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A Rare Case of Ocular Syphilis with Syphilitic Cerebral Mycotic Aneurysm: A Case Report

Abstract – Infection of the central nervous system in a syphilis patient is known as neurosyphilis. Dire consequences can lead to both ocular morbidity and mortality. Due to the lack of specific symptoms associated with this disease, neurosyphilis poses a challenge to diagnosis. The management of syphilitic uveitis has remained controversial among physicians, as it is debatable whether ocular syphilis is a subtype of neurosyphilis. A 49-years-old male presented with two weeks history of sudden onset of painless, generalized blurring of vision of the left eye with a visual acuity of 6/6 over the right eye and 1/60 over the left eye. Slit lamp examination revealed a normal bilateral anterior segment however fundus examination of the left eye showed hyperemic and swollen optic discs with macula star. An infectious screening panel revealed a serum rapid plasma reagin (RPR) titre of 1:256 and raised erythrocyte sedimentation rate (ESR) of 88 mm/h. Leptospirosis, bartonella, toxoplasmosis and viral screening serologies were negative. Lumbar puncture was normal with negative CSF VDRL. Computed tomography angiography scan showed a fusiform aneurysm of the M2 segment of right middle cerebral artery (MCA). In keeping with the current examination findings, blood investigations and imaging test, the patient was diagnosed with ocular syphilis with syphilitic cerebral mycotic aneurysm and was treated with intravenous aqueous crystal penicillin G**.** Cerebral angiogram done after completion of antibiotics revealed resolved vascular malformation. Syphilis has the ability to mimic different ocular diseases, and this can lead to a misdiagnosis and also a delay in appropriate antimicrobial treatment.

Keywords – *Intracranial aneurysm, syphilis, neurosyphilis*

1 INTRODUCTION

Syphilis is a sexually transmitted disease (STD) caused by *Treponema pallidum,* a bacterium of the order of spirochetes, and human beings is the only host. There are four stages of syphilis which are primary, secondary, tertiary and latent syphilis (1). Latent syphilis is usually detected by serologic testing as patients do not manifest any symptoms and they are further classified as early latent syphilis, late latent syphilis or latent syphilis of unknown duration (2).

Ocular syphilis is known as the “Great Masquerader” as it has the potential to mimic a variety of ocular diseases, most commonly uveitis, chorioretinitis, retinitis, retinal vasculitis and interstitial keratitis among many others (3).

Ocular manifestations occur in about 0.6-2% of all patients with syphilis at any stage of disease (4). Study done by Vadboncoeur *et al*, showed that posterior uveitis (29%) was the most common presentation of ocular syphilis followed by anterior uveitis and panuveitis (5).

Mycotic aneurysms are localized, irreversible vascular dilatations caused by weakening and destruction of the vessel wall by an invasive organism such as treponema pallidum establishing an infective arteritis. It is associated with neurosyphilis and is rarely reported due to effective and prompt antibiotic therapy but is also potentially life threatening (6,7). Mycotic aneurysms were also found in 3–10% of patients with active infective endocarditis and also in drug abusers (8).

In 2015, Center for disease control and prevention (CDC) reported a 7.5 per 100,000 population of primary and secondary syphilis in the United States of America (9). In Malaysia, incidence rate of syphilis being only 5.7 per 100,000 population in 2012 but had increased to 8.0 per 100,000 population in 2017 (10,11). There has been a recent resurgence in cases of syphilis in the last few years and in 2018, the total reported cases of syphilis were the highest recorded worldwide since 1991 from 101,584 cases to 115,045 cases (12).

2 CASE REPORT

A 49-years-old male presented with two weeks history of sudden onset of painless, generalized blurring of vision of the left eye that was associated with intermittent floaters, glaring and reduced night vision. There was no fever, headache, vomiting, arthralgia or myalgia. He also had no symptoms of chronic cough, night sweats or tuberculosis contact. Otherwise, he denied any constitutional symptoms such as loss of appetite or loss of weight. He does not rare cats and never had a history of being scratched by a cat. He denied sexual promiscuity or drug usage. There were no oral or genital ulcers. There were no reddish spots over the palms and soles of his feet.

General evaluation showed a well-built gentleman with normal blood pressure and heart rate and no focal neurological deficits or meningeal signs.

Ocular examination demonstrated a visual acuity of 6/6 over the right eye and 1/60 over the left eye. Relative afferent pupillary defect (RAPD) was positive over the left eye with reduced light brightness and red saturation. Slit lamp biomicroscopy revealed a normal bilateral anterior segment with no features of granulomatous anterior uveitis. Fundus examination of the left eye showed hyperemic and swollen optic discs with macula star. However, there was no vitritis, retinitis, choroiditis or choroidal granulomas seen (Figure 1). The vessels were normal with no features of occlusive vasculitis. Fundus examination was unremarkable over the right eye. Confrontation visual field examination and bjerrum test revealed an enlarged blind spot over the left eye corresponding to the swollen optic disc. Intraocular pressure was 15 over both eyes (Figure 2).

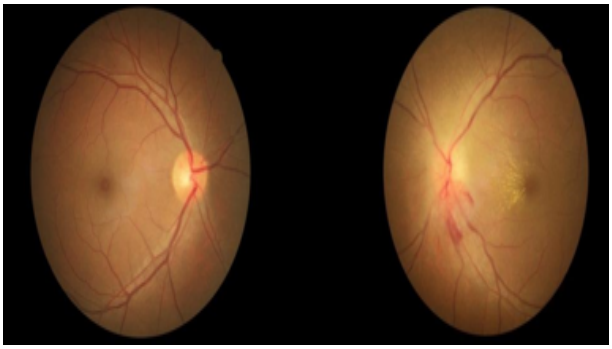

Figure 1. Left optic disc swelling with macula star and a normal right optic disc

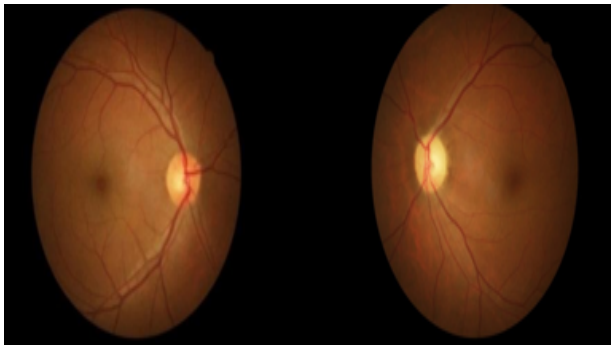

Figure 2. Palish left optic disc with complete resolution of the macula star after completion of antibiotics

A brain computed tomography scan showed prominent vascular calcification in the right sylvian fissure region with no focal enhancing brain parenchymal lesion (Figure 3). Subsequently a CTA/CTV revealed a fusiform aneurysm of the M2 segment of right middle cerebral artery (MCA). No aortic aneurysm was found on an echocardiogram.

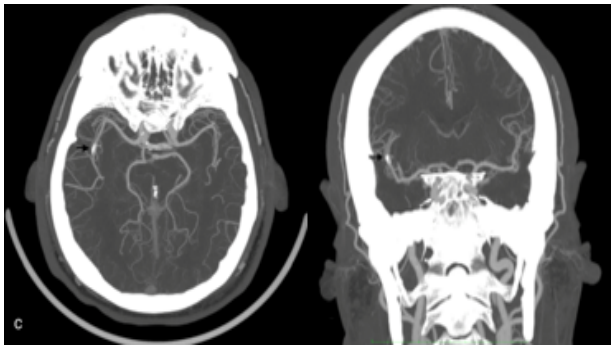

Figure 3. CTA Brain showing fusiform dilatation of the right M2 segment (arrow)

An infectious screening panel revealed a serum rapid plasma reagin (RPR) titre of 1:256. Other abnormal laboratory results included an elevated erythrocyte sedimentation rate (ESR) of 88 mm/h. Leptospirosis, bartonella, toxoplasmosis and viral screening serologies were negative. Lumbar puncture done with a normal opening pressure revealed crystalline liquor, no pleocytosis with protein and glucose at the normal range. However, his CSF VDRL results were negative. Bedside echocardiogram done was normal.

A diagnosis of ocular syphilis with cerebral syphilitic aneurysm was made based on clinical and imaging findings. He was co-managed with infectious disease (ID) team and was started on 24 million units (MU) of intravenous aqueous crystal penicillin G per day for 14 days. Subsequently oral prednisolone was started at a dose of 0.5mg/kg

(35 mg) per day for 1 week followed by a tapering dose of 10 mg weekly.

After a 14-day course of intravenous penicillin therapy, his vision improved to 6/18 (BCVA) OS and remained the same at last follow-up 6 months ago. A diagnostic cerebral angiogram done after completion of the antibiotics revealed resolved vascular malformation and a repeated serum RPR titre was 1:1 (Figure 4).

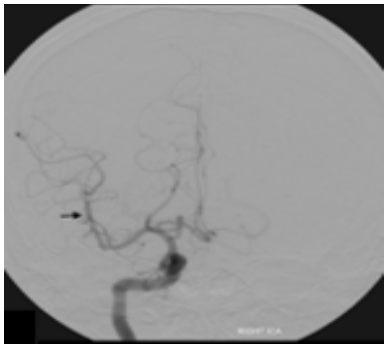

Figure 4. Right internal carotid artery angiogram showing dilatation of the right MCA (arrow)

3 DISCUSSION

Neurosyphilis is challenging to diagnose due to the variety of clinical signs and symptoms (13,14). The serological findings in this case are insufficient to diagnose neurosyphilis because the CSF study was normal. However, we cannot exclude neurosyphilis only with non-reactive CSF FTA-ABS tests as regressed activity of syphilitic infection may show sero-negativity. Instead, a clinical diagnosis can be made.

Syphilitic optic neuropathy is one of the late manifestations of syphilis and this is seen in our case report. Hence this explains his non-reactive CSF FTA-ABS as he presented to us during the latent stage of syphilis. It is rare to have syphilitic optic neuropathy as most cases present with either anterior or posterior uveitis (15). Optic nerve involvement in patients with syphilis can be either unilateral or bilateral and they can have variable presentations, such as anterior optic neuritis, retrobulbar optic neuritis, or optic perineuritis (15).

Treatment of syphilitic optic neuropathy is the same regimen as given in neurosyphilis, which is intravenous administration of benzyl penicillin 14.4 g (penicillin G 24 million IU) per day for 10–14 days. Corticosteroid treatment given as an adjunctive either in oral and intravenous forms has no proven benefit (16). However, in our case report, he was prescribed with oral prednisolone to decrease the optic nerve inflammation and disc edema.

Mycotic aneurysms are rare inflammatory neurovascular lesions that account for 0.7–6.5% of all intracranial aneurysms (17). According to Parkhurst GF et al, these aneurysms have a preference for the more peripheral branch points (M2 and beyond), especially in the distal middle cerebral artery in 50-70% of patients and are usually caused by infectious endocarditis (18). This can be seen in our patient as well who had fusiform dilatation of the right M2 segment. However, his echocardiogram did not reveal any vegetations thus ruling out infectious endocarditis as the source of infection.

Most common organism causing mycotic aneurysms today is *Staphylococcus aureus* (19). In aortic aneurysm, syphilis forms inflammatory infiltrate around the vasa vasorum of adventitia, followed by endarteritis obliterans leading to ischemic injury of the media thus destroying the smooth muscle and elastic tissue of the media. It is assumed that the development of intracranial syphilitic aneurysms would be similar (20).

Kannoth et al in his case series states that the diagnosis of infectious intracranial aneurysms can be challenging as patients can be asymptomatic just like our case report or present with subacute, nonspecific symptoms such as fever, headache, nausea, vomiting, chills, malaise, and minor focal deficits from intermittent shedding of septic emboli (21). To date, cases of intracranial syphilitic mycotic aneurysm has been rarely reported most probably due to their low probability of rupture, thus remaining asymptomatic (17). The mortality rate prior to rupture is 30% and increases to 80% with rupture (21,22).

Unruptured CMA may have a spontaneous obliteration in most cases (23). As antimicobial therapy may take effect for CMAs, conservative regimens are therefore preferred (24). Studies found that 30% of aneurysms disappear, 20% decrease in size, 15-30% have no significant change in size, and 20% actually increase in size (25–28). However, serial angiographic follow-up is required to assess efficacy of treatment on aneurysm size.

4 CONCLUSION

This report shows a rare case of CNS manifestation from syphilitic infection, presenting as intracranial aneurysms which were incidentally found when patient presented with features of syphilitic optic neuropathy. Cerebral mycotic aneurysm is rare but universally fatal without appropriate management. Diagnosis and surveillance remain clinically challenging, and CT

angiography is currently considered the modality of choice.

REFERENCES

[1] O'Byrne P, MacPherson P. Syphilis. BMJ. 2019 Jun 28;l4159.

[2] Workowski KA, Bachmann LH, Chan PA, Johnston CM, Muzny CA, Park I, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recommendations and Reports. 2021 Jul 23;70(4):1–187.

[3] Woolston SL, Dhanireddy S, Marrazzo J. Ocular Syphilis: a Clinical Review. Curr Infect Dis Rep. 2016 Nov 30;18(11):36.

[4] Teixeira AM, Meireles E, Fontes CP, Manuel M. Ocular Syphilis: A Case Report. Cureus. 2022 Mar 26;14(3).

[5] Vadboncoeur J, Labbé AC, Fortin C, Serhir B, Rabia Y, Najem K, et al. Ocular syphilis: case series (2000–2015) from 2 tertiary care centres in Montreal, Canada. Canadian Journal of Ophthalmology. 2020 Feb;55(1):30–7.

[6] Ielapi N, Caprino F, Malizia B, Sisinni A, Ssempijja L, Andreucci M, et al. Infection, Infectious Agents and Vascular Disease. Rev Recent Clin Trials. 2021 Jul 16;16(3):262–71.

[7] Carod Artal FJ. Clinical management of infectious cerebral vasculitides. Expert Rev Neurother. 2016 Feb 19;16(2):205–21.

[8] González I, Sarriá C, López J, Vilacosta I, San Román A, Olmos C, et al. Symptomatic Peripheral Mycotic Aneurysms Due to Infective Endocarditis. Medicine. 2014 Jan;93(1):42–52.

[9] Tsuboi M, Nishijima T, Yashiro S, Teruya K, Kikuchi Y, Katai N, et al. Prognosis of ocular syphilis in patients infected with HIV in the antiretroviral therapy era. Sex Transm Infect. 2016 Dec;92(8):605–10.

[10] Mansor N, Ahmad N, Rahman HA. Determinants of knowledge on sexually transmitted infections among students in public higher education institutions in Melaka state, Malaysia. PLoS One. 2020 Oct 29;15(10):e0240842.

[11] Zamli AK, Ngah NS, Chew-Ean T, Muhammed J, Hitam WH, Hussein A, Zunaina E. Clinical profile and visual outcomes of ocular syphilis: a five-year review in hospital Universiti Sains, Malaysia. Cureus. 2019 Feb 5;11(2).

[12] Tyagi M, Kaza H, Pathengay A, Agrawal H, Behera S, Lodha D, et al. Clinical manifestations and outcomes of ocular syphilis in Asian Indian population: Analysis of cases presenting to a tertiary referral center. Indian J Ophthalmol. 2020;68(9):1881.

[13] Boog GHP, Lopes JVZ, Mahler JV, Solti M, Kawahara LT, Teng AK, et al. Diagnostic tools for neurosyphilis: a systematic review. BMC Infect Dis. 2021 Dec 1;21(1).

[14] Abkur TM, Ahmed GS, Alfaki NO, O'Connor M. Neurosyphilis presenting with a stroke-like syndrome. BMJ Case Rep. 2015 Mar 4;2015.

[15] Puech C, Gennai S, Pavese P, Pelloux I, Maurin M, Romanet JP, et al. Ocular manifestations of syphilis: recent cases over a 2.5-year period. Graefe's Archive for Clinical and Experimental Ophthalmology. 2010 Nov 12;248(11):1623–9.

[16] Smith GT, Goldmeier D, Migdal C. Neurosyphilis with optic neuritis: An update. Vol. 82, Postgraduate Medical Journal. 2006. p. 36–9.

[17] Kannoth S, Thomas S v. Intracranial Microbial Aneurysm (Infectious Aneurysm): Current Options for Diagnosis and Management. Neurocrit Care. 2009 Aug 26;11(1):120–9.

[18] Revest M, Decaux O, Cazalets C, Verohye JP, Jégo P, Grosbois B. Aortites thoraciques infectieuses : implications microbiologiques, physiopathologiques et thérapeutiques. Rev Med Interne. 2007 Feb;28(2):108–15.

[19] Carvalho PMS, Mota JD, Dias PGD, da Mota AOC, de Moura JJA. Mycotic aneurysm of the femoral artery complicating Staphylococcus aureus bacteremia: A case report. Cases J. 2009 Dec;2(12).

[20] Tomey MI, Murthy VL, Beckman JA. Giant syphilitic aortic aneurysm: A case report and review of the literature. Vascular Medicine. 2011 Oct 15;16(5):360–4.

[21] Kannoth S, Iyer R, Thomas S v., Furtado S v., Rajesh BJ, Kesavadas C, et al. Intracranial infectious aneurysm: Presentation, management and outcome. J Neurol Sci. 2007 May;256(1–2):3–9.

[22] Wardlaw JM, White PM. The detection and management of unruptured intracranial aneurysms. Brain. 2000 Feb 1;123(2):205–21.

[23] Lucas JTM, Elhamdani S, Jeong SW, Yu A. Mycotic aneurysm presenting as subdural empyema: illustrative case. Journal of Neurosurgery: Case Lessons. 2022 Jan 24;3(4).

[24] Nakahara I, Taha MM, Higashi T, Iwamuro Y, Iwaasa M, Watanabe Y, et al. Different modalities of treatment of intracranial mycotic aneurysms: report of 4 cases. Surg Neurol. 2006 Oct;66(4):405–9.

[25] Peters PJ, Harrison T, Lennox JL. A dangerous dilemma: management of infectious intracranial aneurysms complicating endocarditis. Lancet Infect Dis. 2006 Nov;6(11):742–8.

[26] Zanaty M, Chalouhi N, Starke RM, Tjoumakaris S, Gonzalez LF, Hasan D, et al. Endovascular Treatment of Cerebral Mycotic Aneurysm: A Review of the Literature and Single Center Experience. Biomed Res Int. 2013;2013:1–8.

[27] Kuo I, Long T, Nguyen N, Chaudry B, Karp M, Sanossian N. Ruptured intracranial mycotic aneurysm in infective endocarditis: a natural history. Case reports in medicine. 2010 Oct;2010.

[28] Ducruet AF, Hickman ZL, Zacharia BE, Narula R, Grobelny BT, Gorski J, et al. Intracranial infectious aneurysms: a comprehensive review. Neurosurg Rev. 2010 Jan 16;33(1):37.