Conclusion: This case emphasizes the need for a careful clinical and imagiologic investigation in children presenting with signs of pituitary hormone deficiency. Early diagnosis can prevent further evolution and complications of hypopituitarism.

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MEASUREMENT OF HEPATIC TISSULAR rSO_2 USING NEAR INFRARED SPECTROSCOPY AS A WITNESS OF HEPATIC TUMOR REGRESSION

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Background and aims: Near InfraRed Spectroscopy (NIRS) is a tool for evaluation of local blood flow and oxygen consumption (VO_2) using measurement of regional oxygen saturation (rSO_2).

Purpose: To describe the feasibility and accuracy of the measurement of hepatic rSO_2 ($lirSO_2$) in an infant with tumoral syndrome in acute leukemia.

Methods: A 7 weeks old girl was admitted with asthenia, bleeding, respiratory distress and hepatomegaly. Hemogram showed 117000 leucoblasts/mm³, Hb=7.1g/100 ml, 24000 platelets/mm³. Blood gaz analysis showed : pH=7.37, HCO_3^- =18 mmol/l, $PaCO_2$ =31 mmHg and lactatemia=888 mg/l. Sonography showed a heterogeneous hepatomegaly. Diagnosis of acute monocytic leukemia (AML-M5) was made. Chemotherapy was started (ELAM 02 protocol). Infant was monitored using cardiac monitoring, continuous measurement of oxygen saturation (SpO_2) and invasive blood pressure. $CerSO_2$ and $lirSO_2$ were measured using NIRS. rSO_2 values were recorded every 6 seconds, hemoglobin and central venous SO_2 (SvO_2) in *vena cava superior* every 6 hours.

Results: rSO_2 measurement began 10 hours after the first chemotherapy (H0). SpO_2 value was $96.4 \pm 2.0\%$, $CerSO_2$ was $75.8 \pm 3.9\%$ SvO_2 values were stable around 70%, suggesting that there was no variation in systemic oxygen transport (TO_2). $lirSO_2$ value at H0 was $24.7 \pm 7.6\%$ and raised up to $74.0 \pm 2.5\%$ at H12.

Conclusions: NIRS provides a non-invasive assessment of $lirSO_2$ in acute hemopathies. The decrease in $lirSO_2$ could be the witness of tissular

hypoxia induced by myeloproliferation. Our data show an increase in $lirSO_2$ under chemotherapy. NIRS could be helpful to evaluate the decrease in VO_2 and the improvement of TO_2 during chemotherapy.

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6-MERCAPTOPURINE INDUCED SYMPTOMATIC HYPOGLYCAEMIA IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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Background & aims: Although the most common cause of SH in paediatric acute lymphoblastic leukaemia (ALL) is over-treatment of hyperglycaemia with insulin, it is also associated with thiopurine usage. The aim of this study was to document the incidence of 6-mercaptopurine (6MP)-related symptomatic hypoglycaemia (SH) in paediatric patients undergoing maintenance treatment for ALL.

Methods: We retrospectively reviewed patients with childhood ALL at our centre to identify those with a history of SH. Hypoglycaemia was defined as a blood glucose level of ≤ 2.7 mmol/l. The mode of presentation, fasting times and laboratory investigations were documented.

Results: Three patients, 1 male and 2 female, were identified from 200 children enrolled in the current MRC-ALL 2003 treatment protocol using 6MP as the sole purine analogue during continuation therapy. The median age at presentation was 3.8 years (range 1.6-4.9) and the median time from commencing 6MP treatment was 107 days (range 82-479). All three presented with seizure-like events and required hospital admission. Fasting times were clearly documented in 2 patients at 15.5 and 12 hours. Critical samples were obtained in all three. All demonstrated an appropriate ketosis with normal gluconeogenic precursors. No definitive endocrine or metabolic abnormality was identified.

Discussion: The mechanism of 6MP-induced SH remains unclear but impaired gluconeogenesis has been hypothesised. Dose modification or discontinuation of 6MP deviates from best practice. Repeated fasting for anaesthesia is the norm for this population. Where possible, fasting times should be limited, and large evening and early-morning meals

encouraged at home. Surveillance for symptoms of hypoglycaemia should be routine.

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T-BET MEDIATED ANTI-NEOPLASTIC EFFECTS OF DENDRITIC CELL-CYTOKINE INDUCED KILLER CELLS IN-VITRO

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Background and aims: To investigate the molecular mechanism underlying T-bet mediated anti-neoplastic effects of cytokine induced killer (CIK) cells.

Methods: Lymphocytes isolated from peripheral blood of leukemic children were induced with IFN- γ , CD3McAb and IL-2 and co-cultured with dendritic cells (DCs) to generate DC-CIK cells. The morphology and immunophenotype of these cells were determined by electron microscopy and flow cytometry, respectively. IL-2 and IFN- γ levels released by DC-CIK cells were quantified by ELISA. Cytotoxicity of DC-CIK cells against leukemia cell lines was measured by the MTT assay. FCM was used to detect CD4+CD25+Treg cells, while RT-PCR and Western blot were used to determine mRNA and protein expressions of Foxp3 and GATA3 in DC-CIK cells treated with T-bet monoclonal antibody.

Results: Induced DC-CIK cells were regular, round and transparent with variable cell volume and cellular aggregation. The main effector cells in this population were CD3+CD8+ cells and CD3+CD56+ cells. We demonstrated a time dependent increase in IL-2 and IFN- γ levels after induction. DC-CIK cells were cytotoxic to B95 cells, Jhhan cells and M07e cells, with the highest cytotoxicity towards B95 cells. Treatment with mouse anti-human T-bet monoclonal antibody resulted in an increase in the proportion of CD4+CD25+Treg cells and elevation of Foxp3 and GATA3 mRNA and protein levels.

Conclusion: DC-CIK cells induced with cytokines were strongly cytotoxic towards a number of cancer cell lines. Foxp3 and GATA3 were implicated in the T-bet mediated anti-neoplastic effects of DC-CIK cells via activation of the Th1 pathway and suppression of the Th2 and Treg pathways.

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PLASMA LEVELS OF LEPTIN AND SOLUBLE LEPTIN RECEPTOR IN SURVIVORS OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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The prevalence of overweight in adolescents and children in Europe is about 20%. Comparing to general population survivors of pediatric acute lymphoblastic leukemia (ALL) have increased risk of being overweight. The purpose of the study was determination of leptin and leptin soluble receptor in ALL survivors. 82 patients (male 55%), aged 5 to 26 (median 13) years were studied. ALL therapy was conducted according to modified German (n=69) or American (n=13) regimens. In 38% cranial radiotherapy (CRT) was used in median dose 18.2Gy. Median age at diagnosis and time from completion of treatment were 5 and 3 years respectively. Patients with BMI $\geq$ 85 percentile were classified as overweight. Correlation of plasma concentration of leptin and leptin soluble receptor, and overweight was analyzed with respect to the intensity of chemotherapy and to CRT. Overweight was observed in 31% of studied group. There was a significant increase in leptin concentrations in entire overweight, overweight girls and radiotherapy subgroups. Reverse relationship was observed for soluble leptin receptor concentrations with significant differences in entire overweight group as well as in overweight boys. There were significant negative correlations ($p < 0.05$) between leptin and leptin receptor in the entire group and in gender subgroups.

Conclusions:

- 1) The prevalence of obesity in our cohort was higher than in European population (31% vs 20%),
- 2) leptin and leptin receptor levels can serve as good markers for high risk of overweight specially for patients treated with cranial radiotherapy.