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temat pracy: „*Wybrane następstwa endokrynologiczne po zakończonym w dzieciństwie leczeniu przeciwnowotworowym*”

Summary

During last years, changes in diagnosis and treatment have caused a significant increase in the number of children and young adults who underwent cancer therapy in childhood. According to one of the world's largest studies there are more than two-thirds of survivors with at least one chronic condition. Endocrine disorders are among the most frequently reported complications in pediatric cancer survivors and they are mainly due to chemotherapy, corticosteroids and radiotherapy. The frequency of endocrine sequelae in Polish survivors is still unknown. Furthermore, the impact of some risk factors associated with the treatment is not fully understood and remains debatable.

The aim of published papers was to assess the frequency of selected endocrine long-term complications after the completion of childhood anticancer therapy. In the first study, we assessed the frequency of low bone mass and the impact of used treatment or endocrine disturbances on bone mass in survivors of childhood Hodgkin disease (HD) and non-Hodgkin lymphoma (NHL) short time (within 1–5 years) after treatment. In the following two publications young adult survivors were examined. We analyzed the frequency of low bone mass, endocrine disorders, insulin resistance (IR) and the association between adipokines (leptin, adiponectin, and resistin), measurement of body fat and received treatment, especially radiotherapy.

The studies were conducted in two groups: 1st group - 43 patients (mean age 16.21 ± 4.4 years) after treatment of Hodgkin's lymphoma ($n = 31$) and non-Hodgkin lymphoma ($n = 12$), and 2nd group - 75 patients (mean age 24.1 ± 3.5 years) after the completion of treatment for childhood cancer (leukemia, $n = 29$; lymphoma, $n = 27$; solid tumor, $n = 19$). Consecutive patients were recruited from the Department of Pediatric Oncology and Hematology of the Medical University of Białystok, Poland. Body mineral density, fat and lean mass were all determined using dual-energy X-ray absorptiometry (DXA). Results of the study subjects were compared to their age- and sex-matched controls (in the form of reference data), and expressed as the means with standard deviations and Z-scores for BMD, in accordance with the local

reference population (473 healthy children). All patients underwent clinical examination with anthropometric assessment (body mass index, height, waist-hip ratio) and laboratory tests that evaluated TSH, fT₃, fT₄, FSH, LH, estradiol and testosterone levels. The concentration of adipokines (leptin, adiponectin and resistin) were also determined in the 2nd group (the control consisted of 49 healthy children). Medical records of each patient were used in order to obtain the patient data concerning type of treatment, cumulative doses of steroids and doses of the radiation therapy. The study was approved by the Ethics Committee of the Medical University of Białystok. Level of statistical significance was set to 0.05.

The study in patients after HL and NHL treatment showed low bone mass (BMD Z-score < 2) in only 7% of patients (3/43). There were no significant differences in analyzed parameters (height, weight, BMD Z-score, radiotherapy, chemotherapy) between the groups in terms of time after cessation of treatment (above and below 2 years). A similar percentage of low bone mass was found in young adults - 9% (7/76), while mild deficits (Z-score < -1) were observed in 25% of patients (19/76). There was no significant correlation between hormone levels and bone mineral density. Subclinical hypothyroidism was diagnosed in 12.5% of patients (9/76). Levels of TSH were also significantly higher in the study group compared with the control group (2.65 mIU / L vs 1.99 ± 1.4 mIU / L ± 0.97, $p = 0.015$). Isolated, high FSH levels were detected in 9% of patients, while increased levels of both FSH and LH were found in 15% of cases. At the follow-up visit overweight was observed in 20% (15/76) and obesity in 9% of survivors (7/76). The analysis has not confirmed the significantly increased incidence of insulin resistance in young adults. No significant differences were found in levels of adipokines according to radiotherapy. Overweight patients had a significantly higher HOMA-IR (0.42 vs 0.14, $p = 0.006$) and decreased the ratio of adiponectin to fat mass (0.26 vs 0.52, $p = 0.003$) compared with patients with normal weight. The multiple regression model for females showed that leptin/adiponectin ratio (LA ratio) significantly affected HOMA-IR (increase of 0.024 per each unit of L/A ratio, $p = 0.019$).

Performed studies do not confirm clinically significant bone deficits among children and adolescents who were treated for HL and NHL, neither in young adults' survivors of childhood cancer. Subclinical abnormalities are a significant problem among young adults, which might predispose to development of the full-blown diseases later in life. Likewise, changes in the levels of adiponectin and leptin adversely affecting HOMA-IR may predispose to insulin resistance and its clinical consequences. None of the enrolled adult patients was aware of the presence of hormonal disturbances. There is a lack of proper clinical assessment among

adult childhood cancer survivors in Poland. Obtained results indicate the need for further, long-term studies in order to monitor and improve quality of life of childhood cancer survivors.