Targeted (biological) therapy in ophthalmology

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The use of targeted/biological therapy in ophthalmology

Indications:

- neovascular (Wet) Age-Related Macular Degeneration (AMD)
- macular edema following Retinal Vein Occlusion (RVO)
- diabetic macular edema (DME) and diabetic retinopathy
- neovascular glaucoma

Pathogenesis:

- dysregulated neovascularisation -> irreversible damage (blindness)

- newly formed blood vessels formed from retinal blood vessels cause ocular vitreous hemorrhage -> conversion to retinal detachment

AMD



-in developed countries a major cause of vision loss in the elderly





"Dry" Mac Degenerat

Wet AMD (10% of patients) → new blood vessels grow into the space between the retinal pigment epithelium or rods and cones, retinal bleeding, swelling and scarring in the macular region

Dry AMD (90 % of patients) → gradual loss of central vision, peripheral vision is preserved

The use of targeted/biological therapy in ophthalmology used primarily substances with antiangiogenic activity (ie.

- used primarily substances with *antiangiogenic activity* (ie block of neovascularization)
- most importance for the process of angiogenesis , VEGF = vascular endothelial growth factor
 - important physiological functions
 - located on the lining of blood and lymph vessels in the body
 - regulates the proliferation and vascular permeability
- several types (A E)
 drugs used
 - monoclonal antibodies (bevacizumab, ranibizumab)
 - small drugs (pegaptanib, vertepofin)
 - aflibercept= fusion protein

The use of targeted/biological therapy in ophthalmology

- intravitreal administration
- therapy usually takes a year or more
- advantages: fewer adverse systemic effects of drugs
- cons: clogging, intraocular infection, atrophy of the retinal pigment sheet, haemophthalmus..



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 Bevacizumab - was developed for the treatment of colorectal cancer, indication AMD is used off-label

 MA : monoclonal antibody against VEGF (binds VEGF1 and VEGF2 , blocks the interaction of DP.)

AE: acceleration of hypertension, proteinuria, thromboembolic events, poor wound healing...

- ranibizumab
 - Indications : AMD , CNV (chorioidal neovascularization)
 - MA : fragment of a monoclonal antibody against VEGF A
 - short plasma half-life
 - Administration 1x per month until the patient's visual acuity is stable (three consecutive monthly assessments)

- pegaptanib synthetic oligonucleotide
- inactivation of the extracellular vascular endothelial growth factor (VEGF165), specific binding
- VEGF165 is responsible for angiogenesis, increased vascular permeability and other inflammatory changes that play a role in the wet form of AMD
- I: therapy of the wet form of AMD
- Cl: eye infection, allergy
- intravitreal drug administration: 0,3 mg pegaptanib (i.e. 90 microliters) (9x per year)
- · aseptic conditions, with a local anaesthetic and an ATB

The use of targeted/biological therapy in ophthalmology

- verteporfin synthetic benzoporphyrin derivative
- photosensitizer for photodynamic therapy to eliminate abnormal blood vessels in the eye (blockage and local damage to the endothelium)
- accumulation in the abnormal blood vessels
- production of highly reactive oxygen radicals when stimulated by nonthermal red light (wavelength of 689nm) in the presence of oxygen
- I: therapy of the wet form of macular degeneration (AMD)
 - also for the therapy of secondary subfoveolar chorioidal neovascularisation in pathologic myopia

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- aflibercept recombinant fusion protein composed of the extracellular domen of the human (vascular endothelial growth factor) VEGF receptor 1+ 2 fusioned with the Fc fragment of the human Ig G1
- as a false soluble "decoy" receptor it binds to the VEGF-A and PIGF (placental growth factor) with high affinity, thus it blocks the angiogenic effect of the VEGR
- · I: intravitreal administration in the wet form of AMD in adults
 - also for the therapy of diabetic macular edema (DME)
 - vision impairment caused by the chorioidal neovascularisation in pathologic myopia
 - vision impairment caused by the macular edeme after retinal vein oclusion
- CI: allergy, eye infections