A case report describing Candida albicans endophthalmitis demonstrated by 16S/18S microbiome sequencing

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Title:

A case report describing *Candida albicans* endophthalmitis demonstrated by 16S/18S microbiome sequencing

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Dear Editor,

We read with interest the letter '*Pathogenic causes and outcomes of endophtalmitis after vitreoretinal surgeries in Finland from 2009 to 2018'* by Loukovaara et al. (Loukovaara et al. 2020). They discuss the problems concerning identification of microorganisms in patients with endophtalmitis (EO) and also mention the future perspective of "…more sensitive modalities for causative pathogen detection including Next Generation Sequencing technique…" (NGS). In this letter we want to highlight the advantages of using NGS (16S/18S microbiome sequencing) as a supplement to culture in the identification of microorganisms. With this technique DNA from bacteria (16S), fungi and parasites (18S) can be used for identification of living and non-living microorganisms (Ring et al. 2017). The technique is already available as a standard method from Statens Serum Institute, Copenhagen, Denmark, for hospitals in Denmark.

Even though infectious EO is a rare condition, it is a serious ocular complication with potentially devastating visual outcomes. Normally, the microbiological diagnosis of EO is based on culture of bacteria or fungi. As others (Ramakrishnan et al. 2009; Melo et al. 2011), Loukovaara and colleagues (Loukovaara et al. 2020) only obtained a positive culture in a limited number of cases (52.9%). The low rate of positive cultures is probably due to the small sample volume, prior antibiotic treatment, insufficient culture techniques or a sterile inflammation.

We performed a quality assurance project regarding the identification of causative microorganisms with culture, supplemented with Sanger sequencing (Hartmeyer & Justesen 2010) in selected cases, compared to 16S/18S microbiome sequencing in all patients with EO. The project included two university hospitals in

Denmark for a period of one year. Vitreous samples were sent to Statens Serum Institute for 16S/18S amplicon-based microbiome sequencing (Ring et al. 2017). Fifteen patients were included and concordance between methods was evaluated to be observed in 13 cases (seven cases were without any microorganisms). In one of the discrepant cases, culture was negative, but *Staphylococcus aureus* was diagnosed with 16S/18S microbiome sequencing after anti-VEGF therapy. The other discrepant case is described below.

An immunocompromised patient with liver failure and a transjugular intrahepatic portosystemic shunt (TIPS) was admitted to hospital with a history of three weeks of blurred vision and a suspicion of retinal detachment. The examination at the hospital showed diffuse unilateral anterior and posterior segment inflammation with posterior synechiae, dense vitritis and blurry white retinal infiltrates (Figure 1), and fungal endophthalmitis was suspected. Acute vitrectomy was performed with injection of vancomycin, ceftazidime and amphotericin B. Culture and 16S Sanger sequencing of the vitreous sample were negative, but 16S/18S microbiome sequencing identified *Candida albicans*. The patient received intravitreal amphotericin B again and started oral treatment with fluconazole.

After one month and during fluconazole treatment the patient developed candidemia. A PET-CT demonstrated a possible site of infection in the thoracic spine (T12) and lumbar spine (L1). A biopsy showed *C. albicans*.

We cannot for sure determine whether the spine or possibly the TIPS was the main site of infection. The patient died two months later from several complications, but without 16S/18S microbiome sequencing, treatment would have been delayed significantly. The case demonstrates the value of 16S/18S microbiome sequencing and superiority to Sanger sequencing and should be considered in culture negative cases where infection with bacteria or fungi is suspected.

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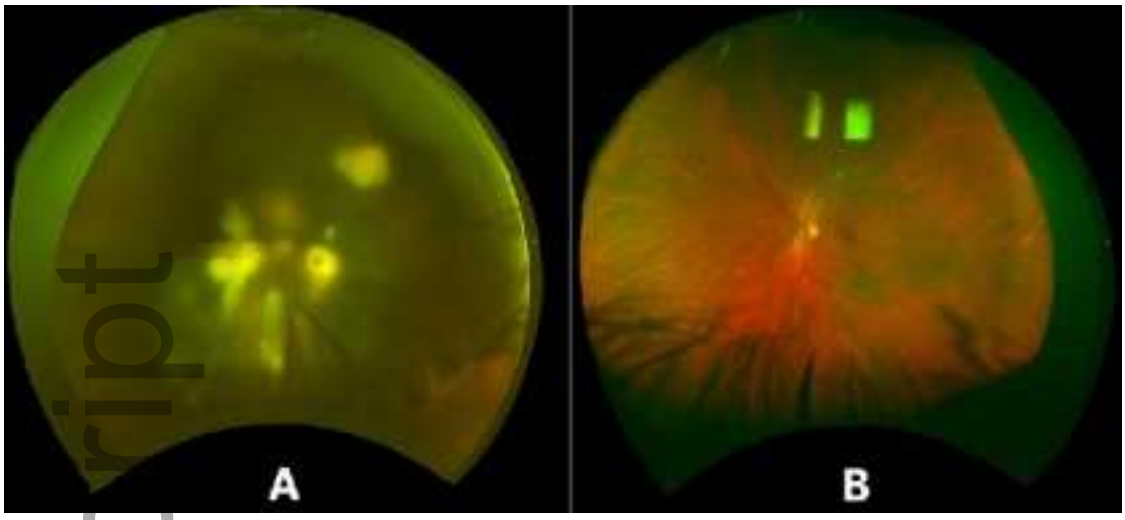
Figure 1. *Candida albicans* endophthalmitis. Bilateral fundus photography at the initial examination. (A) The right eye showed blurry white retinal infiltrates. (B) The left eye showed no abnormalities.



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