European Journal of Cancer Vol. 32A, No. 12, p. 2185, 1996

Printed in Great Britain
0959-8049/96 $15.00 + 0.00

PII: S0959-8049(96)00252-3

Malignant Lymphoma With Severe Hypoglycaemia

C. Camci,[1] S. Paydaş,[1] B. Şahin[1] and E. Coşar[2]

[1]Department of Medical Oncology; and [2]Department of Pathology, Çukurova University, Tıp, Fakültesi Patologi Bilim Dalı, Balcali Hastanesi, Adana, Turkey

HYPOGLYCAEMIA DUE to lymphoproliferative disorders is not a common entity. We present here a patient with splenic lymphoma with severe hypoglycaemic attacks.

A 61 year-old man was admitted to the gastroenterology department because of fatigue and abdominal swelling. Seven months before admission, he noticed fatigue and weight loss (5 kg in 3 months). He had a history of alcohol abuse (70 cl daily) and smoked cigarettes (35 packets/year). His past medical history was unremarkable otherwise, but physical examination revealed huge splenomegaly extending to the pelvis at admission. His abnormal laboratory findings were: haemoglobin (Hb) 9.4 g/dl, haematocrit (Hct) 28%, white blood cells (WBC) 2500/mm^3, platelets (PL) 107.000/mm^3, mean cell volume (MCV) 79 fL, alkaline phosphatase (ALP) 485 IU/l, uric acid 18 mg/dl. His peripheral blood smear was unremarkable and bone marrow aspiration was hypercellular. Abdominal ultrasonography showed hepatosplenomegaly, and an increase in the diameter of the vena porta and vena splenica (v. porta 24 mm, v. splenica 17 mm), but there were no collateral vessels nor intravascular thrombus formation. Abdominal CT scan showed large splenomegaly with multiple infarcts in spleen without retroperitoneal lymphadenomegaly. Percutaneous liver biopsy was reported as chronic persistent hepatitis. Upper gastrointestinal endoscopic examination revealed total gastritis, and gastric biopsy was reported as chronic superficial gastritis with *Helicobacter pylori* infection.

Splenectomy was performed for diagnosis and therapy for possible hypersplenism. The spleen weighed approximately 3.5 kg, and histopathological examination revealed architectural distortion of the spleen, with distension of the white pulp and multiple, irregular, large lymphoid follicles filled with monomorphic large cells with cleaved nuclei, one or two prominent nucleoli and abundant eosinophilic cytoplasm. Cytological atypia and high mitotic activity were noted. Some of the follicles contained polymorphic histocytes and plasma cells were seen at the periphery. Red pulp was totally involved. B- and T-cell markers and immunoglobulins G, M and A were not detected while leucocyte common antigen was positive in lymphoid cells. Final histopathological diagnosis was "non-Hodgkin's lymphoma, follicular Large Cleaved Cell". One week after splenectomy his haematological parameters were as follows; Hb 10.6 g/dl, Hct 33%, WBC 18.400/mm^3, platelets 929.000/mm^3.

One month after the operation the patient was hospitalised suffering from confusion, and his plasma glucose level was 30 mg/dl. Other abnormal biochemical parameters were: ALP 533 IU/l, lactate dehydrogenase (LDH) 2000 IU/l, total Ca^{2+} 12 mg/dl, phosphorus 2.5 mg/dl, uric acid 26.3 mg/dl, serum iron 10 mg/dl, total iron-binding capacity (TIBC) 282 mg/dl, aspartate aminotransferase (AST) 160 U/l, alanine aminotransferase (ALT) 33 U/l, gamma-glutamyltransferase (g-GT) 134 U/l, plasma insulin level 3 μIU/ml (normal range 6–35).

Abdominal CT showed pancreatic enlargement, intra-abdominal ascitic fluid and left pleural fluid collection. Histopathological examination of the peritonoscopic biopsy detected in the peritoneum showed diffuse infiltration of large lymphocytic cells with similar cytologic features with those described in the spleen.

Despite 750 g/day glucose administration, euglycaemia could not be achieved. A chemotherapy regimen containing cyclophosphamide, mitoxantrone, vincristine and prednisone was given. Two days after this treatment, i.v. glucose administration was stopped and there was no hypoglycaemic attack thereafter. Before discharge, blood glucose level was 97 mg/dl.

Association between lymphoproliferative disorders and tumour-induced hypoglycaemia is less clear than epithelial tumours and 5% of tumour-induced hypoglycaemia are due to lymphomas. In Hodgkin's disease, hypoglycaemia induced by circulating auto-antibodies against insulin receptors has been documented, but it is a very uncommon clinical entity [1]. In a small series of lymphomas the measurement of non-suppressible insulin-like activity (NSILA or IGF-like materials) has been found to be within a normal range or lower than normal [2]. In our patient, primary splenic lymphoma was the initial diagnosis. The hypoglycaemic attack after splenic surgery may have resulted due to widespread lymphoma involvement in the peritoneal cavity caused by surgical implantation of lymphoma cells to the peritoneum. We could not measure the amount of IGF-I and IGF-II levels because of technical limitations, but the low insulin levels suggest IGF-II as the causative factor for hypoglycaemia. It is very interesting that the patient did not develop hypoglycaemia before surgical treatment, although the mass was large, but it may be that tumour in the peritoneum resulted in rapid peritoneal and omental fluid exchange with the circulation.

In conclusion, non-Hodgkin's lymphomas may cause severe hypoglycaemia and, without chemotherapy, it is very difficult to correct.

Correspondence to C. Camci.
Received 15 Apr. 1996; revised 28 May 1996; accepted 19 Jun. 1996.

1. Chan JC, Zhu SQ, Ho SK, Cochram CS. Hypoglycemia and Hodgkin's disease. *Br J Haematol* 1990, **76**, 434–436.
2. Khan CR. The riddle of tumor hypoglycemia revisited. *Clin Endocrinol Metab* 1980, **9**, 335–360.