



Letters to the Editor

Mask use by patients in the context of COVID-19 can increase the risk of postinjection endophthalmitis

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Editor,

The close proximity puts ophthalmologists at particular risk for contracting COVID-19 from patients and vice versa. To reduce the risk of postinjection endophthalmitis (PIE), clinicians commonly wear masks when performing intravitreal injections (IVI). In the context of COVID-19, it may seem intuitive to extend this practice to include the patient wearing

a mask. However, observations raise the question as to whether patient masks could paradoxically increase the risk of PIE; masks can leak exhaled air towards the eyes and contaminate the injection site with aerosolized droplets (Hadayer et al. 2020; Raevis et al. 2021).

The suggestion that mask use by patients puts them in peril of PIE is alarming. Consequently, we have compared the risk of PIE at Oslo University Hospital (OUH) since the beginning of the COVID-19 pandemic with the pre-pandemic risk. We defined the pandemic period as March 1, 2020 through January 31, 2021. Mask use by patients was influenced by rules and recommendations from the Norwegian Institute of Public Health and the City of Oslo in particular and occurred sporadically until August. It then gradually became common, and ultimately a majority of our patients wore masks during the IVI procedure. In both the pre-pandemic and pandemic period, the IVI were generally performed ambulatory and took place in positive air pressure cleanrooms. Povidone iodine 5% was used as antiseptic (no antibiotic prophylaxis was used). The standard procedure was to drape the patient after the initial application of povidone iodine, but in the pandemic period clinicians temporarily chose to first drape patients not wearing a mask.

There were five cases of PIE of 68.150 IVI with compounded syringes at OUH in the pre-pandemic period (Blom et al. 2020). A total of 25 904 IVI were given in the pandemic period, 14 649 of these from August 2020 through January 2021. Seven

cases of PIE were identified, six of these after August 2020. Microbiological analyses were positive for pathogens in most of the cases; the bacteria all belonged to the microbiota of the skin and upper respiratory tract. Table 1 displays a summary of the PIE cases. The relative risk (RR) of PIE in the pandemic period compared to the pre-pandemic period was 3.68 (95% CI 1.17–11.60; $p = 0.026$). From August 2020 through January 2021, when mask use by patients gradually became common, the RR of PIE was 5.58 (95% CI 1.70–18.29; $p = 0.005$).

Our findings support the hypothesis that patient masks could redirect exhaled air towards the eyes and contaminate the injection site. Additional aspects may also contribute to an increased risk of PIE. First, the widespread use of masks by the general public has led to a new form of dry eye disease: mask-associated dry eye (MADE). A healthy tear film possesses antimicrobial properties, and air leakage from poorly fitting masks that dries the ocular surface may disrupt the eye's innate immunity and increase its susceptibility to infections (McDermott 2013). Second, a normal ocular microbiota helps prevent pathogenic species from colonizing the ocular surface (Petrillo et al. 2020). Regular mask use may alter the microbiota by contaminating the surface with microbes of higher pathogenic potential.

An increased RR notwithstanding, PIE remains a rare occurrence at OUH. The risk of contracting COVID-19, on the other hand, is still imminent. Accordingly, we do not encourage

Table 1. A summary of the postinjection endophthalmitis cases at Oslo University Hospital in the pre-pandemic and pandemic period.

Pre-pandemic period <i>n</i> = 68 150						Pandemic period <i>n</i> = 25 904					
Case	Age	Sex	Diagnosis	Drug	Pathogen	Case	Age	Sex	Diagnosis	Drug	Pathogen
1	76	M	nAMD	R	Unknown	1	88	F	nAMD	A	<i>S. aureus</i>
2	68	F	nAMD	B	<i>S. epidermidis</i>	2	91	F	nAMD	A	<i>S. epidermidis</i>
3	65	M	RVO	A	<i>S. epidermidis</i>	3	78	F	nAMD	B	<i>S. epidermidis</i>
4	82	M	nAMD	A	<i>S. epidermidis</i>	4	78	F	nAMD	A	<i>S. epidermidis</i>
5	68	F	nAMD	A	Unknown	5	85	F	nAMD	A	<i>S. aureus</i>
						6	89	F	RVO	A	<i>S. gordonii</i>
						7	82	F	RVO	B	Unknown

M, male; F, female; nAMD, neovascular age-related macular degeneration; RVO, retinal vein occlusion; *S. epidermidis*, *Staphylococcus epidermidis*; *S. aureus*, *Staphylococcus aureus*; *S. gordonii*, *Streptococcus gordonii*.

patients to stop using masks but instead advise clinicians to be vigilant about sealing the injection site and counsel patient about properly adjusting their masks and treatment for dry eyes. Ultimately, COVID-19 vaccination would mitigate the risk of transmission in the setting of IVI and allow for safe reimplementation of a procedure for which patients do not wear masks.

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Neovascular age-related macular degeneration inactivated during systemic administration of an immune checkpoint inhibitor pembrolizumab for lung cancer

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Editor,

It has long been known that the immune system is involved in the pathology of neovascular age-related macular degeneration (nAMD). Here, we report a case of nAMD resistance to regular intravitreal injection of vascular endothelial growth factor (VEGF) inhibitor, in which disease activity subsided following systemic administration of an immune checkpoint inhibitor for lung cancer.

A 77-year-old man presented with decreased vision in his left eye. The best-corrected visual acuity (BCVA) of the left eye was 20/32 and fundus examination revealed submacular haemorrhage. Optical coherence tomography (OCT) examination showed retinal pigment epithelium detachment (PED) involving the fovea (Fig. 1A, B). The patient was diagnosed with nAMD, and intravitreal injection of the VEGF inhibitor aflibercept was started. Although no obvious reduction in PED size was obtained during the induction phase, and we judged the patient to be a non-responder to VEGF inhibitor treatment, intravitreal injection of aflibercept was continued at regular intervals of 4 to 8 weeks. A total of 15 doses were administered for a period of 2 years, but the obvious reduction of PED size was not obtained, and BCVA decreased to 20/63 (Fig. 1C). Two years after starting treatment for nAMD, he was diagnosed with squamous cell carcinoma in the lung (Fig. 1D), and systemic therapy with

the immune checkpoint inhibitor, pembrolizumab, was initiated. Six weeks after starting therapy for lung cancer, he visited our hospital for scheduled intravitreal injection. Fundus examination of the affected eye showed that the PED, which had been resistant to treatment with VEGF inhibitor had decreased from 1.5 disc diameter (DD) to 0.5 DD. The exudative lesions in the fovea disappeared and BCVA improved to 20/40 (Fig. 1E). CT scan of the lung cancer at the same time also showed a marked reduction in tumour size (Fig. 1F). Treatment with pembrolizumab continued for one year during that his lung cancer did not progress and nAMD remained stable, despite no additional intravitreal injections of VEGF inhibitor.

Cancer escape from immune destruction has been associated with immunosuppressive mechanisms that inhibit T-cell activation by binding to programmed cell death protein 1 (PD-1), an immune checkpoint molecule on T cells. Pembrolizumab, an anti-PD-1 monoclonal antibody, is one of the immune checkpoint inhibitors that block PD-1 to promote T-cell activation, enabling the activated T cells to attack and diminish the cancer. This immune checkpoint inhibitor is used as a new therapeutic agent for advanced cancers.

Several types of immune cells have been reported to be involved in the pathophysiology of nAMD. CD8⁺ T cells have been found to be abundant in human eyes with drusen, and in eyes with advanced AMD and fibrovascular scarring (Ezzat et al. 2008). A study has shown that CD8⁺ T cells in the blood of nAMD patients express markers indicating accelerated ageing and T-cell differentiation (Subhi et al. 2017). In addition, CD8⁺ T cells have been reported to be involved in the reduction of experimental choroidal neovascularization in mice (Mochimaru et al. 2007). Our patient was a non-responder to VEGF inhibitor treatment. However, nAMD appeared to be inactivated shortly after receiving systemic immune checkpoint inhibitor for lung cancer. Activation and local invasion of CD8⁺ T cells associated with immune checkpoint blockade has been reported to be important for cancer regression (Tumeh et al. 2014). We speculate that treatment with an immune