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Pre-perimetric Optic Neuropathy

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Abstract
We present a case of a 32-year-old male who came with the history of blurring of vision in both eyes. Diagnosed as a glaucoma suspect at another centre, he had a best corrected visual acuity (BCVA) of 20/20 in both eyes and there was no relative afferent pupillary defect (RAPD) in either eye. Intraocular pressure (IOP) was also normal in both eyes. Fundus examination revealed very subtle temporal pallor accompanied by reduced retinal nerve fibre layer (RNFL) striations in the papillomacular bundle (PMB) in both eyes. RNFL optical coherence tomography (OCT) demonstrated thinning of the RNFL in the temporal sector along with thinning of the ganglion cell complex (GCC) on the ganglion cell analysis, whilst his visual fields (24-2) were normal in both eyes. After all necessary laboratory investigations, a diagnosis of vitamin B12 and folate deficiency with nutritional optic neuropathy was made and appropriate management was initiated. Hence, diligent clinical evaluation along with a high level of suspicion goes a long way in diagnosing these almost sub clinical cases with pre-perimetric optic neuropathy and this can help to preserve vision and reverse changes in an otherwise preventable irreversible optic neuropathy.

Keywords: Pre-perimetric optic neuropathy, nutritional optic neuropathy, Vitamin B12 deficiency, Folate deficiency.

Introduction

The prevalence of Vitamin B12 deficiency in the west is estimated to be 6%-20%,[1] whereas studies in the Indian population have shown prevalence as high as 16 to 77%.[2] Causes are numerous ranging from dietary deficiency due to vegetarian diet in a majority of Indians, lack of intrinsic factor, malabsorption, drug interactions, excess alcohol consumption or even following certain gastro-intestinal surgeries.[3,4] The prevalence of optic neuropathy in vitamin B12 deficiency is around 1%[5] but considering the high prevalence rates as stated above, the absolute number of people affected would be significantly high, somewhat indicating the burden of the disease in the population. This miniscule amount of optic neuropathy could also suggest the huge amount of subclinical optic nerve damage, the submerged portion of the iceberg, which is yet to be diagnosed.

Case report

A 32-year-old-male presented with blurring of vision oculus uterque (OU), two months. Onset was insidious, painless and non-progressive. He was diagnosed elsewhere as a glaucoma suspect. There was

no history of head or ocular trauma or a family history of glaucoma/optic neuropathy or any history of use of steroids in any form. He did give a history of pulmonary tuberculosis two years back, for which he was treated with the standard two months of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol and four months of Isoniazid and Rifampicin. Occasional tingling and numbness in upper and lower limbs, along with recurrent mouth ulcers were other complaints cited. His appetite was normal (mixed diet) and he was a non-alcoholic and non-smoker.

On general examination, there was increased pigmentation of the knuckles. His best corrected visual acuity (BCVA) for distance was 20/20, and for near, N6 OU. Colour vision by Ishihara pseudo-isochromatic was 17/17 OU. Goldmann applanation tonometry (GAT) intraocular pressure (IOP) was 15mmHg oculus dexter (OD) and 16mmHg oculus sinister (OS). Gonioscopy revealed open angles OU. On stereoscopic examination of the fundus, both optic discs were average sized, with well-defined margins and cup disc ratio of 0.5:1. The salient findings were the subtle temporal pallor with reduction of retinal nerve fibre layer (RNFL) striations in the papillomacular bundle (PMB) OU (Figure 1 (A) and 1 (B)), more prominently seen with red-free filter (Figure 1(C) and 1(D). Visual fields were done on the Humphrey Field Analyzer, SITA-standard 24-2 (HFA,Model 720, Carl Zeiss Meditec, Dublin CA,USA), and they were unexpectedly normal (Figure 2 (A) and (B)). On optical coherence tomography RNFL (OCT-RNFL, Carl Zeiss Meditec,software version 6.0.2, Dublin, CA,USA) there was RNFL damage in the temporal sector, seen in the deviation map as red and yellow clusters (Figure 3 (A)). Quantitative measurements showed that the temporal neuro-retinal rim thickness was borderline in both eyes. More evidence of the significant temporal RNFL thinning was seen in the quadrant and clock hour map (Fig.3A). Ganglion cell analysis of OCT macula OU showed marked thinning of ganglion cell complex (GCC) (Figure 3 (B)). With these findings, a few blood investigations were ordered. The key findings were, a mean corpuscular volume (MCV)-91fl (79-93.3fl), a mean corpuscular hemoglobin (MCH)-32.5pg/cell (26.7-31.9pg/cell) and a mean corpuscular hemoglobin concentration (MCHC)-35.7g/dl (32.3-35.9g/dl) implying a megaloblastic picture. Serum vitamin B12-95pg/ml (211-911pg/ml), serum folic acid-5.73ng/ml (>6.59ng/ml) and serum homocysteine-41.12µmol/L (3.7-13.9µmol/L) suggested a vitamin B12 and folate deficiency with hyperhomocystenemia.

Parenteral Methylcobalamin was initiated (Injection Methylcobalamin 1500 µg intramuscular for 10 days, then weekly once for 10 weeks, then Tablet Methylcobalamin 750 µg for 2 months) along with folic acid (Tablet Folic acid 5mg once daily for 3 months).

Discussion

Key features of nutritional optic neuropathy (NON) include symmetric painless progressive visual impairment, loss of central visual acuity, dyschromatopsia, decreased contrast sensitivity, with the optic disc being normal or hyperaemic initially and in later stages temporal pallor, when atrophy sets in.[6] RNFL loss is typically in the PMB with central/centrocecal scotomas. RNFL thinning and a reduction in retinal ganglion cell layer (RGL) thickness, both seen on OCT can be helpful in diagnosis of toxic or nutritional optic neuropathy.[7] The greatest decrease in RGL thickness and volume occurs in the inferonasal quadrants, supporting early PMB impairment in its inferotemporal sector as seen in our case as well.[7]

Various patho-mechanisms have been proposed between vitamin B12, folic acid and optic neuropathy, the common factor in all being an increase in oxidative stress.[8] One of the mechanisms for vitamin B12, is the close relationship with homocysteine. It is required for the re-methylation of methionine, failing which there is increased homocysteine, leading to homocysteine induced toxicity (free radical

accumulation) of vascular endothelium.[9] Another mechanism for both vitamin B12 and folic acid, states that a build-up of formic acid causes a disarray in the electron transport chain which would ultimately lead to retardation of adenosine triphosphate (ATP) production and mitochondrial function.[10] The PMB would be the most susceptible to the above changes as the axons here have a high ATP demand.[8]

Toxic optic neuropathy due to the anti-tubercular therapy (ATT) was ruled out in our patient as his complaints were of recent onset, whilst his ATT was completed one and a half years back, visual acuity was maintained and there was no dyschromatopsia or visual field defects.[10] In ATT induced optic neuropathy the effect is linked to dose and duration of the treatment and usually reversible on halting the offending drug.[10]

Conclusion

What needs to be emphasized is the occurrence of OCT changes without any visual field changes, "pre perimetric optic neuropathy". It may be possible to reverse the condition if diagnosed at this stage rather than wait until a perimetric change is detected. Despite visual acuity being 20/20 and N6, patients' complaint of decrease in vision should not be disregarded. They may be complaining about decrease in contrast, field loss or colour vision and needs to be evaluated. Therefore, a high clinical suspicion needs to be maintained in cases of NON. Distinguishing it from glaucoma and other causes of optic neuropathy is of utmost importance. Meticulous fundus evaluation with special attention to the disc and PMB is required. OCT can quantify the thinning of RNFL therefore it can be used as an additional objective test to aid in diagnosis. Prompt diagnosis and simple treatment with vitamin supplementation can prevent sight threatening consequences and permanent optic nerve damage, as it is not an uncommon cause of nutritional optic neuropathy as previously thought.

Conflict of Interest: None for all authors

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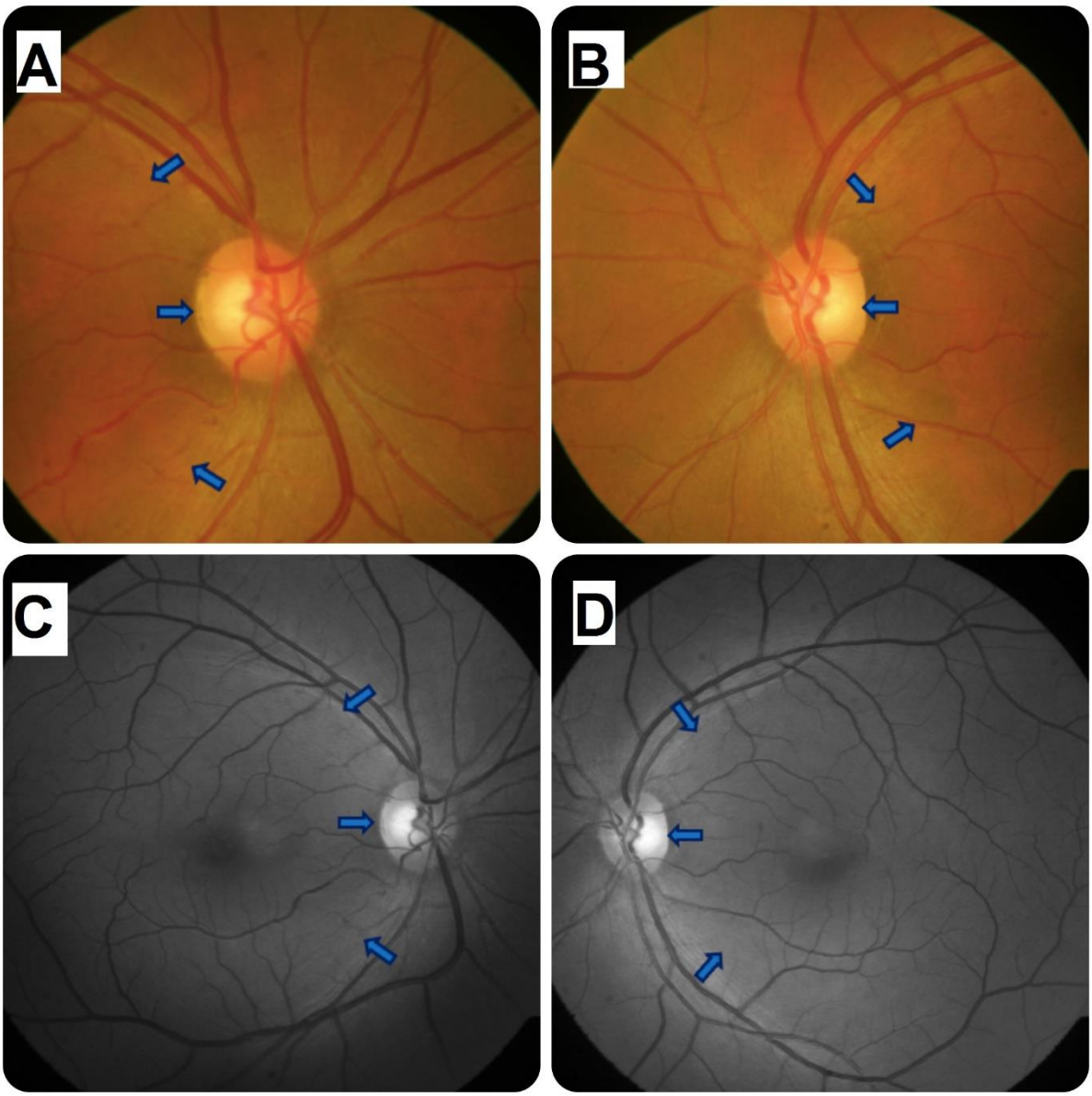
Legends for figures

Figure 1: Fundus photos of the patient (A) OD, (B) OS, showing the subtle temporal pallor with reduction of retinal nerve fibre layer (RNFL) striations in the papillomacular bundle (PMB), seen more prominently with red-free filter (C) OD, (D) OS as shown by the arrows.

Figure 2: Visual fields of the patient on SITA standard 24-2 program (A) OD, (B) OS.

Figure 3: (A) Retinal nerve fibre layer (RNFL) thickness analysis showing significant RNFL thinning in the quadrant and clock hour map. (B) Ganglion Cell analysis of OCT macula shows marked thinning of ganglion cell complex (GCC).



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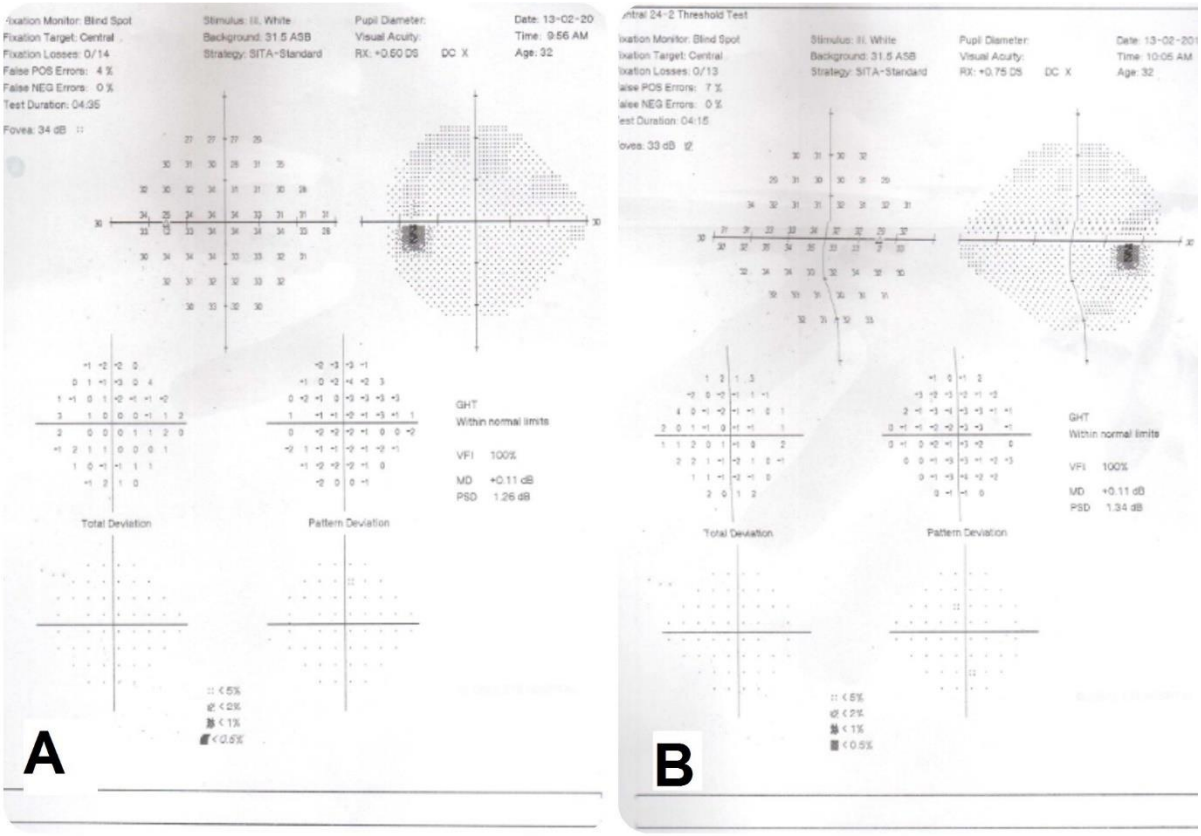

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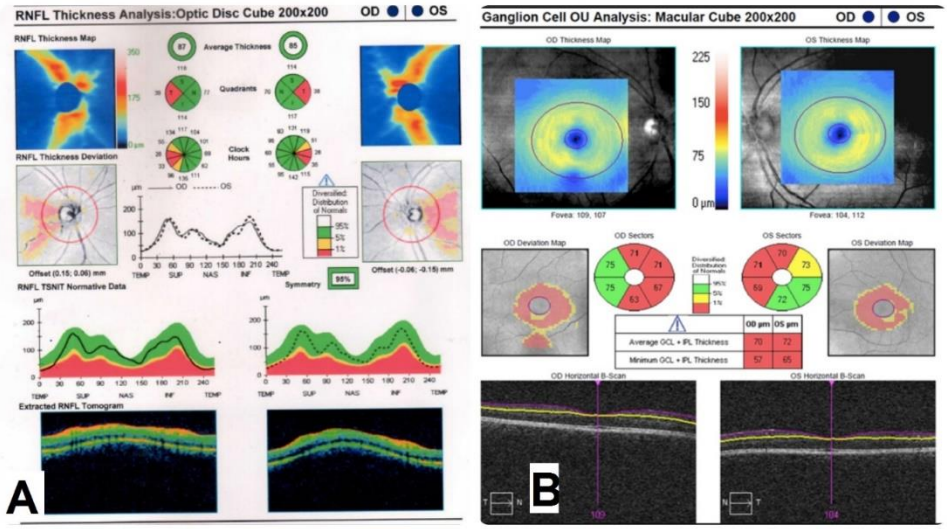

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