Optical Coherence Tomography to Monitor Rebound Intracranial Hypertension with Increased Papilledema after Lumbar Puncture

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Abstract: Objective: We report that lumbar puncture (LP) with removal of cerebrospinal fluid (CSF) induced rebound intracranial hypertension with increased papilledema as monitored by optical coherence tomography (OCT). Background: Severe papilledema causes visual field loss and central vision damage if untreated. Fundoscopy is a key to diagnose papilledema, but is not sensitive enough to monitor therapeutic effects. Methods: OCT was applied to follow a 24-year-old woman with headache, visual dysfunction, severe bilateral papilledema, and elevated CSF opening pressure. She was first treated with serial LP, which led to symptom deterioration, increased CSF pressure, and increased the retinal nerve fiber layer (RNFL) thickness. She was then successfully treated with acetazolamide and furosemide. Results: OCT showed reduction of RNFL thickness directly after LP with CSF removal, accompanied with reduced CSF pressure. Increased RNFL thickness accompanied with worsened headache, visual dysfunction, and increased CSF pressure was observed on the next day after LP. Less than 24 h after start of medication, the symptoms had reversed and RNFL thickness was reduced. The patient was symptom-free 2 weeks after starting on medical treatment. Papilledema had vanished on fundoscopy 6 weeks after the therapy, and RNFL thickness was normalized at 3 months of follow-up. Conclusion: This case provides evidence that OCT is an objective and sensitive tool to monitor papilledema and its response to therapy, and thereby important to help in correct clinical decision-making.

Keywords: rebound intracranial hypertension; papilledema; lumbar puncture; cerebrospinal fluid pressure; optical coherence tomography; retinal nerve fiber layer

1. Introduction

Papilledema refers to optic disc swelling caused only by elevated intracranial pressure (ICP) [1]. Acute elevated ICP with bilateral, symmetric papilledema is often linked to, e.g., intracranial space-occupying lesions, meningitis/encephalitis, cerebral venous sinus thrombosis, or idiopathic intracranial hypertension (IIH) [2]. Meningoencephalitis causes diffuse cerebral edema with increased production of cerebrospinal fluid (CSF) and/or decreased CSF absorption by the arachnoid granulations. Rapid development of high ICP with severe papilledema can lead to visual field defects and eventually to visual loss if not correctly treated in time. Currently used methods to monitor ICP require invasive processes [3]. Papilledema assessment is based on grading of findings seen on fundoscopy or fundus photography, which are semiquantitative, subjective, and not
sensitive enough [4], especially when used to monitor therapeutic effects [5]. Numerical quantitative models might be more accurate and sensitive to monitor papilledema [6].

Optical coherence tomography (OCT) provides direct in vivo real-time, noninvasive, sensitive measurements of the retina [7]. Examination with OCT does not need pupil dilation or direct eye contact. With the help of OCT, optic disc pathology can be demonstrated and monitored both qualitatively and quantitatively at few-micrometer levels [8].

In this paper, we report a patient with papilledema and high ICP secondary to meningocencephalitis who was monitored with OCT during the treatment. Carbonic anhydrase inhibitor combined with loop diuretics rapidly reversed the acute rebound intracranial hypertension (IH) secondary to lumbar puncture (LP) with CSF removal.

2. Case Report

A previously healthy 24-year-old obese (body mass index 32) Caucasian female was referred for neurological consultation due to a 10-day history of headache, nausea, and vomiting after fever for a couple days. These symptoms were accompanied by dizziness, blurred vision and intermittent diplopia for 4 days. The patient was confused and disoriented one day before the consultation. Physical and neurological examinations were normal except for bilateral severe papilledema with hemorrhages as revealed by fundus photography, Frisén grade 4–5 (Figure 1a). Brain CT and MRI with angiography were normal. OCT (SD-OCT, Cirrus 4000, Carl Zeiss Meditec, software version 6.5, CA, USA) showed thickened retinal nerve fiber layer (RNFL) in both eyes (right 469 µm, left 460 µm), and visual fields tested by Humphrey automated perimetry (faster SITA) were 96% in the right and 93% in the left eye (Figure 1a). CSF revealed pleocytosis with 57 mononuclear cells/µL. No pathogen was identified, including herpes viruses and tick-borne encephalitis virus. CSF opening pressure registered via LP was 37 cm H$_2$O. After removal of 10 mL CSF, the pressure dropped to 23 cm H$_2$O. Immediate reduction of RNFL thickness was registered: 20 µm reduction in the right eye and 30 µm in the left. Headache, nausea, and blurred vision were improved. Several hours later, the patient was awakened by intensified headache, double vision, and vomiting. Next day, OCT showed bilaterally increased RNFL thickness (right 497 µm, left 467 µm) (Figure 2). Due to intensified headache and persistent blurred vision, a second LP was performed one day after the first LP. CSF pressure was 36 cm H$_2$O, which dropped to 13 cm H$_2$O after removal of 10 mL CSF. Two days later, OCT revealed further thickened RNFL (right 507 µm, left 497 µm), and visual fields were getting worse (right 83%, left 87%) though fundus photography revealed Frisén grade 4–5 as before (Figure 1b). The symptoms were further worsening. The patient was treated the same day with carbonic anhydrase inhibitor (acetazolamide, 1 g daily) and loop diuretics (furosemide, 40 mg daily). On the next day, the symptoms were improved and RNFL thickness was markedly reduced (right 447 µm, left 470 µm) (Figure 1c), but papilledema remained at Frisén grade 4–5 as assessed by fundus photography (Figure 1c). The RNFL thickness continued to diminish during the course of the medical therapy, as shown by measurements on day 3 (right 407 µm, left 439 µm). Visual fields were improved and papilledema was still unchanged (Frisén grade 4–5) (Figure 1d). Continual reducing of RNFL thickness was observed at follow-up on days 12 and 14, as well as on weeks 4 and 6 (Figures 1e and 2). The patient was symptom-free at week 2 of treatment. Papilledema was reduced from Frisén grade 4–5 to grade 2 at week 6. Visual fields were normal, and RNFL remained slightly thickened (Figure 1e). The medications were then discontinued. At three-month follow-up, RNFL thickness was normal (Figure 2), and the patient had completely recovered.
Figure 1. Digital fundus photography (left) with corresponding OCT thickness map (center) and perimetry (right) showing changes in papilledema, retinal nerve fiber layer (RNFL) thickness, as well as visual field before and after LP followed by medical therapy. Fundus photography showed severe papilledema in both eyes with hemorrhages in (a–d) (Frisén grade 4–5), which were in regression to grade 2 in e. OCT, on the other hand, quantified and discriminated subtle changes of papilledema severity, which were associated with changes of visual field (a,b,d,e). RNFL thickness map is coded by red and yellow colors indicating thickness values.

Figure 2. Rebound RNFL thickening (µm) after LP reversed by medication under monitoring of OCT. RNFL thickness in both eyes was significantly thickened 1 day after first LP, and 2 days after second LP. RNFL thickness was remarkably reduced on days 1, 3, 12, and 14 and on week 4 during medical therapy. RNFL thickness was almost normalized on week 6 when the medication was discontinued. RNFL thickness was normal at three-month follow-up.
3. Discussion

Elevated ICP is the result of increased volume of the brain, CSF, and/or cerebral blood flow in the rigid inelastic cranium. As part of the brain white matter, the optic nerve is surrounded by CSF and enveloped in the meninges. Increased ICP is transmitted to the optic nerve sheath and thus interferes with the axonal flow to the ganglion cells, leading to neuronal dysfunction and injury. At first, elevated ICP causing papilledema provokes an enlargement of the blind spot, which is potentially reversible. If the high ICP is not treated in time, it can lead to irreversible damage to the optic disc with larger scotomas and visual loss [9]. CSF opening pressure measured by LP is a key diagnostic method that is instant with dynamic nature, but it is invasive and not risk-free [3]. As a therapeutic method, LP results in small benefit often followed by exacerbation in patients with idiopathic intracranial hypertension [10].

Our patient developed elevated ICP with severe papilledema. Meningoencephalitis was diagnosed based on the clinical manifestations and findings from the blood and CSF tests, with unknown pathogen. Elevated ICP registered after each LP in this patient was normalized directly after CSF removal. The clinical symptoms were improved simultaneously. OCT examination performed right after LP showed reduced RNFL thickness bilaterally. This improvement was short-lasting, less than 24 h, and was followed by exacerbated clinical symptoms, elevated ICP, increased RNFL thickness, and worsened visual fields. However, papilledema as revealed by fundus photography was unchanged in severity.

Prompt improvement was achieved by medical therapy using a combination of carbonic anhydrase inhibitors and loop diuretics. Improved clinical symptoms were accompanied by quickly reduced RNFL thickness and improved visual fields. The patient was symptom-free two weeks after start of therapy. RNFL thickness was normal at three-month follow-up.

In this case, RNFL thickness measured by OCT provided much more sensitive and accurately quantitative measurements regarding papilledema severity compared to fundus photography. Changes of papilledema severity measured by RNFL thickness were identified at micrometers level and took less than 24 h to be found using OCT. Changes of RNFL thickness correlated directly to changes of ICP, symptomatology, and visual function. It took several days to observe changes of papilledema using fundus photography. In our case, it hardly distinguished papilledema changes using fundoscopy when the change of RNFL thickness was within 100 µm. Moreover, findings of fundus photography were not parallel with clinical and visual findings and were not affected by CSF removal or ICP changes. In addition, assessment using fundoscopy is more subjective and experience- and time-demanding [11]. Therefore, the change of RNFL thickness, in this case, was an objective measure and directly related to ICP and reflected therapeutic effect, accurately and quickly.

In conclusion, through this case we illustrate that OCT provides an easy, quick, accurate, and noninvasive tool to monitor papilledema and therapeutic effect. It enables us to identify minimal changes of papilledema that may take days when funduscopy is applied. OCT may provide a complementary tool to make a quick and correct clinical decision in management of papilledema.

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