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Zakażenie pałeczką *Burkholderia pseudomallei*, rzadka manifestacja oczna – seria przypadków

Ocular *Burkholderia pseudomallei*, a rare variant in presentation – a case series

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Streszczenie

Burkholderia pseudomallei jest Gram-ujemną bakterią beztlenową wywołującą melioidozę. W artykule przedstawiono serię trzech przypadków rzadkiej prezentacji ocznej zakażenia *Burkholderia pseudomallei* u pacjentów z dodatnim wynikiem badania serologicznego w kierunku melioidozy w malezyjskim stanie Pahang. Pierwszy przypadek dotyczył 32-letniego mężczyzny, u którego nagle doszło do pogorszenia widzenia w lewym oku, bez towarzyszących dolegliwości bólowych. Pacjent w wywiadzie podawał pływanie w rzece. W badaniu okulistycznym ujawniono ropień w obrębie naczyniówki wraz z odwarstwieniem dolnej części siatkówki. Drugi przypadek dotyczył 14-letniego chłopca z bezbolesnym pogorszeniem widzenia w lewym oku oraz obrzękiem ślinianki przyusznej w wywiadzie. Badanie dna oka wykazało obrzęk tarczy nerwu wzrokowego i ognisko w plamce w kształcie gwiazdy. Trzeci opisany przypadek dotyczył 10-letniego chłopca z ziarniniakiem w obrębie tarczy nerwu wzrokowego oka lewego i częściowym wysiękowym odwarstwieniem siatkówki oraz zapaleniem naczyń. We wszystkich opisanych przypadkach wdrożono antybiotykoterapię (ceftazydym) z dobrym skutkiem. U każdego pacjenta z podejrzeniem zakaźnego zapalenia błony naczyniowej oka należy zawsze brać pod uwagę wariant oczny melioidozy. Wysokie prawdopodobieństwo takiego zakażenia wymaga wczesnej i odpowiedniej terapii.

Słowa kluczowe: melioidoza, *Burkholderia pseudomallei*, manifestacja oczna

Abstract

Burkholderia pseudomallei is Gram-negative anaerobe causing melioidosis. We report a case series including three cases of rare ocular presentations in patients with positive melioidosis serology in the state of Pahang, Malaysia. The first case involved a 32-year-old male with a sudden onset of painless decrease in vision in the left eye, with a history of swimming in a river. Eye examination revealed a choroidal abscess with inferior retinal detachment. The second case was that of a 14 year-old-male patient with painless reduction of vision in the left eye and a history of parotid gland swelling. Eye fundus examination showed optic disc swelling with macular star. The third case, a 10-year-old male, presented with left eye optic disc granuloma and subtotal exudative retinal detachment with vasculitis. The three cases were successfully treated with the antibiotic ceftazidime. Ocular melioidosis should always be taken into consideration in any patient with suspected infectious uveitis. A high index of suspicion is required to initiate early and prompt treatment.

Keywords: melioidosis, *Burkholderia pseudomallei*, ocular presentation

INTRODUCTION

Melioidosis is an infection caused by the Gram-negative bacillus *Burkholderia pseudomallei* (*B. pseudomallei*) which is an environmental saprophyte. It is endemic in tropical countries including Southeast Asia and Northern Australia[1–3].

The clinical manifestations vary from a latent infection to fulminant sepsis[4]. The infection usually causes a soft tissue abscess. Bacteraemic melioidosis carries poor prognosis, and septic shock is the main cause of mortality[5–7]. Ocular and periocular involvement rarely occurs. The most common presentation mimics orbital cellulitis, followed by endophthalmitis and necrotising fasciitis[5,8].

The aim of this report is to retrospectively describe three rare variant presentations of ocular melioidosis in the state of Pahang, Malaysia.

METHODS

This was a retrospective case series of patients with positive melioidosis serology. The patients presented to the Ophthalmology Clinic, Hospital Tengku Ampuan Afzan, Kuantan, Pahang, in 2018, and were diagnosed with ocular melioidosis.

We analysed the patients' demographic data, clinical presentations, examination results, imaging findings, anterior segment photos, and fundus photos.

RESULTS

Case 1

A 32-year-old male presented with a sudden onset of painless reduction of vision in his left eye. Two weeks prior to the onset of the symptoms, the patient went swimming in a river. His best corrected visual acuity (BCVA) was 6/6 OD, and hand movement OS. His left eye conjunctiva was minimally injected, with AC reaction of 4+ (Fig. 1 *A*) and severe vitritis. The result of right eye examination of the anterior and posterior segments were unremarkable. A B-scan of the left eye showed features of choroidal abscess with inferior retinal detachment (Fig. 1 *B*). The patient's full blood count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were normal. All infectious screenings were negative except for *B. pseudomallei* serology which came back positive with a titre of 1:640. He was treated empirically with intravenous ceftazidime 1 g bid for 2 weeks followed by oral trimethoprim-sulfamethoxazole (Bactrim) for another 6 weeks. He was referred to the vitreoretinal team for unresolved vitritis, but he refused surgery and subsequently defaulted his follow-up examination. At the last review, his left eye vision improved to 6/36.

Case 2

A 14-year-old male complained of painless decrease in vision in his left eye, with preceding history of parotid gland swelling. His visual acuity was 6/6 OD, and 6/36 OS. The results of anterior segment examination of both eyes were unremarkable. Dilated fundus examination of the left eye showed optic disc swelling with a macular star (Fig. 2 A). Optical coherence tomography (OCT) of the left macula showed some subretinal fluid collection (Fig. 2 B). Leptospira, toxoplasma and VDRL serologies were all non-reactive. The *B. pseudomallei* IgM serology was, however, positive with a titre of 1:640. Intravenous ceftazidime and oral prednisolone were empirically commenced, and followed by oral Bactrim. He responded well to treatment, and his latest vision during the clinic follow-up improved to 6/9, while the OCT macula showed resolved subretinal fluid collection (Fig. 2 C).

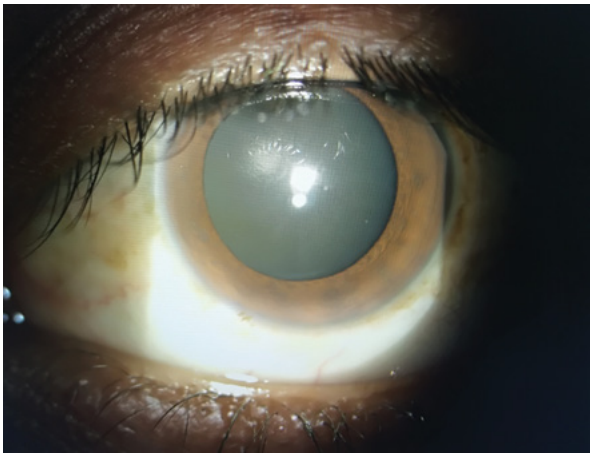

Fig. 1 A. Anterior segment of the left eye; very minimal conjunctival injection

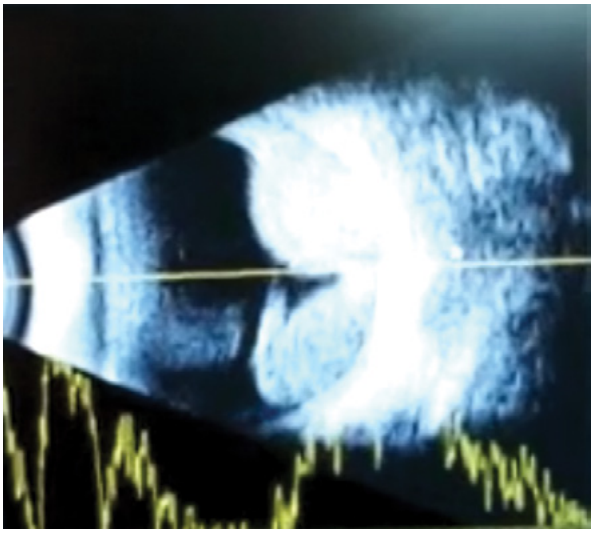

Fig. 1 B. B-scan of the left eye showing a well-defined dome-shaped lesion at the posterior pole, representing choroidal abscess, mimicking choroidal melanoma

Case 3

A 10-year-old boy presented with a sudden onset of painless blurring of vision in his left eye. His visual acuity was

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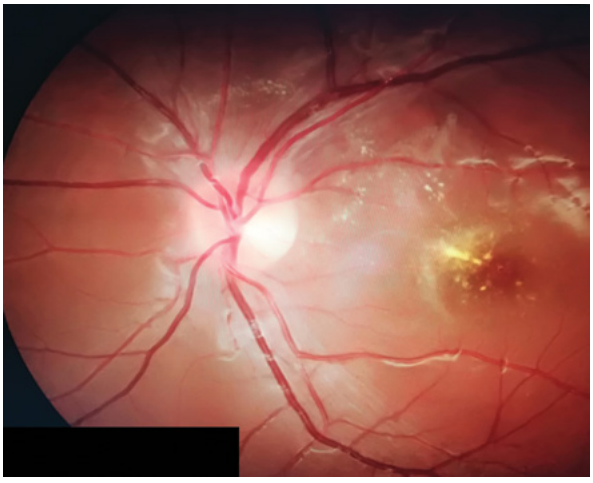

Fig. 2 A. Left eye fundus – blurred margin optic disc with partial macular striation

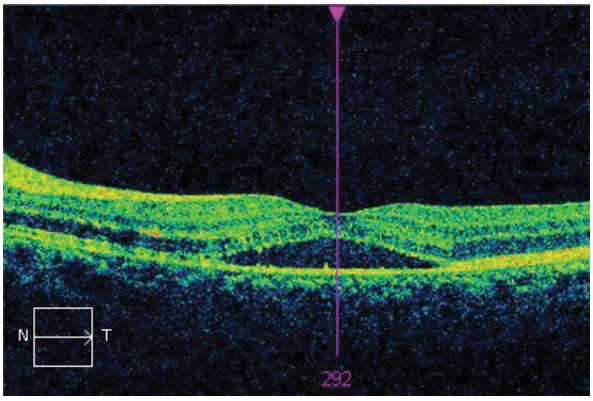

Fig. 2 B. OCT macula of the left eye at presentation

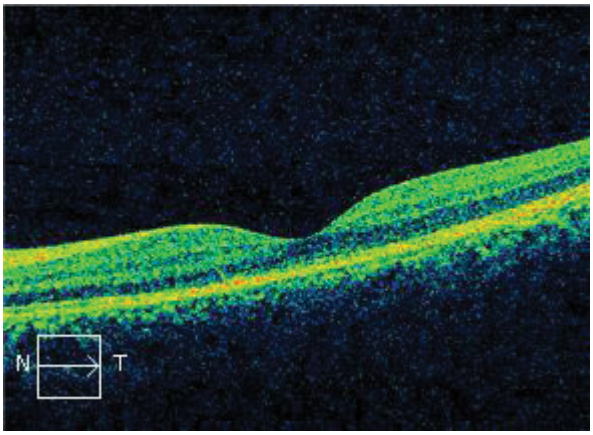

Fig. 2 C. OCT macula of the left eye post treatment at 3 months

6/6 OD and counting finger OS. The results of anterior segment examination were unremarkable in both eyes. The fundus of the left eye showed optic disc granuloma and inferior subtotal exudative retinal detachment with an area of vasculitis (Fig. 3 A). The OCT maculopapular bundle area of the left eye showed the presence of intraretinal fluid collection at the optic disc area, with vitreomacular traction (Fig. 3 C). His ESR and CRP were both significantly elevated. TB QuantiFERON and chest X-ray revealed no evidence of tuberculosis infection. However, the *B. pseudomallei* IgM serology was positive with a titre of 1:320. The patient was also successfully empirically treated with intravenous ceftazidime followed by oral azithromycin. His latest BCVA improved to 6/9, with the left fundus showing resolved optic disc granuloma and exudative retinal detachment after 4 months of treatment (Fig. 3 B). The OCT of the left macula showed resolved intraretinal fluid (Fig. 3 D).

DISCUSSION

Melioidosis is a severe disease caused by *B. pseudomallei* in which infection is acquired by inoculation, inhalation or ingestion[9]. It is endemic in Northern Australia and Southeast Asia, especially Thailand, which is referred to as the "capital of melioidosis" with an incidence of 3.6–5.5 cases per 100,000 per year[3,10].

As this pathogen is commonly found in water and soil, a history of contact must be elicited in a healthy individual; for example, swimming in a river[11] or involvement in an agricultural type of occupation[4]. The most common predisposing factors in the Malaysian setting are diabetes mellitus, chronic renal disease, and an immunocompromised state[4,12,13]. The mode of infection is mostly either by respiratory or direct cutaneous inoculation[8].

Systemically, fever is the commonest presentation associated with isolated pneumonia and followed by other multiorgan involvement[13]. Its clinical presentation can be acute, subacute or chronic[14,15]. Ocular manifestation varies, some located in the eye, presenting as various forms of uveitis in healthy individuals like in our cases mentioned above. Saonanon et al. revealed that periocular involvement is usually preceded by prolonged high-grade fever, and septicaemic illness[8].

Yaisawang et al. revealed from their retrospective review of clinical presentations that cases of ocular melioidosis were initially diagnosed as orbital cellulitis (44%), preseptal cellulitis (13%), endophthalmitis (25%), panophthalmitis (13%), and panuveitis (6%)[5]. Other rare incidences reported on ocular melioidosis include lid abscess, orbital abscess with subdural empyema, and cavernous sinus thrombosis[2,16].

Our case series presented as panuveitis with choroidal abscess (case 1), neuroretinitis (case 2), and posterior uveitis with optic disc granuloma and exudative retinal detachment (case 3).

The gold standard for the confirmation of diagnosis is by isolating *B. pseudomallei* species from clinical specimens[17,18]. As this organism is Gram-negative and oxidase-positive, it grows on blood agar and MacConkey agar[18]. Ashdown's medium containing gentamicin is a selective medium to isolate *B. pseudomallei* specifically[15].

Serological tests that are used include indirect haemagglutination assay (IHA), IgM and IgG enzyme-linked immunosorbent assay (ELISA), and indirect fluorescent antibody

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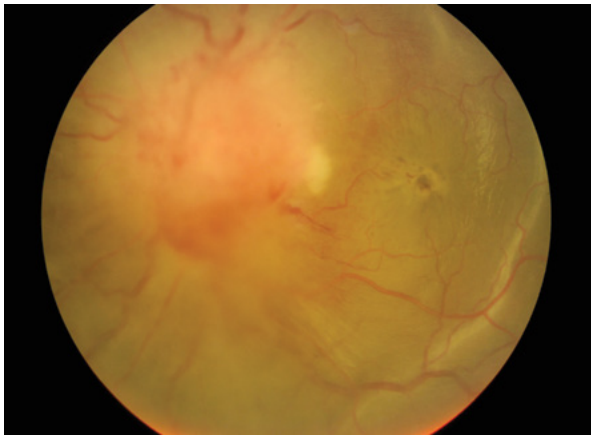

Fig. 3 A. Fundus photo; left eye optic disc granuloma with inferior exudative retinal detachment with vasculitic changes

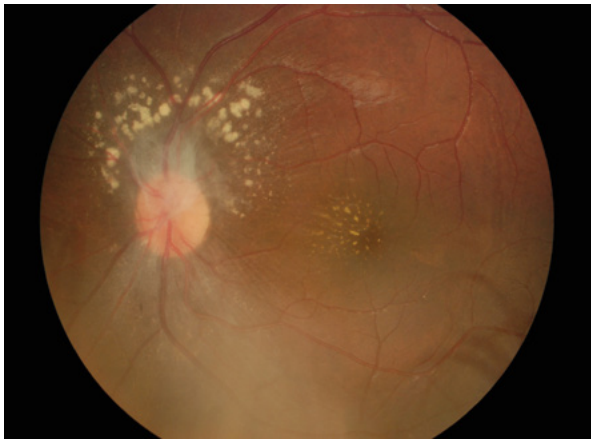

Fig. 3 B. Fundus photo; left eye after 4 months of treatment, showing the resolution of granuloma and exudative retinal detachment

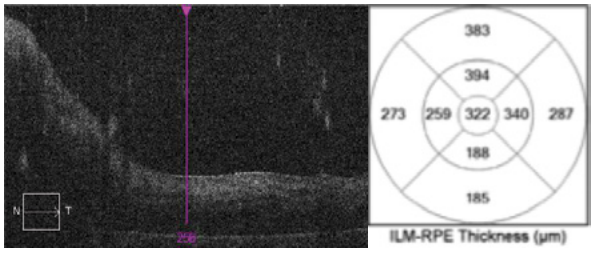

Fig. 3 C. OCT maculopapular bundle area of the left eye; presence of intraretinal fluid collection at the optic disc area with vitreomacular traction at presentation

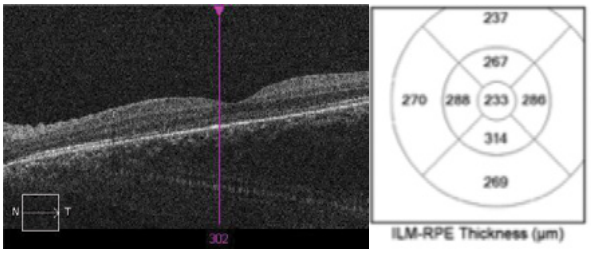

Fig. 3 D. OCT macula of the left eye; post-treatment image showing resolved intraretinal fluid

test (IFAT)[18]. Malaysia applies a titre of 1:80 as the determining value for IHA to indicate true infection[19]. However, other countries such as Thailand and Australia use a 1:160 titre and 1:40 titre, respectively, for the diagnostic sensitivity of melioidosis[20–22]. Recently, PCR amplification and gene sequencing; namely, groEL and MALDI-TOF MS have been used to achieve higher specificity and sensitivity which accelerate the confirmation of diagnosis[17]. However, in our cases, the diagnosis of ocular melioidosis was confirmed by ELISA IgM, which is 74% sensitive and 99% specific[23].

A standard regime for the treatment of melioidosis consists of an intensive phase of at least 10 to 14 days of intravenous ceftazidime, meropenem or imipenem, followed by oral eradication therapy, usually Bactrim for 3 to 6 months[14]. In Malaysia, Hassan et al. found in 2014 that out of 228 isolates of *B. pseudomallei*, 98.2% were sensitive to cefoperazone, 97.8% to ceftazidime, 95.2% to imipenem, 93.4% to chloramphenicol and 47.4% to Bactrim[24]. Our three local cases were successfully treated with intravenous ceftazidime followed by oral eradication therapy.

CONCLUSIONS

Ocular melioidosis comes with various presentations causing multiple incapacitating organ and ocular complications. Therefore, a high index of suspicion is required in order to initiate early and prompt treatment resulting in an excellent visual outcome.

Conflict of interest

The authors have no conflict of interest.

Piśmiennictwo

1. Royan J, Teo KSS, Hashim H: Variants of ocular meliodosis in Hospital Selayang. Eye South East Asia 2018; 13: 73–79.
2. Wadwekar B, Ninan RS, Bhat S et al.: Lid abscess: an unusual presentation of melioidosis. AMJ 2018; 11: 322–325.
3. Currie BJ, Dance DAB, Cheng AC: The global distribution of *Burkholderia pseudomallei* and melioidosis: an update. Trans R Soc Trop Med Hyg 2008; 102 Suppl 1: S1–S4.
4. Tipre M, Sathiakumar N, Kingsley PV et al.: Melioidosis in Malaysia: a review of case reports. PLoS Negl Trop Dis 2016; 10: e0005182.
5. Yaisawang S, Asawaphureekorn S, Chetchotisakd P et al.: Ocular involvement in melioidosis: a 23-year retrospective review. J Ophthalmic Inflamm Infect 2018; 8: 5.
6. Puthucheary SD, Parasakthi N, Lee MK: Septicaemic melioidosis: a review of 50 cases from Malaysia. Trans R Soc Trop Med Hyg 1992; 86: 683–685.
7. Trinh TT, Hoang TS, Tran DA et al.: A simple laboratory algorithm for diagnosis of melioidosis in resource-constrained areas: a study from north-central Vietnam. Clin Microbiol Infect 2018; 24: 84.e1–84.e4.
8. Saonanon P, Tirakunwichcha S, Chierakul W: Case report of orbital cellulitis and necrotizing fasciitis from melioidosis. Ophthalmic Plast Reconstr Surg 2013; 29: e81–e84.
9. Inglis TJJ, Merritt AJ: *Burkholderia pseudomallei* and *Burkholderia mallei*. In: Tang IW, Sussman M, Liu D et al. (eds.): Molecular Medical Microbiology. Vol. 2, Academic Press, 2015: 769–791.

DOI: 10.15557/PiMR.2020.0061

10. Suputtamongkol Y, Hall AJ, Dance DA et al.: The epidemiology of melioidosis in Ubon Ratchatani, northeast Thailand. Int J Epidemiol 1994; 23: 1082–1090.

11. Ahmad SS: Water related ocular diseases. Saudi J Ophthalmol 2018; 32: 227–233.

12. Yee KC, Lee MK, Chua CT et al.: Melioidosis, the great mimicker: a report of 10 cases from Malaysia. J Trop Med Hyg 1988; 91: 249–254.

13. How SH, Ng KH, Jamalludin AR et al.: Melioidosis in Pahang, Malaysia. Med J Malaysia 2005; 60: 606–613.

14. Joseph MM, Balingi, Menon J et al.: Clinical manifestations, diagnosis, and treatment of Melioidosis. IOSR J Pharm 2015; 5: 13–19.

15. Howe C, Sampath A, Spotnitz M: The pseudomallei group: a review. J Infect Dis 1971; 124: 598–606.

16. Kogilavaani J, Shatriah I, Regunath K et al.: Bilateral orbital abscesses with subdural empyema and cavernous sinus thrombosis due to melioidosis in a child. Asian Pac J Trop Dis 2014; 4 Suppl 2: S851–S853.

17. Kritsiriwuthinan K, Wajanarogana S, Choosang K et al.: Production and evaluation of recombinant *Burkholderia pseudomallei* GroEL and OmpA proteins for serodiagnosis of melioidosis. Acta Trop 2018; 178: 333–339.

18. Lau SK, Sridhar S, Ho CC et al.: Laboratory diagnosis of melioidosis: past, present and future. Exp Biol Med (Maywood) 2015; 240: 742–751.

19. Puthucheary SD: Melioidosis in Malaysia. Med J Malaysia 2009; 64: 266–274.

20. Cheng AC, Peacock SJ, Limmathurotsakul D et al.: Prospective evaluation of a rapid immunochromogenic cassette test for the diagnosis of melioidosis in northeast Thailand. Trans R Soc Trop Med Hyg 2006; 100: 64–67.

21. Wuthiekanun V, Pheaktra N, Putchhat H et al.: *Burkholderia pseudomallei* antibodies in children, Cambodia. Emerg Infect Dis 2008; 14: 301–303.

22. Cheng AC, O'Brien M, Freeman K et al.: Indirect hemagglutination assay in patients with melioidosis in northern Australia. Am J Trop Med Hyg 2006; 74: 330–334.

23. Chenthamarakshan V, Vadivelu J, Puthucheary SD: Detection of immunoglobulins M and G using culture filtrate antigen of *Burkholderia pseudomallei*. Diagn Microbiol Infect Dis 2001; 39: 1–7.

24. Hassan MR, Vijayalakshmi N, Pani SP et al.: Antimicrobial susceptibility patterns of *Burkholderia pseudomallei* among melioidosis cases in Kedah, Malaysia. Southeast Asian J Trop Med Public Health 2014; 45: 680–688.