Very encouraging results with radioactive peptides for cancer imaging and therapy

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Since the introduction (Rotterdam, 1987) in nuclear medicine of a radioactive peptide - derived from somatostatin - a number of sort-like peptides have been synthesized - leading to new ways to identify, localize and treat neuroendocrine tumours. Although these tumours are relatively uncommon, their impact upon the daily life of patients can be tremendous. Overproduction of various hormones from these tumours results in symptoms such as uncontrollable diarrhoea and hot flushes. At the time of the initial diagnosis, about 3/4 of the patients have already spread of the disease, very often to the liver.
After administration of a radioactive protein in the bloodstream and the use of a γ-camera it is possible to search for the tumour location. The protein ("key") binds only to cells where the correct receptors ("lock") are situated. In this way the protein carries the radioactivity ("key ring") into the target cells through "the opened door". The rest of the radioactivity is quickly removed from the body into the urine. Not only can the extent of the disease be established in this way, but therapy can also be performed by the internal radiation of the target cells.
Since about 10 years the technique of "somatostatin receptor scintigraphy" (SRS), is worldwide in use and the National Institute of Health (USA) has investigated its application for staging of neuroendocrine tumours in comparison with data from CT, MRI, ultrasound and angiography. SRS appeared superior and the NIH advises SRS to be the initial imaging choice in neuroendocrine tumour staging.
As a sequela to imaging, the same principle has been applied for therapy of neuroendocrine tumours. In Rotterdam radiation therapy was carried out since 1992 in more than 400 patients with neuroendocrine tumours expressing somatostatin receptors. Three generations of somatostin-like peptides have been used in collaboration with the universities of Brussels (Prof. Dr S Pauwels) and Tampa (Prof Dr LK Kvols) and with Mallinckrodt, Novartis and NRG Petten. Treatment is given starting with a 4 h infusion with amino acids which block accumulation of the radioactive peptide in the kidneys. This is followed by the administration of high doses of radioactive peptide for up to 30 min. Only 15% of patients vomit during therapy, caused by the infusion of the amino acids for kidney protection. In general, patients undergo such treatments 3 to 4 times with intervals up to 9 weeks. Especially, with the second and third generation of somatostatin-like peptides impressive tumour shrinkage (up to 50%) and tumour growth stabilization have been observed which last for at least 36 months on average. Overall quality of life of the patients appears to improve with less fatigue, insomnia and pain, and following treatment with the second generation peptide, 50% of the patients are still alive at 5 years.
Not only neuroendocrine tumours are candidates for the second and third generation radioactive somatostatin-like peptides treatment. Also preliminary good results have been obtained in metastatic thyroid cancers whereas other cancer candidates for treatment are small cell lung and renal cell cancer and malignant lymphomas. Since autoimmune diseases also may express somatostatin receptors, we are investigating the possibility to treat patients with, for instance, intractable rheumatoid arthritis.

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