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Case Reports

An Unusual Case of Pyrexia with Blindness

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Abstract: Pyrexia is a common clinical problem; causes may vary depending on the clinico- epidemiological settings. Infectious diseases form the most common cause of fever especially in the immunocompromised category. The cause may not be obvious from the initial presentation and a stepwise workup is usually required. Potential diagnostic clues are very important in this regard. Our patient had a fever for 2 months and blindness for 1 month. The etiology of pyrexia with blindness can be linked to ophthalmic infections like viral, bacterial, parasitic, and fungal retinitis or micro vasculopathy (disease of small vessels) of retinal vessels or central nervous system causes like stroke, tuberculosis, toxoplasmosis, syphilis, and John Cunningham Virus infection. We report a case of a 60-year-old female who presented with complaints of fever, productive cough, burning micturition, and loss of vision. A stepwise workup was done in search of the causes of pyrexia with blindness. The serum was negative for toxoplasma and cytomegalovirus antibodies, the Venereal disease research laboratory test was negative, and the cerebral fluid CBNAAT for tuberculosis was negative. After the extensive workup, the patient was found reactive to Human Immunodeficiency Virus – 1 antibody, and her CD4 count was 66 only.

Keywords: Fever, Blindness, Immunocompromised, HIV

Introduction

Infections are the dominant cause of fever in the developing countries (Mulders-Manders *et al*., 2015). Among the causes of Fever of Unknown Origin (FUO), infections contribute to a maximum number of cases (Unger *et al*., 2016; Ryan, 2024). In the immunocompromised category like Human Immunodeficiency Virus (HIV) infection, opportunistic infections are the most common cause of fever though HIV itself can be a cause of fever in 40-90% of cases (De Munter *et al*., 2017). The etiology of blindness in HIV can be ocular or central. Ocular causes include infections involving the retina or cornea, retinal microangiopathy, and Kaposi sarcoma (Feroze and Wang, 2023). Central causes include infarction (ischemic necrosis) of the occipital lobe, infections like toxoplasma, John Cunningham Virus (JCV), syphilis, tuberculosis involving the brain parenchyma, and lymphoma of the central nervous system (Sarkar and Tripathy, 2023). We report an unusual case of pyrexia with blindness in a 60-year-old female.

Aim and Objective

We present an unusual case of pyrexia with blindness, illustrating the diagnostic challenges and clinical implications in an immunocompromised patient.

Case Description

A 60-year-old female who was a home-maker presented with complaints of continuous high-grade fever associated with chills documented up to 102ºF, chronic productive cough without hemoptysis, burning micturition associated with increased frequency and nocturia for 2 months and acute onset, painless progressive loss of vision without any complaints of floaters or flashes of light in both the eyes for 1 month (Fig. 1). No History Of (H/O) headache, sore throat, abdominal pain, joint pain, skin rash or any other comorbidities like diabetes mellitus, hypertension or previous H/O tuberculosis. No H/O multiple sexual partners, blood transfusions, or any substance abuse. Her husband died around five years back due to some respiratory illness.

On examination, she had pallor and Bilateral (B/L) pedal oedema. Chest auscultation showed B/L inspiratory crackles in the lower lobes. Neurological examination-sensory and motor examination is unremarkable. Deep tendon reflexes were normal. Cerebellar signs couldn't be assessed except for nystagmus which was absent. In the ocular examination, only perception of light was present, and ocular movements were normal. Fundoscopy and slit lamp examination was unremarkable.

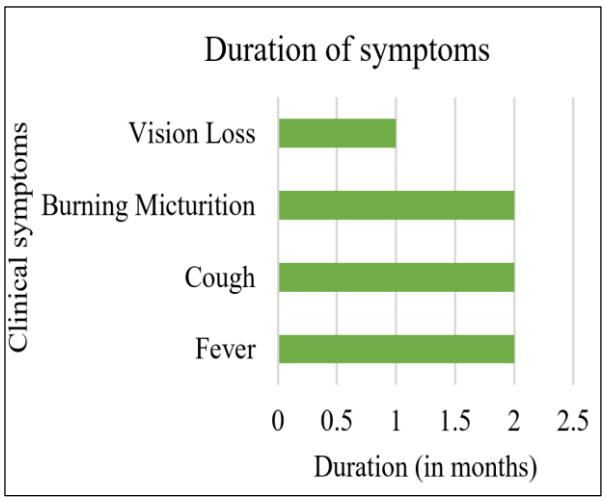

Fig. 1: Duration of symptoms

Laboratory investigations showed Hb- 8.7 g/dL, TLC- 5.6×10^3/µL, ESR- 35 mm in Ist h, Albumin-2.1 g/dL, urine microscopy showed 12-14 pus cells, urine culture was positive for *Escherichia coli* sensitive to Nitrofurantoin, Amikacin and Imipenem. Blood and Sputum cultures were sterile. CT thorax shows fibro-reticular parenchymal opacities in B/L lungs suggestive of pneumonia. Contrast MRI brain showed multiple ill-defined hyperintensities involving B/L fronto-parietal, temporo-occipital, and thalamic region on T2 and FLAIR images without diffusion restriction and enhancement (Fig. 2). No ring-enhanced lesions were seen on MRI brain. MRI of the spine didn't show any evidence of demyelination and Visual Evoked Potential (VEP) was also normal. B/L carotid artery Doppler is normal. Cerebrospinal Fluid (CSF) analysis showed 5 WBCs, no RBCs, Protein-59.8 mg/dl, Glucose -29.9 mg/dL, and Cl^- -97.7 mmol/L. CSF CBNAAT for tuberculosis was negative. The serum was negative for toxoplasma and cytomegalovirus antibodies. Venereal Disease Research Laboratory (VDRL) was also negative. She was found to be reactive to HIV-1 antibodies and her CD4 count was 66 cells/µL. Progressive Multifocal Leukoencephalopathy (PML) was suspected but RT-PCR for JCV in CSF couldn't be possible due to limited clinical setup. Taking into consideration the advanced clinical condition of the patient, a brain biopsy was not done.

A provisional diagnosis of PML secondary to AIDS was made on the basis of clinical and radiological findings after ruling out other causes. Anti-retroviral therapy (ART) was started. But the patient's condition deteriorated and she died in the following week.

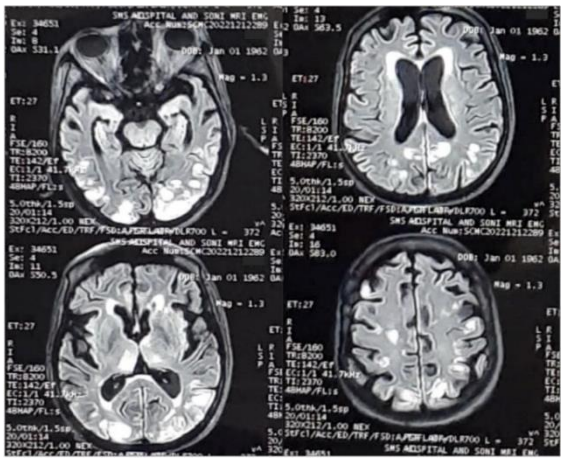

Fig. 2: FLAIR image showing PML lesions

Discussion

Nowadays, FUO requires a documented temperature of ≥101°F on multiple occasions without any identifiable cause after extensive diagnostic workup (Ryan, 2024). Infectious etiology remains the most common cause (Unger *et al*., 2016; Ryan, 2024). In our case also, the etiology was linked to multiple opportunistic infections like pneumonia, UTI, and encephalopathy in an immunocompromised host due to HIV. Pneumonia and UTI can be easily diagnosed but the workup for blindness was extensive and challenging. Negative history of floaters and flashes, slit lamp examination, and fundoscopy ruled out the ocular causes like CMV retinitis, toxoplasma retinochoroiditis (inflammation of retina and choroid), retinal microangiopathy (disease of small blood vessels) due to HIV (Feroze and Wang, 2023). Perimetry (measurement of light sensitivity in the visual field) could not be possible as the patient was left with a perception of light only. The differential diagnosis of central causes of blindness includes occipital lobe infarction, HIV encephalopathy, and opportunistic infections infecting the brain parenchyma like toxoplasma, tuberculosis, syphilis, cryptococcosis, JCV and Primary CNS Lymphoma (PCNSL) (Sarkar and Tripathy, 2023). The infarct can be easily diagnosed using diffusion-weighted images of the MRI brain. HIV encephalopathy generally presents with cognitive impairment and MRI brain shows diffuse and B/L cerebral atrophy with hyperintense areas in the periventricular white matter on T2 and FLAIR images and iso to low signal intensities on T1 images (Sakai *et al*., 2021). The diagnosis of CNS infections causing blindness was narrowed down by using a combination of CSF analysis, brain imaging, and serological tests. Among the opportunistic infections CNS cryptococcosis and tuberculosis present with meningitis or meningoencephalitis (Sakai *et al*., 2021).

PCNSL, toxoplasmosis, and PML present with focal brain lesions on the MRI. Brain lesions show peripheral ring enhancement and perilesional edema in the case of cerebral toxoplasmosis and the size of the lesion is >4 cm in PCNSL (Sakai *et al*., 2021). PML manifests as focal neurological deficits and the MRI shows typical lesions in brain areas which are hyperintense on T2 weighted and FLAIR images, and hypointense on T1 weighted sequences indicating white matter destruction (Sakai *et al*., 2021; Choudhary *et al*., 2018). PML was first described in 1958 and since then, it has been considered a cause of opportunistic infection in immunocompromised patients with HIV (Shishido-Hara, 2010). It is a rare and fatal neurological disorder due to the reactivation of polyoma JCV (Bernard-Valnet *et al*., 2021). The JCV infection occurs in healthy subjects and remains asymptomatic but once the patient gets immunosuppressed, the latent infection gets reactivated. It targets the oligodendrocytes and causes widespread demyelination and morphological changes in astrocytes (Snopková *et al*., 2019). A reduction in CD4 lymphocyte count to <200 cells/µL and a low CD4/CD8 ratio are the risk factors for PML in HIV-reactive patients (Badura *et al*., 2023). PML is the only known clinical manifestation of JCV (Choudhary *et al*., 2018). Its clinical features include cognitive dysfunction, motor deficits, visual disturbances, and seizures (Tan and Koralnik, 2010). Few case reports of PML presenting as blindness have been reported in the past (Jeyaraman *et al*., 2013; Finsterer *et al*., 2011). Diagnosis involves neuroimaging and JCV DNA can be demonstrated through PCR in CSF (Badura *et al*., 2023).

The PML cases are referred to as:

(i) Histology confirmed
(ii) Laboratory confirmed
(iii) Possible with the presence of typical clinical and radiological features but no demonstration of JCV (Choudhary *et al*., 2018)

No specific therapy is available for PML. The JCV infection can be eliminated by reconstituting the immunity (Snopková *et al*., 2019). Programmed cell Death –1 (PD-1) protein is expressed on CD4+ and CD8+ lymphocytes. Its expression is increased in PML. Pembrolizumab is an anti-PD1 immune checkpoint inhibitor and has been tried for the treatment of PML but has not been approved (Chatterjee *et al*., 2022). The 1-year survival rate has increased to 50% after the introduction of ART (Tan and Koralnik, 2010).

Conclusion

Our case illustrates the complex interplay between the fever and ophthalmic symptoms in an immunocompromised host. It highlights the challenges faced during the diagnosis of underlying causes of fever in the context of blindness. The diagnostic journey of such case scenarios requires a thorough understanding of the potential infectious agents in an immunocompromised host.

Future Recommendations

Healthcare providers should maintain a high index of suspicion for HIV and other immunocompromising conditions in patients presenting with prolonged fever and neurological or ophthalmological symptoms. Implementing routine screening for HIV in at-risk populations, along with a standardized protocol for the investigation of pyrexia with unusual presentations may facilitate earlier diagnosis and treatment.

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Author's Contributions

Naveen: Concept, manuscript preparation.
Bharat Bhushan Sharma: Manuscript edited and reviewed.
Annu Kumari Saw: Design, literature search.
Akash Paruthi: Intellectual content, literature search.

Ethics

The patient's medical team prescribed all of her medications.

Consent for Publication

Written consent was obtained from the patient for the publication of this report, in accordance with the journal's policy. Our institution does not require ethics approval for reporting individual cases.

Conflicts of Interest

The author declares no conflict of interest.

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