict visual acuity improvement both in early-phase neuropathy and at later period, i.e. 12 months after cessation of ethambutol.

Furthermore, the results of this study suggest that the toxic effect of ethambutol is not limited only to the papillomacular bundle, as the damage was observed in both nasal and temporal GCIPL.

An OCT study of patients who received ethambutol at a dose of 15–19 mg/kg/day for approximately 5 months demonstrated that the treatment contributed to an increase in RNFL thickness. The thickness of RNFL returned to its baseline level within 12 months of ethambutol discontinuation. This implies that OCT

may be a useful test for early detection of subclinical ethambutol-induced optic neuropathy [18].

Another OCT study of two patients with ethambutol-induced optic neuropathy (developed within 8 and 12 months of the treatment) demonstrated a significant decrease in retinal thickness (especially at the inner ring) when combined RNFL, GCL and IPL map was subjected to the analysis. However, when only the thickness of RNFL was considered, no abnormalities were found in 1 out of the 2 patients. These results suggest that ethambutol may affect both RNFL and retinal GCL [19].

The OCT analysis of pre- and post-treatment RNFL thickness of 38 patients with ethambutol-induced optic neuropathy, who received combined therapy with Boqihuoxue Formula + Methycobal, demonstrated increase of this parameter in all quadrants, especially in the lower and temporal quadrant. These findings imply that OCT may be a useful instrument for the monitoring of treatment effects, and perhaps also recovery after ethambutol discontinuation [20].

In summary, OCT is a potentially interesting tool to assess the degree of optic nerve damage in the ethambutol induced optic neuropathy, especially in the early stages of the condition, when the optic disc has a normal ophthalmoscopic appearance. However, large studies are missing to confirm these preliminary findings, especially regarding early localized temporal RNFL thickening, as an early sign of the disease. Therefore, OCT is not recommended as the sole method for monitoring potential ethambutol optic nerve toxicity.

18.1.2 Methanol

Methanol is a common cause of toxic optic neuropathy especially in the developing world. It is also the most dreaded cause, due to its systemic consequences, potentially leading to metabolic acidosis, visual loss, coma and death. These adverse effects are due to indirect toxicity related to formic acid, catabolised from methyl alcohol via formaldehyde by the enzyme alcohol dehydrogenase in the liver and red blood cells.

The changes in the optic nerves are mostly due to cytotoxic oedema within the retina and the optic nerve, occurring during the first 48 h after methanol ingestion. The retinal ganglion cells and the retrolaminar myelin sheath are also affected due to degeneration of optic nerve axons. Several animal studies also supported these findings by identifying demyelination of optic nerve sheath [21]. The treatment of methanol intoxication is based on ethanol, B-group vitamins, and systemic steroids; however, the prognosis is usually poor and the final visual acuity is counting fingers or worse [22]. It was shown that fomepizole is safe and effective in the treatment of methanol poisoning [23], but high costs limits its availability. The visual improvement after treatment of 2 patients with a combination of intravenous erythropoietin, systemic corticosteroids, vitamins, and folic acid was reported [24]. OCT has been used for exploring macula and peripapillary retina in methanol-induced retinal toxicity, showing peripapillary nerve fibre swelling and accumulation of intraretinal fluid in the acute phase, with subsequent thinning in the chronic phase (Fig. 18.1).

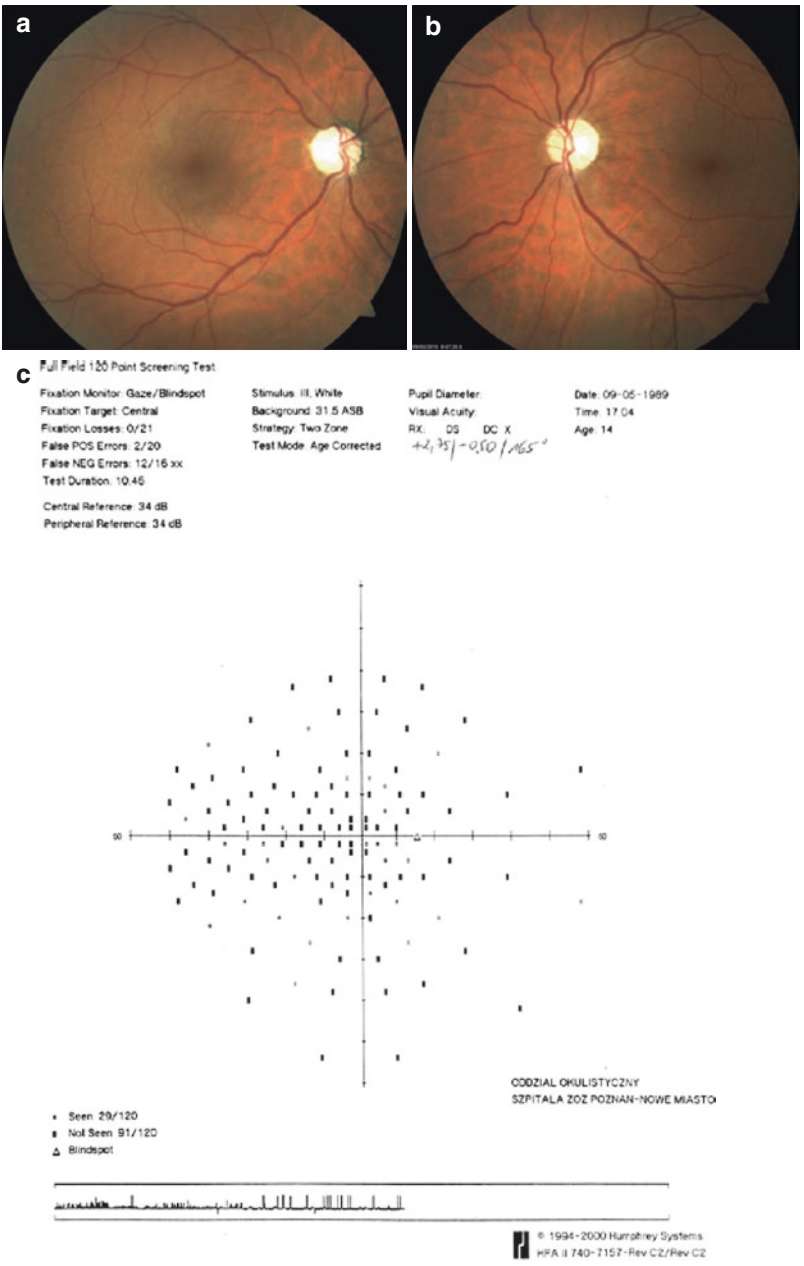
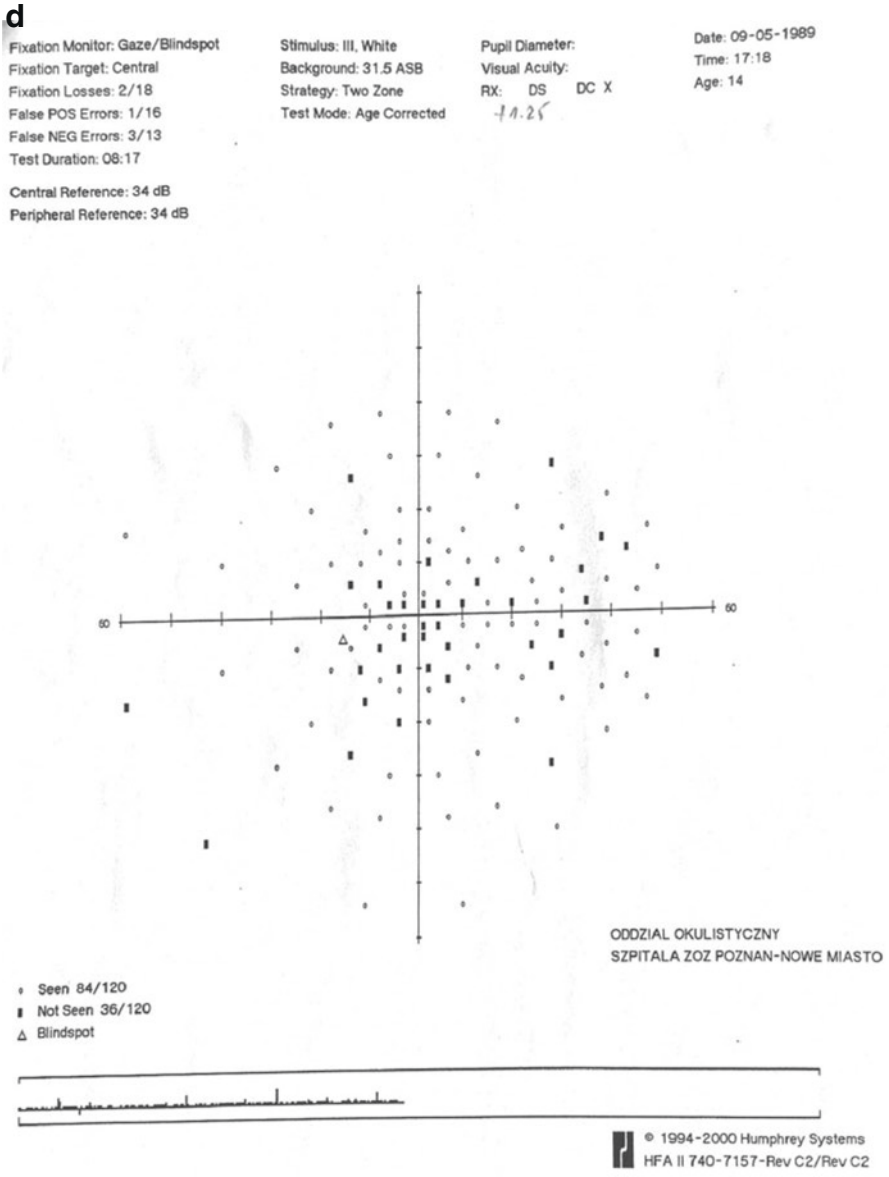


Fig. 18.1 Case report of Methanol Optic Neuropathy. A 40 year old patient with no light perception in both eyes and dilated non-responsive pupils transferred from Toxicology Department after accidental methanol intoxication. After 1-month follow up patient presented improvement of VA in both eyes (counting fingers in right eye and 0.16 in left eye) and kept stable. After 3 months optic nerve atrophy was clearly recognized with pale optic discs in fundoscopy (**a**, **b**), centrocecal scotoma in both eyes (**c**, **d**), decrease in RNFL thickness in both eyes (**e**), and decreased volume of ganglion cells in both eyes (**f**, **g**)



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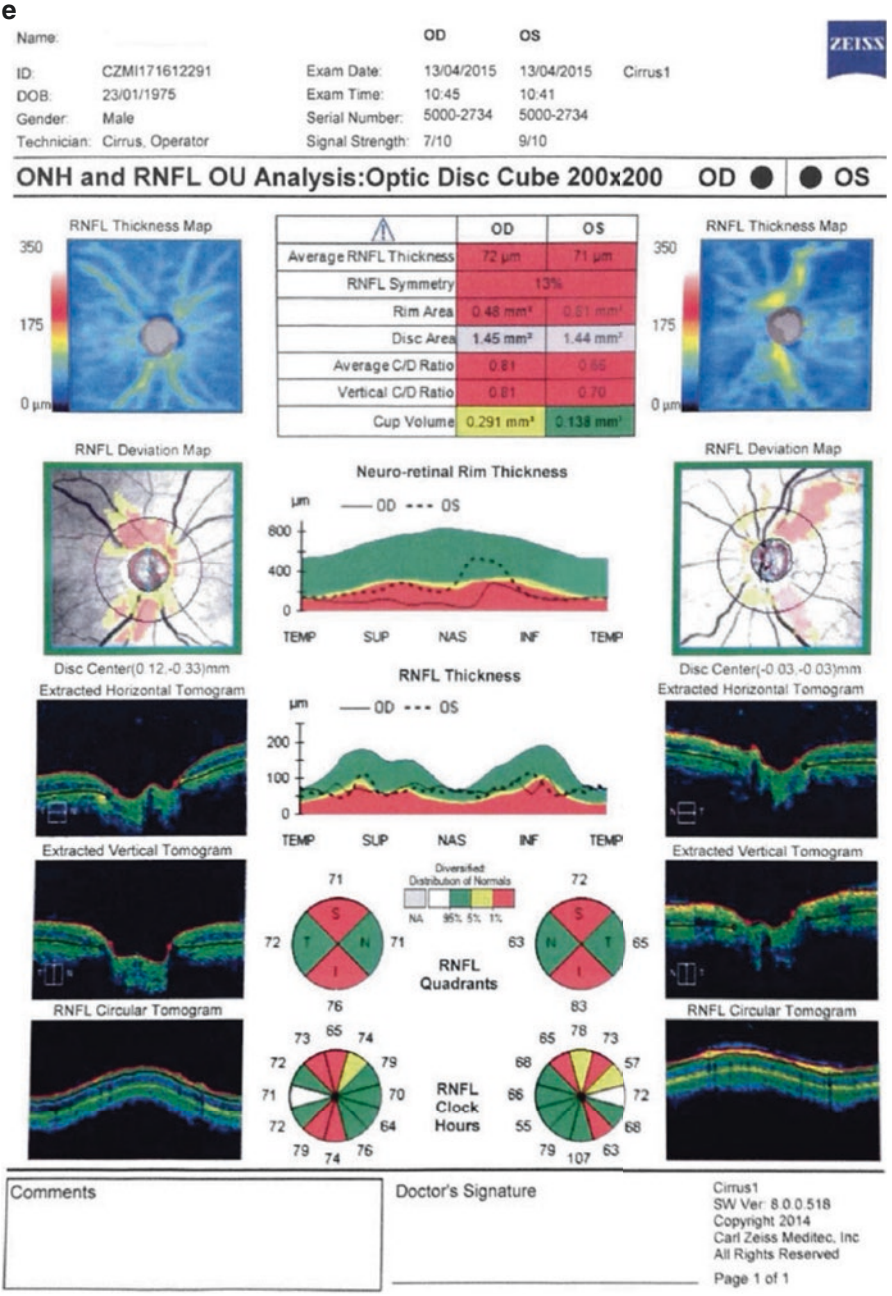

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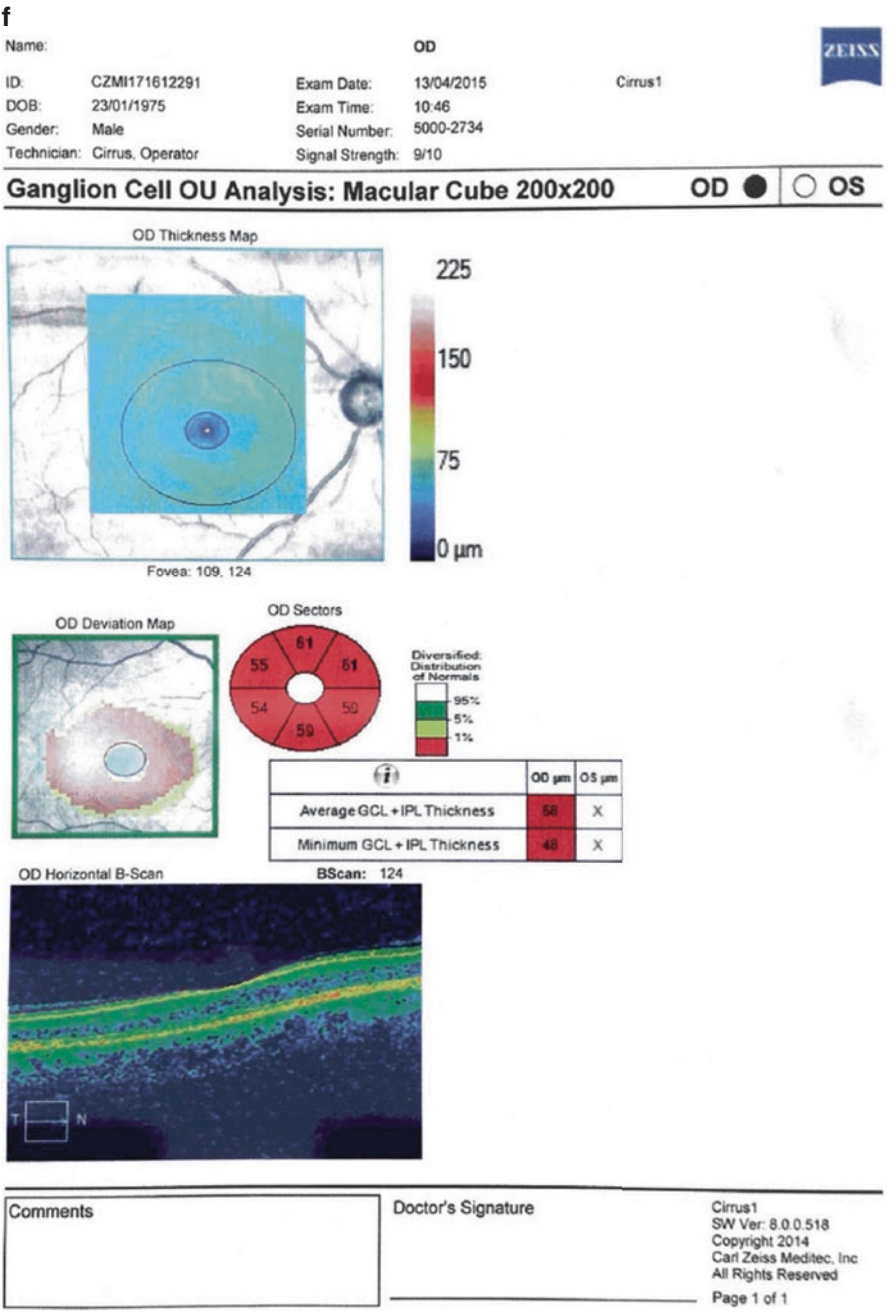

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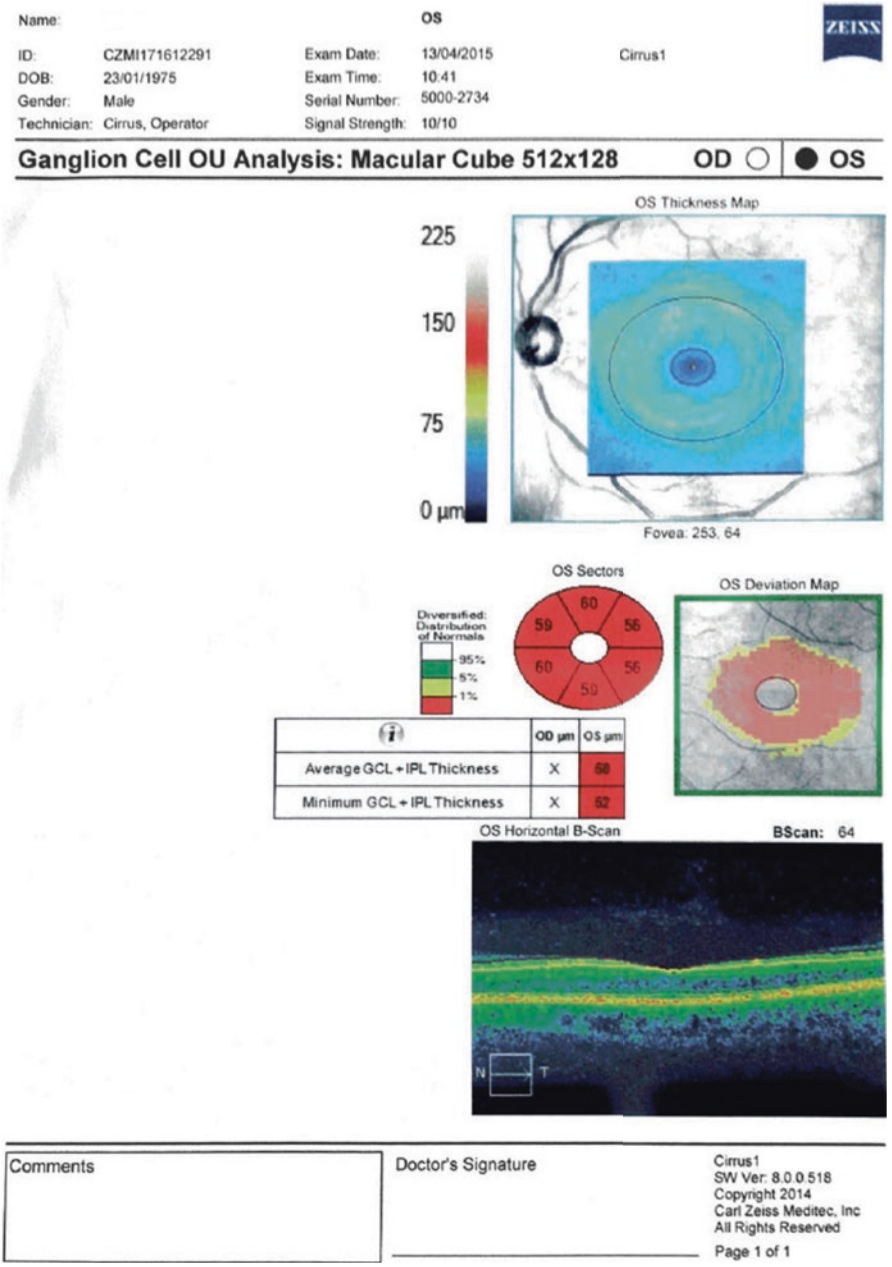

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Therefore, OCT could he a useful tool in this setting, for evaluation of the severity of retinal edema and the temporal changes in the retinal profile [25].

18.1.2.1 Methanol Toxicity in a 19-Year-Old Female Student: A Case Report

Examination of the patient's right eye revealed inferonasal colobomatous defect of the iris, inferonasal chorioretinal coloboma and tilting and mild peripapillary atrophy of the optic nerve. In the left eye, trace segmental pallor of the temporal optic nerve head was observed during the examination conducted 4 weeks after the methanol ingestion. OCT conducted 4 weeks after the methanol intoxication revealed right ocular changes that corresponded to the coloboma. Neither thinning nor thickening of the RNFL were found in the left eye, other than a mild thinning in the nasal macula. OCT of the macula conducted 8 months after the acute intoxication with methanol revealed multiple retinal microcysts in nasal segments of both eyes. The microcysts appeared highly uniform and localized to the inner nuclear layer. OCT scan of the RNFL was normal, but bilateral wedge-shaped segmental defects of the papillomacular bundles were found during the assessment of ganglion cell layer [26].

The microcysts found on OCT in patients with methanol intoxication are characteristic and unlikely to be confused with those observed in cystoid macular edema. They are highly uniform, small, have characteristic shape and are located in the inner nuclear layer. The microcysts are found in both eyes, occur symmetrically and are not accompanied by macular thickening. In contrast, the cysts observed in cystoid macular edema are larger, more irregular and can also be found in the outer plexiform layer. The lesions are either unilateral or bilateral, asymmetrical.

Several mechanisms of microcyst formation have been proposed thus far, including trans-synaptic retrograde degeneration, glial cell activation and mitochondrial dysfunction. Fluorescein angiography suggests that the lesions have nonvascular etiology. Presence of microcysts in the inner nuclear layer might correspond to retinal ganglion cell loss, and represent a damage to small caliber axons rich in mitochondria in the papillomacular bundle [26].

The OCT study of patients with methanol-induced optic neuropathy demonstrated significant decrease of global RNFL thickness during the following years. The most remarkable loss was detectable in the temporal segments. The highest rate of thickness was seen in the most severely poisoned patients [27]. Therefore, OCT could be a potentially interesting tool to assess the degree of chronic retinal axonal loss in patients with acute methanol-induced optic neuropathy.

18.1.3 Tobacco

The toxic optic neuropathy caused by tobacco seems to be mysterious entity since all confirmed cases were reported many years ago, in the era before OCT and genetic studies. It was shown that at least part of this disorder in fact was Leber's

Hereditary Optic Neuropathy (LHON) [28–30]. It was proposed that smoking, especially in genetically susceptible individuals might affect sulphur metabolism, leading to chronic cyanide intoxication [31, 32]. The disorder was characterized by slowly progressive papillomacular bundle damage, centrocecal scotoma and visual loss. The appearance of the optic nerve is usually normal at the initial stages, with occasional peripapillary dilated vessels and haemorrhages, while pallor ensues only in the later stages [32]. Since the clinical picture of TON is similar to other optic neuropathies, the diagnosis of TON is by exclusion only of other toxic, nutritional and hereditary optic neuropathies. A few new articles [33–35] claimed that they presented patients with tobacco optic neuropathy, but they were undermined as they did not convincingly proofed the diagnosis [36–40].

18.1.4 Amiodarone

Amiodarone is a very efficient antiarrhythmic agent primarily used to treat atrial or ventricular tachyarrhythmias and fibrillation. The clinical presentation of amiodarone induced optic neuropathy may be sometimes indistinguishable from that of non-arteritic anterior ischaemic optic neuropathy (NAION) [41]. Amiodarone induced optic neuropathy has typically an insidious onset with a milder degree of visual loss, a longer duration of disc edema, and is more commonly bilateral than typical NAION, though there can be a considerable overlapping between these two conditions. Furthermore, disc edema and optic neuropathy may continue to progress even after cessation of the drug [41]. The mechanism of amiodarone-induced optic neuropathy is possibly due to the accumulation of cytoplasmic lamellar inclusions in the lysosomes due to binding of amiodarone with phospholipids. These complexes are not degraded by phospholipase enzymes leading to deposition of amiodarone deposits in the optic nerve as well as in other ocular tissues, including cornea and lens.

OCT has shown that in amiodarone-related optic neuropathy, there is transient RNFL thickening, during the initial months of therapy, followed by subsequent axonal loss and optic nerve atrophy [42]. OCT has been proposed as follow-up method for documenting edema or RNFL thinning in this setting.

18.1.5 Linezolid

Linezolid is a widely used broad-spectrum antibiotic. OCT studies demonstrated that patients with the signs of linezolid-induced optic neuropathy presented with microcystic spaces in the retinal nerve fiber layer and at the border of the RNFL and the retinal ganglion cell layer. The microcystic spaces in the RNFL resolved within 6 weeks of linezolid discontinuation. The degree of changes documented on OCT was shown to be proportional to deterioration of visual acuity [43, 44].

18.1.6 Chemotherapy

There is a published case report of neuropathy induced by intravenous chemotherapy (cytarabine and daunorubicin) in a patient with acute myeloid leukemia. OCT, conducted 6 weeks after the onset of symptoms, demonstrated thinning of the retinal nerve fiber layer in both eyes. Moreover, thinning and alteration of the foveal contour were observed in both eyes on OCT of the macula. The progression of changes documented on OCT was no longer observed when the patient was switched to another chemotherapy regimen [45].

18.2 OCT and Nutritional Optic Neuropathies

Nutritional optic neuropathy is more common among alcohol abusers and those who are undernourished [46]. Isolated nutritional optic neuropathies are rare, they are more frequent in regions of famine, where they may be epidemic. Nutritional optic neuropathies may be associated with various causes, including unbalanced diet, bariatric surgery, hunger strike, anorexia nervosa, absorption deficiency of vitamin B [47].

As in toxic neuropathies, the anterior visual pathways are susceptible to nutritional deficiency associating papillomacular bundle damage, central or cecocentral scotoma and reduction of color vision. The primary lesion is not necessarily localized into the optic nerve itself; it may be located at various levels, such as the retinal ganglion cells, nerve fiber layers, chiasm, or the optic tracts [48].

The exact mechanism by which nutritional deficits damage the optic nerve remains largely unknown. Specific deficiencies of vitamin B-12 (cyanocobalamin), thiamine (vitamin B-1) [49], other vitamins (riboflavin, niacin, and pyridoxine), folic acid, copper [50, 51] and other proteins with sulfur-containing amino acids have been associated with optic neuropathies [52]. It has been postulated that these deficiencies affect mitochondrial oxidative phosphorylation, and therefore nutritional optic neuropathies may be part of the acquired mitochondrial optic neuropathies spectrum [53]. The visual prognosis depends on multiple factors, including the cause and the duration of symptoms. At advanced stages of the condition, associated with optic atrophy, recovery is less likely to occur than at early stages [50]. Nutritional optic neuropathies are very rare in children.

Nutritional and toxic optic neuropathies have similar clinical presentations, i.e. bilateral, painless visual loss associated with colour vision disturbances and central scotoma. When an optic neuropathy is suspected, a thorough history should cover diet, drug/toxin exposure, social history (including alcohol consumption) and the professional environment. Treatment of any chronic disease such as pernicious anemia should be elucidated. Sensory symptoms and gait disturbance may be associated, due to either peripheral neuropathy or cerebellar dysfunction. A family history should be taken, to identify environmental factors or predisposition for hereditary optic neuropathies.

Clinically, patients with nutritional optic neuropathies complain of gradual blurring of vision, at far and near. Often, the slow progression of the symptoms delays diagnosis and treatment. Rarely, the visual symptoms may be asymmetric, but

almost never strictly unilateral. Dyschromatopsia can be the initial symptom in nutritional optic neuropathies. In case of orbital pain, pain on ocular movement, unilateral vision loss, other diagnoses should be considered.

In nutritional optic neuropathies, visual acuity may vary from minimal reduction of vision to no light perception (NLP). However, most patients have 20/200 vision or better. Both pupils are sluggish to light, and there is no relative afferent pupillary defect due to the bilateral involvement, The optic disc may be normal or slightly hyperemic (Fig. 18.2) in the early stages, with small peripapillary hemorrhages.

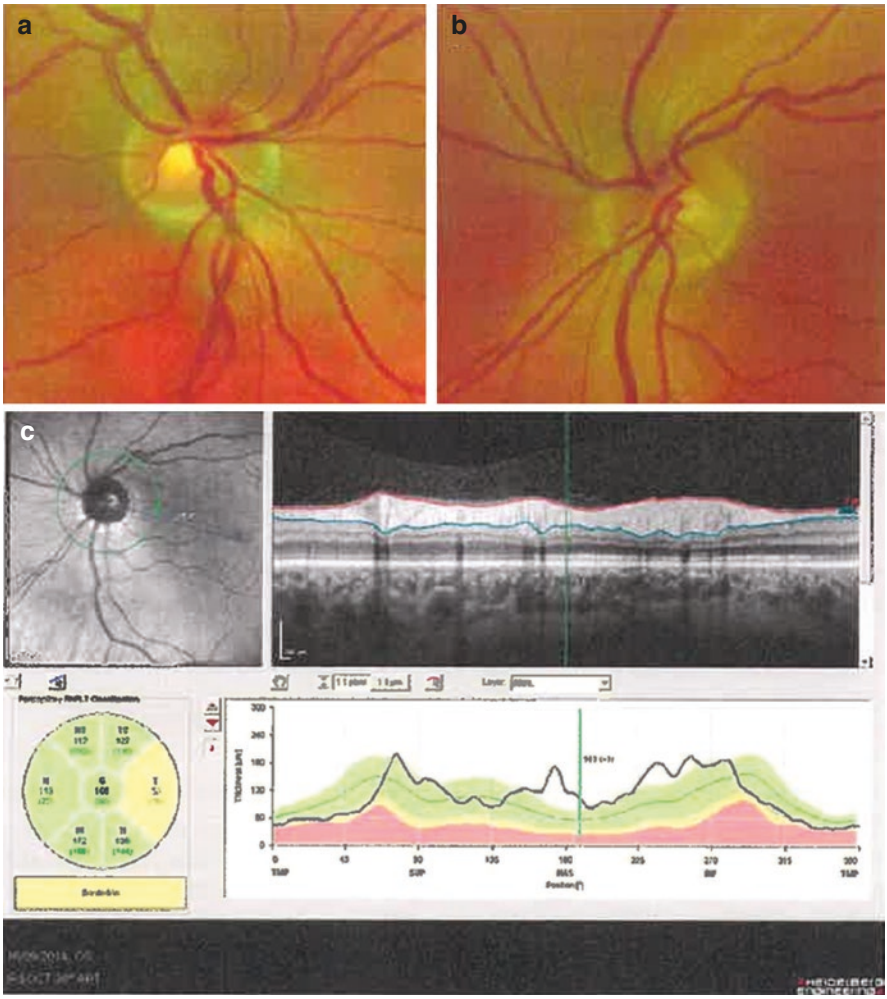


Fig. 18.2 Nutritional optic neuropathy, associated with reduced serum thiamine (Vitamin B l), in a 30-year-old male patient presenting with blurred vision, painful dysesthesia in both legs and gait instability. Visual acuity was 20/200 in both eyes. Bilateral temporal pallor of the optic discs (**a**, **b**) and moderate reduction of the temporal retinal nerve fibre layer, visible on OCT (**c**, **d**). Vision recovered after intramuscular vitamin Bl administration

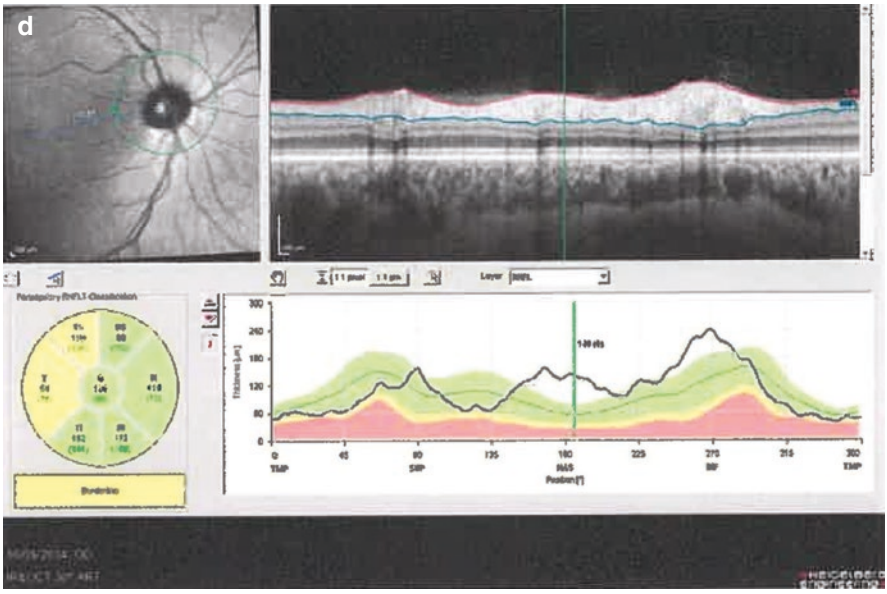


Fig. 18.2 (continued)

After several weeks to months, a papillomacular bundle dropout and temporal disc pallor may occur, followed by optic atrophy (Fig. 18.2). Isolated, purely nutritional optic neuropathies have been rarely explored with OCT, which might be able to closely monitor subtle RNFL changes, i.e. thickening at initial stages, followed at later stages by RML thinning, predominantly encountered in the temporal sector [51] (Figs. 18.3 and 18.4).

A recent OCT study conducted in chronic alcohol and tobacco users demonstrated substantial thinning of the RNFL in all quadrants except the nasal quadrant. The severity of axonal loss in ganglion cells was shown to be proportional to the degree of nicotine dependence. In the case of alcohol abuse, however, the relationship was not as straightforward [54]. These findings suggest that OCT may be a useful screening instrument to predict visual morbidities in persons with nutritional optic neuropathies.

18.2.1 Copper Deficiency

Copper deficiency is an extremely rare finding in patients after bariatric surgeries. According to one published case report, a woman subjected to Roux-en-Y bypass surgery and partial gastrectomy, approximately 3 years after the procedure showed the signs of progressive binocular loss of visual acuity and disorders of color vision with central visual field scotoma in both eyes. OCT conducted 2 months after the

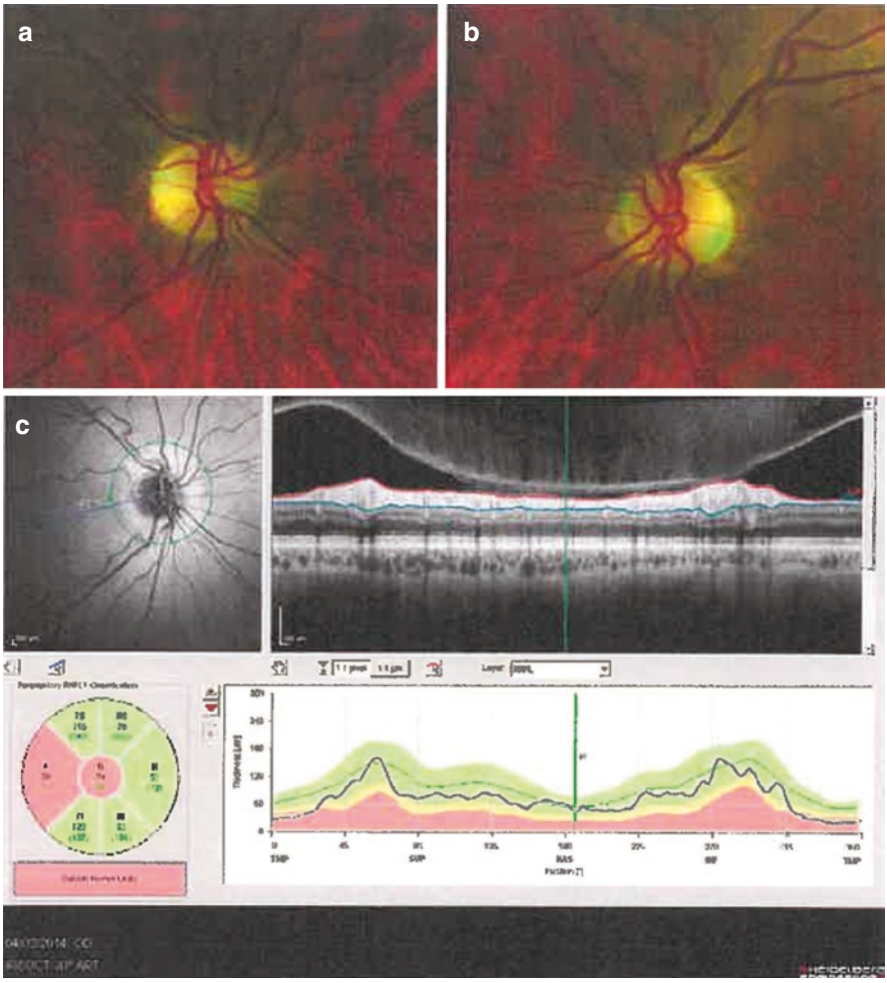
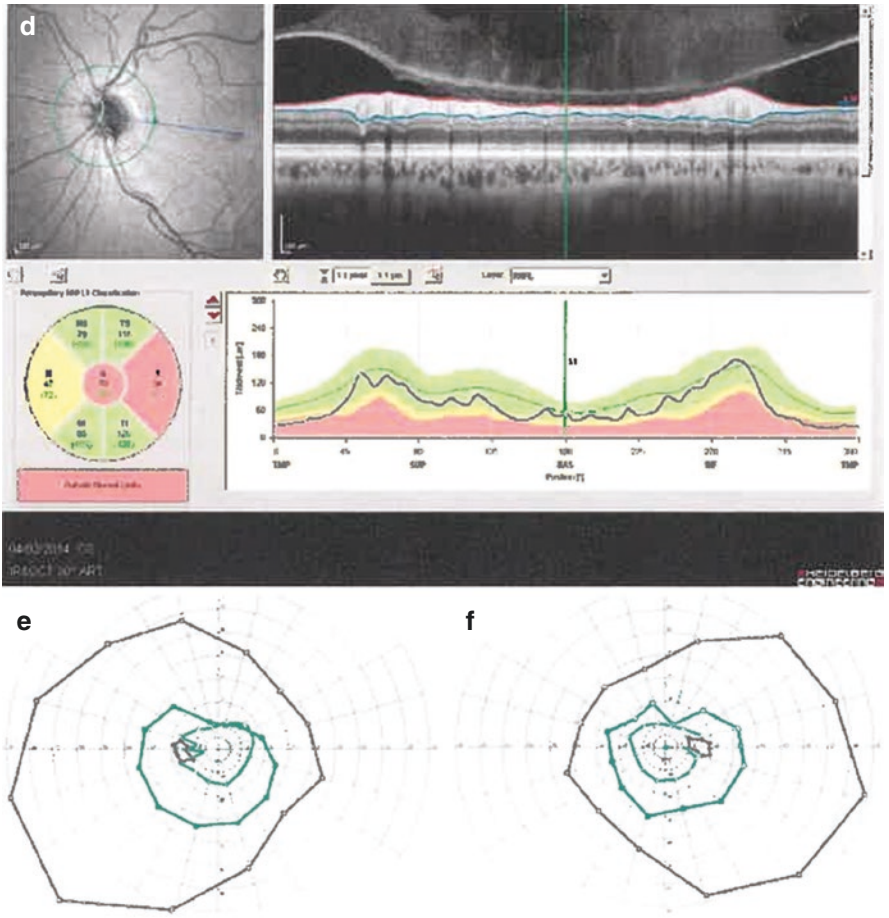


Fig. 18.3 A 60-ycar-old patient presented with bilateral visual loss ongoing for 6 months, (visual acuity was 20/200 in the right eye and 20/400 in the left eye), temporal disc pallor (**a**, **b**) and severe weight loss. There was no history of smoking or alcohol abuse. Decreased RNFL thickness was selectively located in the temporal area (**c**, **d**). Bilateral centrocaecal scotomas were encountered on Goldmann perimetry in both eyes (**e**, **f**). A megaloblastic anemia and folate deficiency was found on the blood test. Eventually a glucagonoma was discovered on abdominal MRI. Malabsorption responsible for malnutrition and particularly for folate deficiency was the suspected mechanism, After successful surgery and folate supplementation, visual acuity improved to 20/30 in the right eye and 20/80 in the left eye

onset of the symptoms revealed binocular thinning of the retinal ganglion cell-inner plexiform layer in the macula. However, the average peripapillary retinal nerve fiber layer thickness was normal. The authors of the report did not provide an explanation for such result of the OCT [55].



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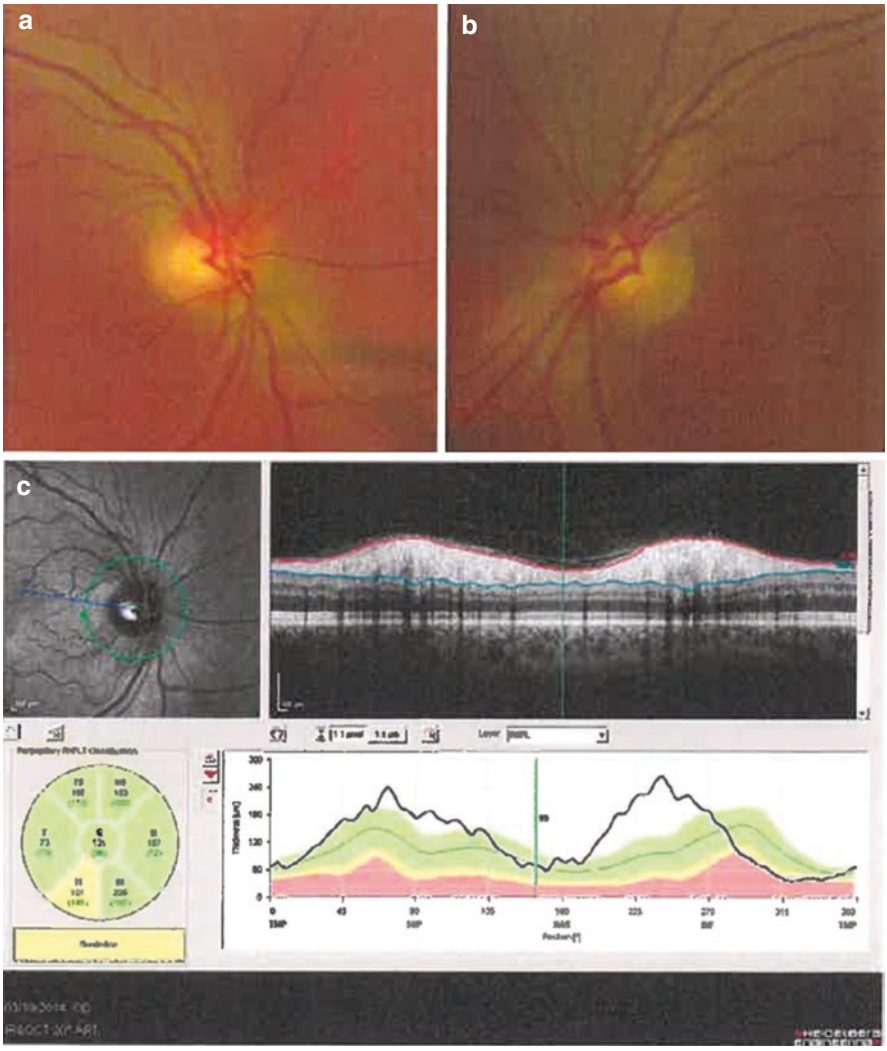
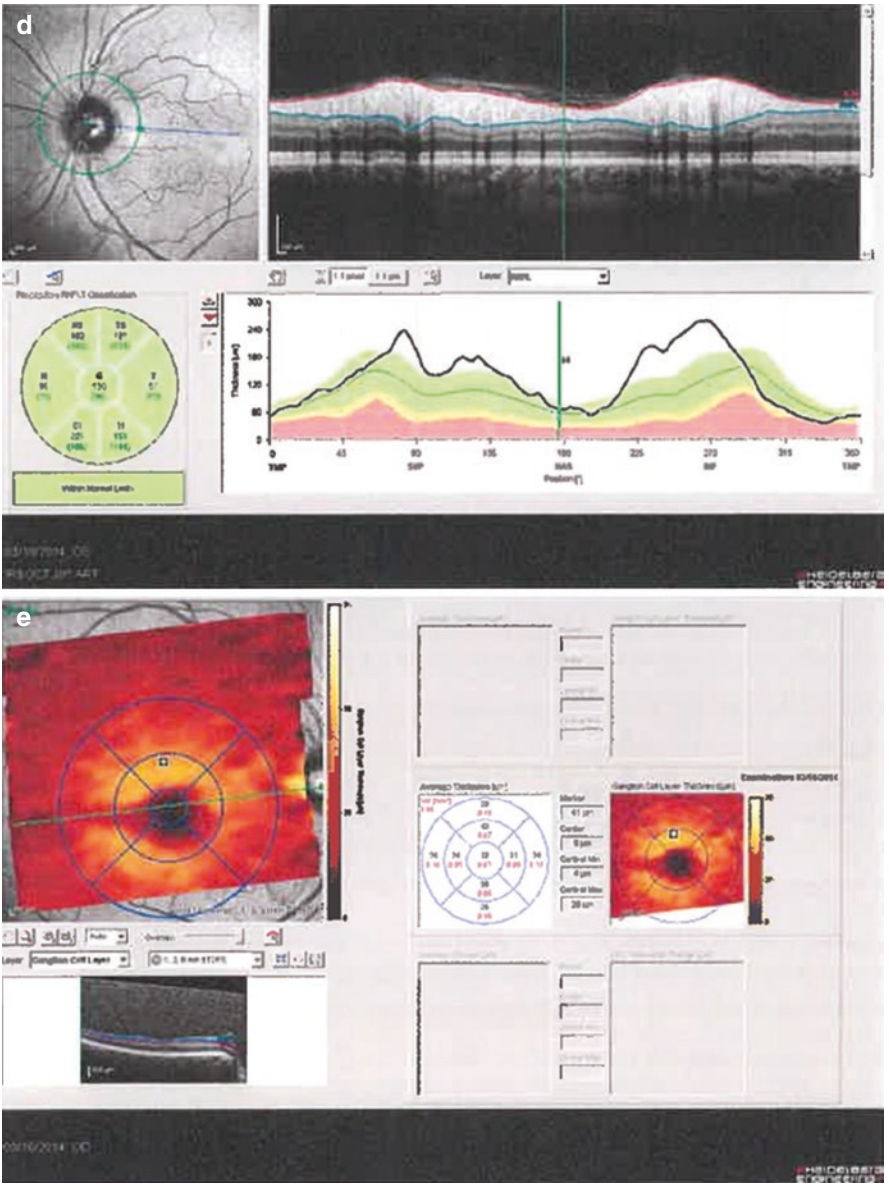


Fig. 18.4 A 40-year-old female patient presented with isolated severe visual loss and a history of mental anorexia in her teens. She stated being well aware of her irregular and unbalanced food intake. Visual acuity was 20/200 in both eyes. The optic disc are slightly hyperaemic with telangiectasia in the peripapillar retina (**a**, **b**). RNFL thickness was at higher normal limit in both eyes (**c**, **d**). The ganglion cell layer was normal in both eyes (**e**, **f**). Leber's hereditary optic neuropathy was ruled out, and the work-up disclosed low vitamin pp and carnitine levels. Six months after supplementation, visual acuity dramatically improved to 20/30 in the right eye and 20/40 in the left eye, although bilateral optic disc pallor had developed and temporal RNFL loss (**g**, **h**) and central ganglion cell loss in both eyes had occurred (**i**, **j**)



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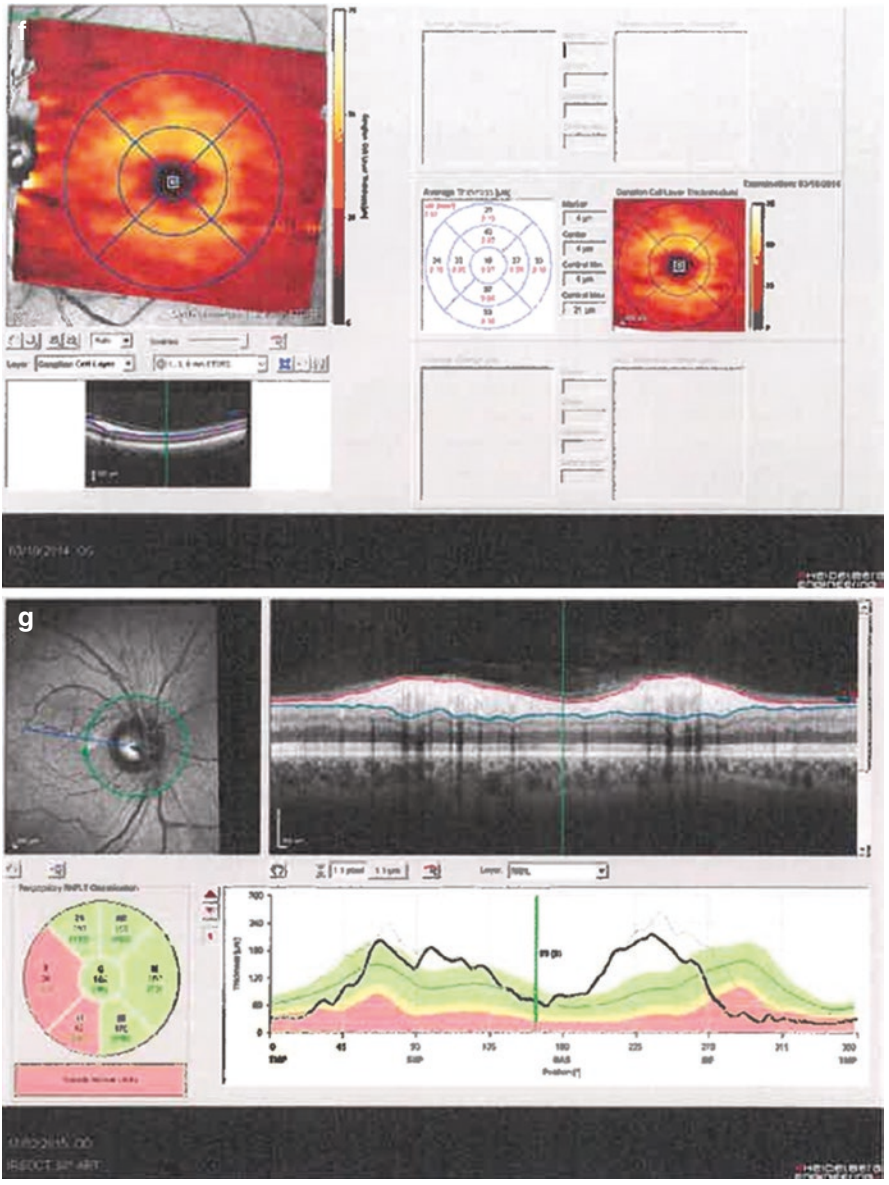

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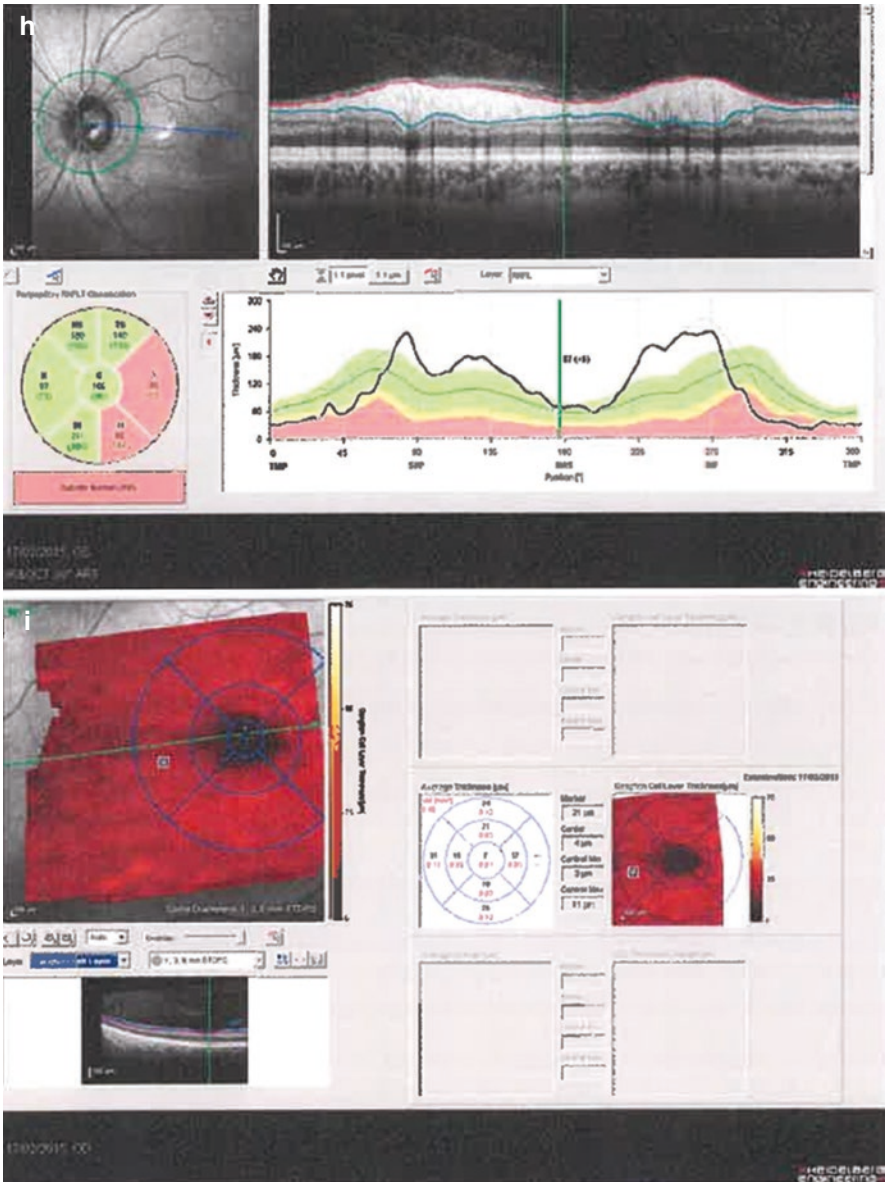

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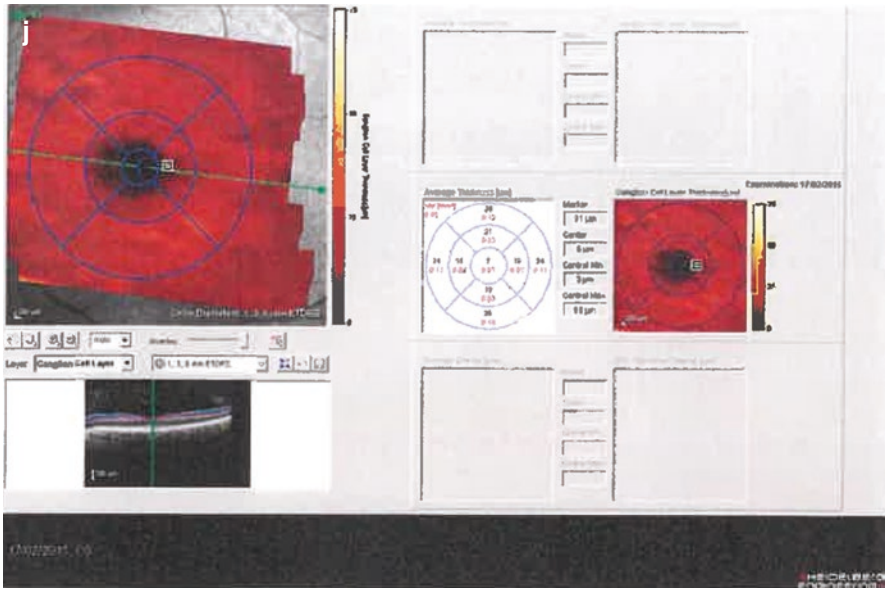

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18.3 OCT and Antiepileptic Drug Toxic Maculopathy

Vigabatrin (Sabril) is a second-line anti-epileptic drug prescribed in partial epilepsy, with or without secondary generalization (mainly after failure of other drugs). As a first-line/monotherapy, Vigabatrin is licensed only for the treatment of infantile spasms (West's syndrome). Vigabatrin acts as a selective irreversible inhibitor of GABA-transaminase. Treatment therefore causes an increase in the concentration of GABA (gamma aminobutyric acid), the major inhibitory neurotransmitter in the brain but also in the retina. Maximal efficacy in adults is usually seen in the 2–3 g/day range. The recommended maintenance dose in children is 50–100 mg/kg/day.

During its clinical development, vigabatrin has rarely been associated with symptomatic visual field constriction and retinal disorders. In 1997, 3 cases of severe, symptomatic, persistent visual field constriction attributed to vigabatrin (VAVFC) were described by Eke [56].

Vigabatrin toxicity is typically associated with bilateral, concentric, predominantly nasal constriction of visual fields. However, patients with perimetric loss due to vigabatrin exhibit normal visual acuity and are unaware of the visual field constriction unless it extends into the central field [57]. The prevalence of VAVFC varies widely between studies, but is generally estimated to be 30–40% [58, 59].

The precise site of toxicity is controversial, but retina is involved in this condition.

Previous studies have shown correlations between the severity of the ERG changes and duration of therapy, as well as with severity of VAVFC. The amplitude of the cone flicker response has the best predictive value for VAVFC, with a sensitivity of 100% and a specificity of 75% [59]. Therefore, ERG screening is currently used for toxicity detection in patients unable to perform perimetry.

Although visual field (VF) loss may occur in this setting despite any clinically detectable retinal changes, patients on Vigabatrin may exhibit optic nerve head pallor and RNFL thinning (Fig. 18.5) [60]. RNFL loss displayed on time domain OCT has previously shown a significant correlation between VAVFC and cumulative vigabatrin doses [61]. Patients with VAVFC displayed a reduced mean RNFL thickness compared with those under Vigabatrin but without field loss. Since none of the patients with VAVFC had normal RNFL thickness, the OCT sensitivity for detecting VF changes was 100% and specificity 70% [60].

Thickness of the nasal quadrant of RNFL appears to be particularly interesting in predicting vigabatrin associated visual filed constriction, with comparable results in terms of sensitivity (67–100%) and specificity (66–73%) [61, 62]. On the opposite, the temporal RNFL sector was not significantly different from control patients with epilepsy (not treated with gabaergic medications) and healthy volunteers [61, 62].

Thus, time domain and spectral domain optical coherence tomography seem to be reliable, in terms of sensitivity, for detecting RNFL thinning associated with vigabatrin-related visual field loss. It appears that both time domain and spectral domain OCT screening for vigabatrin treated patients may accurately monitor those at risk for VAVFC, especially when they are unable to perform perimetry.

In conclusion, OCT may be useful for quantifying the RNFL and retinal ganglion cells complex parameters in toxic and nutritional optic neuropathies [63]. Several studies have suggested that at early stages, localized, subtle RNFL thickening may be detected with OCT, prior to ophthalmoscopically visible changes. In the long term, localized, followed by diffuse RNFL thinning may occur, witnessing global axonal death.

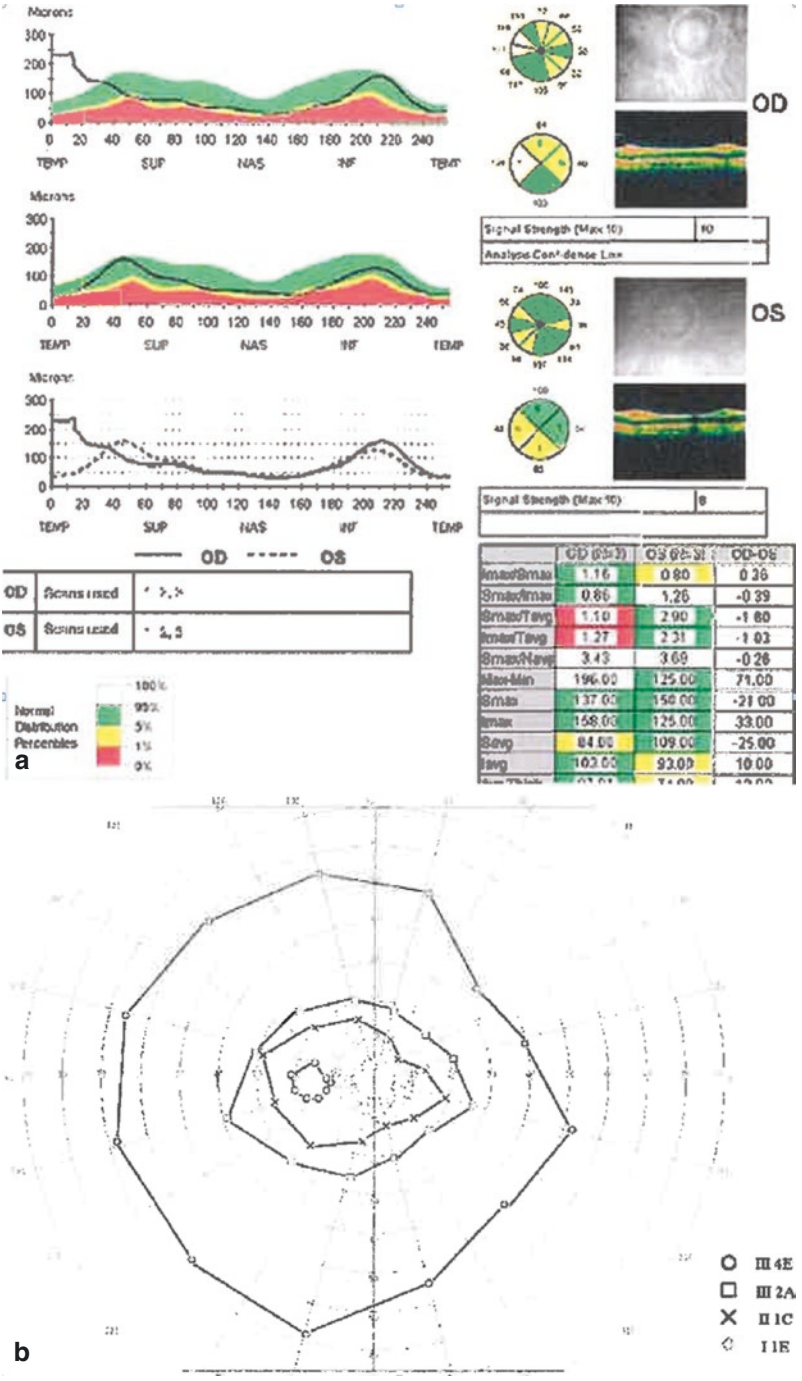

Fig. 18.5 Reduced nasal thickness on time domain OCT (**a**) in a patient treated with vigabatrin and presenting with vigabatrin associated visual field constriction in the nasal hemifield of the left eye (**b**)

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