Medical Xpress

Radiotherapy can cause lasting vascular disease

March 22 2010

For an as yet unknown reason, cancer radiotherapy can increase the risk of cardiovascular disease later in life, a problem that is growing as more and more people survive their cancer diagnosis. New research from Karolinska Institutet now suggests that sustained inflammation induced by post-radiotherapy changes in the gene expression in the arteries could be the cause.

Epidemiological studies have shown that a course of radiotherapy increases the risk of cardiovascular disease in the same part of the body; for example, myocardial infarction after left-side breast cancer treatment, or stroke after the treatment of head and neck or brain tumours. Scientists know very little, however, about the biological causes of these serious side-effects, which often do not appear until many years following treatment.

"Studies have been hampered by the fact that the disease process is so slow," says Martin Halle, researcher at Karolinska Institutet. "Cell studies and animal studies are best suited to the more immediate effects, and studies on human subjects have been ruled out for ethical reasons."

By studying autografts that have been carried out after cancer, Martin Halle and colleagues have now for the first time managed to study the long-term effects of radiotherapy on human blood vessels. This type of autograft involves the transplantation of skin, muscle or bone tissue from one part of a patient's body to reconstruct defects that arise after the removal of a tumour in another, often irradiated, part. By harvesting

biopsies from previously irradiated branches of the carotid arteries and non-irradiated arteries from grafts, the researchers have been able to compare the difference in global gene expression between irradiated and non-irradiated arteries from the same patient at the same time.

They found that the irradiated arteries showed signs of chronic inflammation and an increase in activity of Nuclear Factor- kappaB (NF-kappaB), a transcription factor known for playing a key part in the development of atherosclerosis. The greater inflammatory gene expression was visible for several years after irradiation, and might, the researchers believe, explain why cancer patients can suffer cardiovascular disease many years after radiotherapy.

"Hopefully, these findings will one day help medicine to mitigate the side effects by administering radiotherapy in combination with an anti-inflammatory treatment," says Dr Halle.

The importance of the results is underscored by the publication of an explanatory commentary in the journal's editorial.

More information: "Sustained Inflammation Due to NF-Kappa B Activation in Irradiated Human Arteries" , Halle M, Gabrielsen A, Paulsson-Berne G, Gahm C, Agardh HE, Farnebo F, Tornvall P, Journal of the American College of Cardiology, 23 March 2010; 55:1227-1236, doi:10.1016/j.jacc.2009.10.047

Provided by Karolinska Institutet