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Letters to the Editor

Cancer is associated with a 2.7 higher risk for intravitreal injection therapy in patients with age-related, diabetic, or vascular occlusive macular edema

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Dear Editor,

Macular oedema (ME) is the final common pathway of various systemic diseases as well as intraocular conditions such as diabetic retinopathy, and venous occlusive disease. ME can also be a side effect of many local and systemic medications including anticancer agents.

Cancer-associated retinopathy (CAR) is a paraneoplastic syndrome, occurring in the setting of systemic malignancy (Shildkrot et al. 2011; Bussat et al. 2018). Traditionally, the most common primary tumour associated with CAR has been a small cell carcinoma of the lung or melanoma. Exact pathogenesis of CAR is unknown, antibodies are directed against retinal antigens. Sometimes CAR can be associated with ME without leakage (Rahman et al.2013).

Our study population consisted of 9135 eyes with ME that were treated with intravitreal anti-VEGF and/or cortisone injections due to age-related macular degeneration (AMD) (50.7%), diabetic maculopathy (13.8%), vascular occlusion (10.5%), or other ophthalmic reason (25%) in Finland between January 1st 2010 and December 31st 2017. Altogether, 5109 (55.9 %) of the patients were female, and 3005 (32.9%) were older than 80 years. Of the patients 54.6% used statin treatment, 24.4% used insulin, and 29.3% used oral antidiabetic drug (OAD).

Noteworthy, 2.6% of these ophthalmic patients had been diagnosed with cancer in 5 years before operation: 21 (0.2%) had colon cancer, 20 (0.2%) had melanoma, 46 (0.5%) had other skin cancer, 68 (0.7%) had breast cancer, and 90 (1.0%) had prostate cancer.

After adjusting for age, chronic diseases, systemic medication (insulin, OAD, statin) and years after cancer diagnosis, we found that three years after the original cancer diagnosis with Poisson regression, there was a 2.7 times higher risk for intravitreal injection for ME in the eyes of cancer patients as compared with controls (Incidence Rate Ratio (IRR) 2.7, 95% CI 2.15–3.33).

Cancer (colon, melanoma, breast, prostate) seems to associate with a statistically significantly increased risk of intravitreal injection for ME in patients suffering from various macular diseases. Pathogenesis of DME, AMD, and vascular occlusion with macular leakage together with cancer comorbidity (potentially even with CAR-related ME without leakage) is complex, but generally poorly understood and less studied. However, ophthalmologists need to take this complexity of ME pathogenesis into account while treating elderly patients with complex systemic diseases.

Generally, response to therapeutic intervention in ME eyes is variable (Grewal et al. 2014). Numerous immune-modulatory local treatments with repeated or sustained-release intravitreal corticosteroid agents and implants as well as anti-VEGF can be used to treat ME. These local treatments can be combined with systemic intravenous immunoglobulin therapy to improve visual prognosis in cancer patients (Cao & Cao 2010; Ramos-Ruperto 2019; Kim. et al 2019).

We wish to increase awareness of combined systemic disease, cancer and ophthalmic ME, and to encourage further studies.

Ethics

This is a register-based study without patient contact. The study was approved by the ethics committees of the Hjelt Institute, University of Helsinki, and the Hospital District of Helsinki and Uusimaa, Helsinki, Finland.

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