CASE REPORT

Infiltrative Optic Neuropathies: Opening Doors to Sinister Pathologies

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ABSTRACT

Optic disc edema may be caused by a number of conditions. A commonly ignored but important aspect is the presence of “infiltration” of disc; that may closely mimic disc edema. Disc edema, optic nerve dysfunction and a normal appearing disc in any combination may occur in infiltrative optic neuropathies. Identifying disc infiltration can aid in diagnosis of many sinister pathologies even in the absence of other specific clinical features. We describe two patients presenting with optic nerve dysfunction and infiltrated disc appearance, which on investigations were found to have underlying malignancies thereby underscoring the importance of detecting infiltrative optic neuropathies.

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Introduction

Optic disc oedema may be seen in a number of conditions; optic neuritis, increased intracranial pressure (ICP), ischaemic optic neuropathy, toxic and nutritional optic neuropathies are common aetiologies. A commonly ignored but important aspect is the presence of “infiltration” of disc, which may closely mimic disc oedema. Disc oedema, optic nerve dysfunction, and a normal-appearing disc in any combination may occur in infiltrative optic neuropathies.¹ The presence of optic nerve infiltration portends a nodular and irregular appearance to the disc. A yellowish white mass involving the disc with peripapillary haemorrhages may be seen. Identifying disc infiltration can aid in diagnosis of many sinister pathologies even in the absence of other specific clinical features.

We describe two patients presenting with optic nerve dysfunction and infiltrated disc appearance, which on investigations were found to have underlying malignancies, thereby underscoring the importance of detecting infiltrative optic neuropathies.

Case reports

Case 1

A 42-year-old male presented with history of bilateral gradually progressive painless loss of vision of 15 days duration. There was no history suggestive of recent febrile illness, connective tissue disease, or any focal neurological deficit. Systemic and neurological examination was normal. Visual acuity was no light perception in both eyes, and there was bilateral disc oedema with exudates and peripapillary haemorrhages (Figure 1a, b). Pupils were sluggishly reacting to light in both eyes. The ophthalmological examination including fundus fluorescein angiography was normal. Haemogram and metabolic panel were within normal limits. Gadolinium-enhanced magnetic resonance imaging (Gd-MRI) of the brain suggested features of increased intracranial pressure (posterior scleral flattening) with nodular enhancement of bilateral optic nerve sheaths (Figure 1c). Opening pressure of cerebrospinal fluid (CSF) on lumbar puncture was 260 mm of

Figure 1. (a, b) Disc oedema in both eyes with peripapillary haemorrhages and exudates. (c) T1-weighted contrast-enhanced MRI of the brain suggestive of nodular appearance of right optic nerve (red arrow) and posterior scleral flattening of left globe. (yellow arrow). (d) Contrast-enhanced CT of the abdomen depicting circumferential thickening of the anal canal with mass (blue arrow). (e) Biopsy of the supraclavicular lymph node demonstrates clusters of signet ring cells infiltrating the lymph node surrounded by pools of mucin (haematoxylin and eosin [H&E]; 200 $\times$). (f) Biopsy of the rectal mass showing sheets of signet ring cell filling up the lamina propria (H&E; 400 $\times$). (g) Periodic acid Schiff–Alcian blue (PAS-AB) stain highlights the intracellular mucin within the signet ring cells on rectal biopsy (PAS-AB; 400 $\times$).

H₂O. CSF was acellular, with raised protein (109 mg/dL) and sterile on cultures. Three consecutive CSF samples were acellular with normal CSF pressures (180 mm H₂O; 210 mm H₂O) and negative malignant cytology.

During the hospital course, the patient developed loose stools with tenesmus. On reviewing, patient history revealed suggestive of similar recurrent episodes of tenesmus with loose stools for past 2 years. A per-rectal examination was done, which revealed a circumferential mass 3 cm from

the anal verge with blood stain. Contrast-enhanced computed tomography (CT) of the chest and abdomen revealed localised area of mucosal circumferential soft tissue density in the rectal region with multiple mediastinal, left supraclavicular, and abdominal lymphadenopathy (Figure 1d). Biopsy of anal mass revealed a signet ring cell carcinoma (Figure 1f, g) with metastasis to left supraclavicular lymph node (Figure 1e). The temporal profile and the nodular appearance of the optic disc with exudates and haemorrhages strongly suggested

presence of optic nerve infiltration by malignant cells. Although increased intracranial pressure could have been contributory, the extent of vision loss and the optic disc appearance point towards optic nerve infiltration. Despite treatment with steroid pulse (methylprednisolone 1 g daily for 5 days), the patient showed no clinical response. The aetiology of bilateral vision loss was understood to be malignant optic nerve infiltration with probable meningeal carcinomatosis.

Case 2

A 32-year-old female was recently diagnosed with mixed connective tissue disorder in view of her complaints of malar skin rash, recurrent arthritis, and positive antinuclear antibodies (ANA 3+, speckled). She was initiated on treatment and after 2 months of starting immunomodulation presented with history of holocranial headache. CT of the head suggested the presence of a small pineal cyst 1.2×1.5 cm in size (Figure 2c), and Gd-MRI of the brain confirmed its presence (Figure 2d). The cyst was considered benign, and because it was not amenable for biopsy, the patient was advised close follow-up. Four months into her illness, she presented to the neuro-ophthalmology clinic with sequential painless loss of vision in right followed by left eye.

The patient could only appreciate hand motions close to face in the right eye and could only perceive light from her left eye. Both pupils were sluggishly reacting to light, with relative afferent pupillary defect in the left eye. Fundus examination revealed presence of disc oedema, with irregular appearance of optic disc along with peripapillary haemorrhages and exudates in both eyes (Figure 2a, b). Systemic examination was normal except for absence of deep tendon reflexes in bilateral lower limbs.

Metabolic panel and haemogram were normal. Repeat Gd-MRI of the brain showed normal optic nerves, and no interval change was noted in the pineal lesion. Opening pressure of CSF measured at two occasions was normal (17 and 15 cm H₂O), with a high protein level of 273 mg/dL and low sugar level of 20 mg/dL. The Gram stain, India ink, and cryptococcal antigen were negative, with ADA (adenosine deaminase) of 1.0 unit per liter. Bacterial culture, polymerase chain reaction

(PCR)-based assay for tuberculosis and pan-viral screening were negative. Two consecutive CSF samples for malignant cytology revealed clusters of small, round blue cells with moderately pleomorphic nuclei and scanty to moderate cytoplasm suggestive of malignant/metastatic cells (Figure 2h, 2i). MRI of the spine revealed presence of metastasis in the form of multiple enhancing nodular lesions along the cauda equina nerve roots (Figure 2e).

Whole-body ¹⁸F-FDG PET/CT ([¹⁸F]fludeoxyglucose positron emission tomography/computed tomography) revealed FDG-avid lesions in the pineal gland, with focal FDG-avid ill-defined densities in the spinal canal likely to be of metastatic origin (Figure 2e). The rest of the body (including optic nerves [Figure 2f, g]) showed normal FDG uptake. Tumours markers, including alpha-fetoprotein and human chorionic gonadotrophin (hCG), were also negative. A provisional diagnosis of pinealoblastoma with optic nerve infiltrates with drop metastasis in the spinal cord was made, and the patient was started on intravenous methylprednisolone and chemotherapy (vincristine, etoposide, and cisplatin). After completion of six cycles of chemotherapy, repeat PET scan showed no area of increased FDG uptake in either the brain or the spinal cord. At 8 months' follow-up, the patient is doing well with no headache. Her visual acuity improved to 6/18 in the right eye and 6/24 in the left eye.

Discussion

Presence of disc oedema with clinical features of increased intracranial pressure necessitates the need of ruling out an intracranial space-occupying lesion. If ruled out on neuroimaging, suspicion of infectious or inflammatory meningeal process must be kept. Carcinomatous meningitis remains a possibility in patients in which sudden severe vision loss is seen along with the infiltrated optic disc appearance. Direct involvement of the optic nerve with tumour cells must be considered in these patients. Both the patients discussed above were middle-aged individuals with a subacute history and almost complete vision loss at presentation. The optic nerve appearance suggested an infiltrative nature and prompted the investigation for metastatic disease. Intracranial or leptomeningeal metastatic spread is not commonly associated with

Figure 2 (a, b) Bilateral disc oedema with nodular and irregular disc margins, haemorrhages, and exudates. Non-contrast-enhanced (c) CT of the head and (d) T2-weighted MRI of the brain showing pineal space-occupying lesion (red arrow). (e) Whole-body ^{18}F -FDG PET/CT showing focally increased FDG uptake in ill-defined densities in the spinal canal extending from L1 to L5 vertebrae (SUVmax 8.3 at L3–L4 vertebrae) (yellow arrow). (f, g) ^{18}F -FDG PET/CT showing normal FDG uptake in both optic nerves. (h) Tight cluster of tumour cells in a background of blood (40 $\times$) and (i) tumour cells with high nuclear cytoplasmic ratio, opened-up chromatin, and one to two prominent nucleoli; occasional atypical mitotic figure (MGG; 100 $\times$) noted on CSF analysis.

gastrointestinal malignancies.^{2–4} Further, the optic nerve infiltration by these tumours is less common. Case 1 describes a distant spread of colorectal carcinoma presenting with infiltrating optic neuropathy.

Although meningeal metastasis contributing to increased intracranial pressure cannot be completely ruled out, the nodular appearance of the optic disc with exudates and haemorrhages strongly suggests

presence of optic nerve infiltration by malignant cells. Also, the temporal profile and extent of vision loss point towards optic nerve infiltration and not merely increased intracranial pressure

Pineoblastomas are characterised by aggressive clinical course with frequent metastases along the craniospinal axis.⁵ The most common route of metastasis is the dissemination of tumour cells via CSF; therefore, spinal drop metastases and leptomeningeal metastases are common.

Although pineal mass was identified in the second case, it was considered a benign pineal cyst until vision loss and the extensive disc involvement occurred. Identifying infiltrative optic disc pathologies may aid diagnosis of sinister aetiologies earlier in their course.

Conclusion

An “odd-looking” disc oedema should raise suspicion of infiltrative optic neuropathies. Infiltrative ocular neuropathy may provide early clues in

patients of malignancies, aiding prompt diagnosis and early management of these patients.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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