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Single Case – General Neurology

Acute HIV Infection Masquerading as Idiopathic Intracranial Hypertension: A Case Report and Literature Review

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Keywords
Raised intracranial pressure · Aseptic meningitis · Acellular CSF · Acute HIV infection · Idiopathic intracranial hypertension

Abstract
We describe a previously healthy 21-year-old man who presented acutely with signs and symptoms of raised intracranial pressure (ICP). Lumbar puncture yielded an elevated opening pressure and an acellular CSF analysis. Radiological images showed bilateral flattening of the posterior eye globes and an empty sella turcica. His serum HIV antigen/antibody was reactive. We provide a review of published cases that have been labeled as idiopathic intracranial hypertension (IIH) in HIV-infected patients, addressing the appropriateness of labeling such cases as truly idiopathic. We also discuss the importance of a thorough clinical evaluation of raised ICP in those who do not fulfil the typical IIH demographic.

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Introduction

Raised intracranial pressure (ICP) can occur at different stages of HIV infection, mostly arising in advanced stages attributed to opportunistic infections such as cryptococcus meningitis, tuberculosis, and syphilis or from neoplasms [1]. Elevation in ICP occurs much less frequently in early stages of illness during a lymphocytic meningitis acute HIV infection (AHI) [2]. On the other hand, idiopathic intracranial hypertension (IIH), sometimes referred to as "pseudotumor cerebri," is a condition where an unexplained elevation in ICP leads to headache, tinnitus, and papilledema. It is most commonly encountered in obese young women and can threaten visual function if left untreated [3]. Interestingly, there have been several reports of IIH developing in HIV-infected patients over the past few decades [4–6]. We aim to demonstrate and review with this case that prompt recognition of historical red flags and strict adherence to IIH criteria will help identify secondary causes of increased ICP not due to intracranial structural abnormalities. Second, the application of the terms "idiopathic intracranial hypertension," "pseudotumor cerebri," or "benign intracranial hypertension" might have been used more liberally in previous reports to describe HIV-infected patients who exhibited an increase in ICP. Using these terms, especially without specifying if the condition is primary or secondary, is misleading in the setting of an HIV-infected patient. Prompt recognition and early intervention are required in any condition leading to increased ICP, whether secondary or primary. Here, we report the discovery of AHI with aseptic meningitis in a patient who presented with raised ICP and an acellular CSF analysis.

Case Report

A 21-year-old gentleman with no prior medical illness presented to our emergency department with a 4-day history of holocephalic headache and severe bilateral eye pain, with binocular double vision, tinnitus, and nausea. He had had a recent upper respiratory tract infection following unprotected sexual intercourse 4 weeks prior to his presentation. Initial examination revealed a temperature of 37.0°C with normal vital signs and a body mass index of 26. Visual acuity was 20/60 OU and improved to 20/28.5 OD and 20/30 OS when measured with pinhole. Intraocular pressure was 16 mm Hg in both eyes, and fundoscopic examination showed bilateral grade III papilledema (Fig. 1a). There were no other cranial nerve deficits. Remaining motor and sensory neurological examination were normal. Complete blood count showed WBC 11.7 × 10^9/L with 6.3 × 10^9/L lymphocytes; creatinine and electrolytes were normal. A computed tomography scan of the brain with venogram showed an empty sella turcica and normal patent cerebral veins. A lumbar puncture (LP) revealed an opening pressure >55 cm H_2O and no WBC or RBC were detected. CSF protein concentration was 0.8 (normal 0.15–0.45 g/L). The CSF glucose level was 4.2 mmol/L (normal for the patient's serum blood sugar). CSF Gram stain, fungal stain, and acid-fast bacilli smears did not show any organisms, and CSF Cryptococcus antigen was negative; ultimately all cultures for bacteria, fungi, and tuberculosis had no growth. Polymerase chain reaction for herpes simplex virus and varicella zoster virus was not detected. Venereal Disease Research Laboratory and serum cryptococcal antigen were also negative. His autoimmune workup including antinuclear, anti-dsDNA, and anti-ENAS was negative.

A presumptive diagnosis of IIH was made, and while awaiting investigation results, therapy with acetazolamide 500 mg twice daily was started. Both his headache and diplopia had improved after the LP and acetazolamide therapy. Magnetic resonance imaging of the brain

and orbit and magnetic resonance angiography of cerebral vessels were all normal apart from the observation of an empty sella turcica and flattening of the globes. On the fifth day from presentation, his HIV antigen/antibody serology was reactive. His plasma viral load was 173,444 copies/mL. A second LP was performed on day 6 after admission due to worsening visual symptoms and the opening pressure was 48 cm H_2O. Similar to the previous tap, neither WBCs nor RBCs were detected. The glucose level was again normal at 4.01 mmol/L and protein was slightly lower at 0.56 (normal 0.15–0.45 g/L). Repeated microbiological studies were similarly negative. Repeat funduscopic examination showed worsening papilledema with hemorrhages and exudates (Fig. 1b). His visual field assessment revealed bilateral arcuate defects and an enlarged blind spot OS (Fig. 2a). As his headaches did not remit with worsening papilledema, acetazolamide was increased to 1,000 mg twice a day, and furosemide was added to his treatment regimen at a dose of 40 mg once daily.

His CD4 T lymphocyte count was 485 cells/mm^3, and antiretroviral therapy (ART) with a combination pill of efavirenz 600 mg, tenofovir disoproxil fumarate 300 mg, and emtricitabine 200 mg once daily was initiated. That same day, he reported worsening of his symptoms, and he underwent a third LP for CSF withdrawal to alleviate symptoms which still showed an acellular CSF with a protein level of 0.51 g/L. A lumbar drain was then placed with CSF output at 50 ml per day until a permanent ventriculoperitoneal shunt was surgically placed with no complications 18 days from his initial presentation. His headaches significantly improved and repeat neuro-ophthalmologic examination showed an improved corrected visual acuity of 20/20 bilaterally. His fundus examination showed significant improvement of previous edema (Fig. 1c) and his visual field test showed improvement in the inferior arcuate defect and size of blind spot OS (Fig. 2b). He continued to do well with no recurrences over subsequent months with a well-functioning shunt with decreasing viral load and improving CD4 levels.

Discussion

We present a patient diagnosed with intracranial hypertension due to AHI that initially had a clinical profile similar to that of IIH. Neurological manifestations of AHI appear to be widely varied. Aseptic meningitis, facial palsy, Guillain-Barré syndrome, and transverse myelitis are the most commonly reported neurological manifestations in AHI [1]. About 5–24% of HIV-infected patients may have meningitis during their seroconversion period [7, 8]. Aseptic meningitis in HIV is usually characterized by the presence of mononuclear cells and elevated protein in the CSF [9]. However, raised ICP, which is an entity commonly seen with bacterial meningitis, is not frequently reported in viral meningitis [10].

IIH is primarily a diagnosis of exclusion. Over the past decades, the criteria have been modified to incorporate more recent diagnostic modalities. The latest modified Dandy criteria, revised by Friedman et al. [3], specify the presence of papilledema, normal neurological examination apart from cranial nerve abnormalities, no radiological findings that could explain increased ICP, and normal composition of CSF with an elevated opening pressure measured by LP at ≥250 mm H_2O. Our patient demonstrated all these elements except that he did not exhibit an entirely normal CSF composition as the protein level was above normal [3, 11, 12]. More importantly, subsequent diagnosis of HIV added further evidence that there was a secondary cause for an increase in ICP due to the AHI, given there was no microbiological evidence for Cryptococcus meningitis, and his CD4 T lymphocyte count was >100 cells/mm^3. As

such, this presentation does not fulfil the criteria of IIH, and atypical presentation of an aseptic meningitis was a more likely diagnosis.

Raised ICP appears to be a rare early presentation of AHI. Two cases reported in 1997, in which intracranial hypertension was the first manifestation of an HIV infection [2], demonstrated a lymphocytic meningitis picture on CSF analysis. Another published case reported an HIV-infected patient who developed increased ICP with papilledema, albeit this was in a setting of Guillain-Barré syndrome with elevated CSF protein and lymphocytosis [4]. Furthermore, we identified additional published cases with increased ICP developing in patients infected with HIV in the absence of structural radiological findings or opportunistic infections [5, 6, 13–17]. Two cases were attributed to the use of co-trimoxazole [6, 13] and one was linked to amphotericin B [14]. One patient developed intracranial hypertension after initiating ART [15] and another one after developing anemia as a side effect of zidovudine-based ART [16]. On the other hand, no specific cause was identified in the remaining cases [5, 17]. The report by Traverso et al. [17] showed an acellular CSF, although this patient was known to have been HIV-infected prior to presentation. Among these reports only the patients described by Schwarz et al. [13] and Heudier et al. [14] had a normal CSF composition, and both of these conditions were thought to be related to drug use. The remaining had either incomplete reports on CSF composition, abnormal protein levels, or CSF pleocytosis, suggesting that a diagnosis of primary IIH could not have been established according to the criteria [3], and conditions were compatible with either a secondary type of increased ICP or an aseptic meningitis.

The importance of this case is highlighted by the severe increase in ICP that threatened the patient's vision and did not resolve until a shunt was placed. This aggressive increase in ICP with an acellular CSF should raise the possibility of an AHI in similar cases. Even mild elevations in CSF protein, as seen here, should argue against typical forms of IIH and should be taken as a red flag in order to investigate further for secondary causes of increased ICP. Our patient's symptoms did not remit with the use of acetazolamide [18] and furosemide; while resistance to diuretics can occur in some cases of IIH, it did raise a concern of a secondary etiology, in addition to the atypical demographic profile of the patient. Fortunately, he recovered well after ventriculoperitoneal shunt placement.

We emphasize that the development of increased ICP with no obvious etiology on brain imaging in a patient who does not follow the typical IIH demographic, in this case a non-obese male with no response to high-dose diuretics, requires further investigations to rule out secondary causes even if CSF analysis demonstrates an acellular picture with high opening pressure. Multiple CSF analyses might be required with careful inspection for lymphocytes or other cells. Even modest elevations in protein levels require further exploration. More importantly, a detailed history will usually reveal clues about the underlying process, as it did in our case, further emphasizing liberal universal testing for HIV infection.

Statement of Ethics

This work was conducted in accordance with the World Medical Association Declaration of Helsinki and ethical approval was received from the institutional review board at King Saud University. The patient was informed of the purpose of the case presentation and gave his written informed consent for publication of his case (including publication of images).

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Writing of the manuscript was primarily done by A.M. Alqahtani. Z.F. Al-Saaran aided in the case report writing and in interviewing the patient. M.H. Alanazy contributed in revising the manuscript, especially the section on neurological assessment. N.H. AlOtaibi, M. Barry, and K. AlJerian revised the final version and provided valuable contributions in their fields (infectious diseases and pathology). T.A. Muayqil aided in the writing of the manuscript and supervised the whole process of this report's production.

References

1 Hogan C, Wilkins E. Neurological complications in HIV. Clin Med (Lond). 2011 Dec;11(6):571–5.
2 Prevett MC, Plant GT. Intracranial hypertension and HIV associated meningoradiculitis. J Neurol Neurosurg Psychiatry. 1997 Apr;62(4):407–9.
3 Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology. 2013 Sep;81(13):1159–65.
4 Gross FJ, Mindel JS. Pseudotumor cerebri and Guillain-Barré syndrome associated with human immunodeficiency virus infection. Neurology. 1991 Nov;41(11):1845–6.
5 Le C, DeFreitas D. HIV-associated pseudotumor cerebri: a case report and literature review. AIDS Read. 2008 Dec;18(12):611–2.
6 Javeed N, Shaikh J, Jayaram S. Recurrent pseudotumor cerebri in an HIV-positive patient. AIDS. 1995 Jul; 9(7):817–9.
7 de Almeida SM, Nogueira MB, Raboni SM, Vidal LR. Laboratorial diagnosis of lymphocytic meningitis. Braz J Infect Dis. 2007 Oct;11(5):489–95.
8 Schacker T, Collier AC, Hughes J, Shea T, Corey L. Clinical and epidemiologic features of primary HIV infection. Ann Intern Med. 1996 Aug;125(4):257–64.
9 Atwood WJ, Berger JR, Kaderman R, Tornatore CS, Major EO. Human immunodeficiency virus type 1 infection of the brain. Clin Microbiol Rev. 1993 Oct;6(4):339–66.
10 Beal JC. Increased intracranial pressure in the setting of enterovirus and other viral meningitides. Neurol Res Int. 2017;2017:2854043.
11 Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. Neurology. 2002 Nov;59(10):1492–5.
12 Smith JL. Whence pseudotumor cerebri? J Clin Neuroophthalmol. 1985 Mar;5(1):55–6.
13 Schwarz S, Husstedt IW, Georgiadis D, Reichelt D, Zidek W. Benign intracranial hypertension in an HIV-infected patient: headache as the only presenting sign. AIDS. 1995 Jun;9(6):657–8.
14 Heudier P, Chichmanian RM, Taillan B, Gratecos N, Fuzibet JG, Dujardin P. Drug-induced benign intracranial hypertension. Apropos of a case with amphotericin B. Review of the literature. Therapie. 1992 Sep–Oct; 47(5):403–7. French.
15 Lisk DR, Cummings CC, Charles CC, Foley E, Ujah U. Rapid weight gain and benign intracranial hypertension in an AIDS patient on treatment with highly active anti-retroviral therapy (HAART). West Indian Med J. 2000 Dec;49(4):338–9.
16 Ananth JV, Sudharshan S, Selvakumar A, Devaleenal BJ, Kalaivani K, Biswas J. Idiopathic intracranial hypertension associated with anaemia, secondary to antiretroviral drug in a human immunodeficiency virus positive patient. Indian J Ophthalmol. 2018 Jan;66(1):168–9.

17 Traverso F, Stagnaro R, Fazio B. Benign intracranial hypertension associated with HIV infection. Eur Neurol. 1993;33(3):191–2.
18 Wall M, McDermott MP, Kieburtz KD, Corbett JJ, Feldon SE, Friedman DI, et al.; NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee. Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: the Idiopathic Intracranial Hypertension Treatment Trial. JAMA. 2014 Apr;311(16):1641–51.

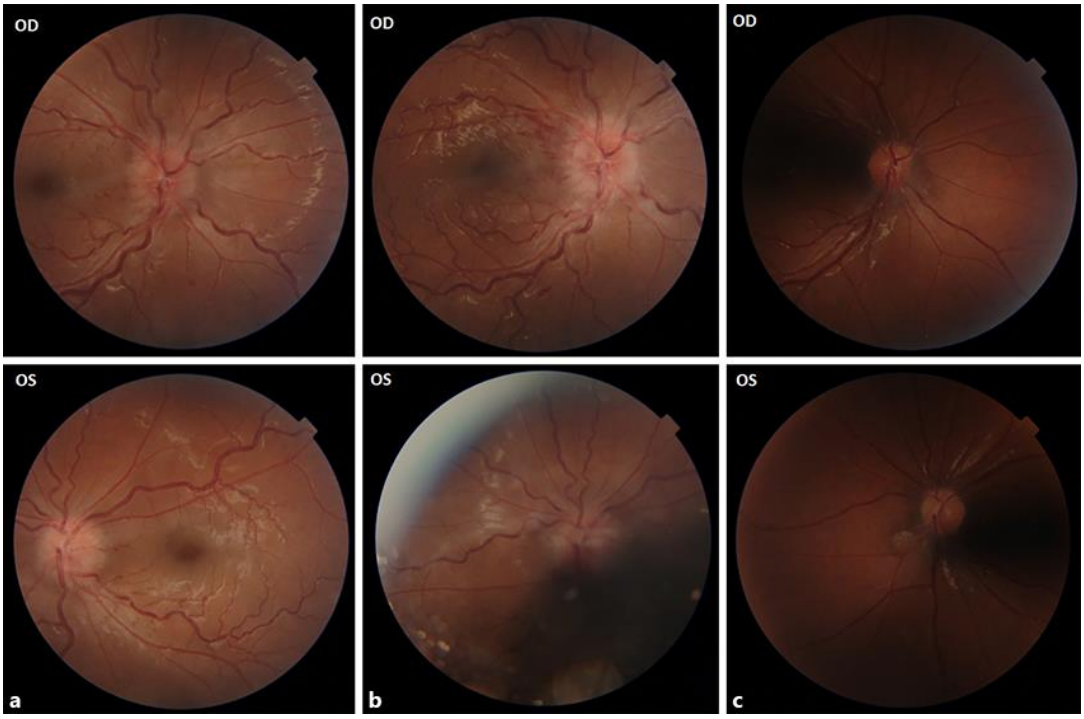

Fig. 1. **a** Fundus photographs at initial presentation: bilateral grade III papilledema. **b** Fundus examination revealed worsening papilledema with hemorrhages and exudates. **c** Fundus examination after ventriculoperitoneal shunt placement revealed improvement of previous edema.

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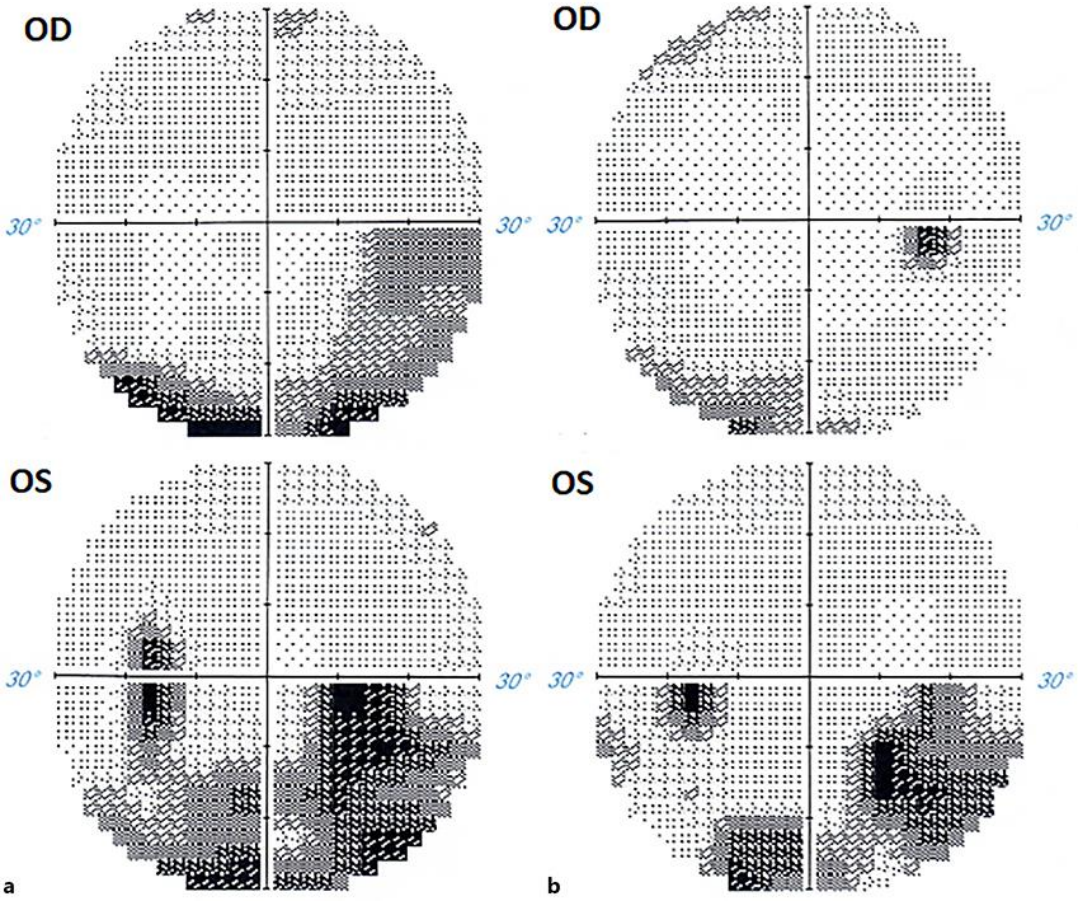

Fig. 2. **a** Visual field test showed bilateral inferior arcuate defects and enlarged blind spot OS. **b** Visual field test showed an improvement in the size of the blind spot OS and the inferior arcuate defect.