Childhood cancer survivors at heightened risk of several autoimmune diseases

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Childhood cancer survivors are at heightened risk of a wide range of autoimmune diseases, reveals research published online in the *Annals of the Rheumatic Diseases*.

Diabetes and Addison's disease—a condition in which the adrenal gland doesn't work properly—make up almost half of the excess cases, the findings show.

Over the past 40 years, the number of childhood cancer survivors has risen sharply, resulting in a five year survival rate of 80% among children who succumb to the disease.

But mounting evidence suggests that these survivors are at heightened risk of various health problems as adults, which increase in number and severity as they get older.

The researchers looked at the risk of developing a wide range of autoimmune diseases among more than 20,000 adults who had had cancer before the age of 20, and survived for at least a year, and nearly 126,000 people, matched for age, gender, and country of birth, who had not had cancer as children.

They used national cancer registry data from Denmark, Iceland, and Sweden, dating back to the 1940s up until 2008, to identify those who had had cancer as a child.

And they used hospital records to work out the difference between the expected and excess number of cases of autoimmune disease, expressed as a standardised hospitalisation rate ratio (SHRR).

The health of all the participants was tracked for an average of between 15 and 19 years.

In all, 724 (3.6%) childhood cancer survivors had at least one episode of hospital treatment for any autoimmune condition, when 516 would have been expected ordinarily, amounting to a 40% increased risk.

Or put another way, seven extra cancer survivors were treated for every 1000 patients tracked over a decade.

The SHRRs were significantly higher for 11 out of 33 autoimmune diseases investigated among the childhood cancer survivors, particularly for the rarer forms.

The analysis revealed that autoimmune haemolytic anaemia was 17 times more likely, Addison's disease 14 times more likely, and polyarteritis nodosa, which describes inflammation of the small muscular arteries, six times more likely, among those who had had cancer as a child.

Similarly, cases of rheumatic heart disease, scleroderma—connective tissue disease—idiopathic thrombocytopenic purpura—tendency to bleed and bruise easily as a result of low clotting factor levels—Hashimoto's thryroiditis—a thyroid gland disorder—pernicious anaemia, sarcoidosis—abnormal cell clumping—Sjögren's syndrome—a tear duct and salivary gland disorder—and diabetes, were all significantly higher than would be expected among the childhood cancer survivors.

Those who had had leukaemia, Hodgkin's lymphoma, kidney cancer, and

central nervous system tumours seemed to be at greatest risk of developing an autoimmune disorder in later life. They were up to 60% more likely to do so than those who had not had cancer in childhood.

The excess risk for all autoimmune diseases combined peaked during the first five years after a cancer diagnosis, which may be a consequence of closer medical monitoring, explain the researchers.

However, the excess persisted for up to 30 years later for most conditions, and up to 50 years later for some conditions, they point out.

One possible explanation for the findings is that "persistent immune abnormalities after treatment with chemotherapy predispose to the development of autoantibodies, which are central to the pathogenesis of many autoimmune diseases," they write.

"Both the cancer itself and the immunosuppressive treatment, as well as the increased number and types of infections during cancer treatment, could alter the immune system as a whole and also result in immunologically different antigens, leading to the production of autoantibodies," they add.

Radiotherapy may also help to explain the development of autoimmunity, they suggest.

"Cure is no longer a sufficient goal in childhood cancer care," they emphasise. "As the vast majority of these patients survive, attention must be paid to their long term quality of life and health challenges."

More information: Autoimmune diseases in adult life after childhood cancer in Scandinavia (ALiCCS), DOI: 10.1136/annrheumdis-2015-207659