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Haematology

ELEVATED LEVEL OF BETA HUMAN CHORIONIC GONADOTROPHIN (B-HCG) IN THE SERUM OF A PATIENT WITH NON-HODGKIN'S LYMPHOMA: A CASE REPORT AND REVIEW OF LITEREATURE

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ABSTRACT **Background:** Reports about raise level of beta human chorionic gonadotrophin (β-hCG) is rare in the non-Hodgkins lymphoma (NHL), with few reports of elevated level in both men and post-menopausal women with NHL. We report a case of a young woman diagnosed with high grade NHL presenting with elevated level of β-hCG.

Case report: The patient was a 16-year-old nulliparous woman who presented with cervical lymphadenopathy and multiple abdominal masses of varying sizes, involving the spleen, ovaries and peritoneal cavity. The serum and urinary HCG test was positive. Cytology of the splenic, ovarian masses and biopsy of the node were consistent with a high grade Non-Hodgkin lymphoma. She received two cycles of chemotherapy using CHOP regimen. Her peripheral lymphadenopathy resolved after two courses of chemotherapy and the β-hCG became negative; however, abdomino-pelvic USS showed only minimal change in the spleen size and intra-abdominal masses. She defaulted follow up thereafter, due to financial constrain.

Conclusion: raised level of b HCG is rare in NHL and often associated with the high grade forms.

KEYWORDS : β-hCG , High Grade, Non-hodgkins Lymphoma

Background: The Non-Hodgkin lymphomas (NHL) comprise a heterogeneous group of clonal lymphoid malignancy arising from either B lymphocytes (85%) or T lymphocytes (15%). They are divided into low-grade and high-grade disease (1). The clinical manifestation of the high grade forms is with a rapidly progressive disease, usually with extra nodal involvement. Several clinical and laboratory parameters are associated with its prognosis. There are some reports of elevated level of the pregnancy hormone - beta human chorionic gonadotrophin (β-hCG) in both men and post-menopausal women with NHL (2,3). It's unclear what prognostic significance this finding connotes, especially that most of the patients reported had a high international prognostic index (IPI) score (3). Herein, we report a case of a young woman diagnosed with high grade NHL presenting with elevated level of β-hCG.

Place of study: Department of haematology and blood transfusion, UMTH, Maiduguri. Borno Nigeria

Case report: A 16-year-old nulliparous woman was admitted to the accident and emergency unit, on account of four week history of progressive abdominal swelling and pain. There was associated history of B symptoms, anorexia and vomiting. Systemic review and past medical history were unremarkable. On examination, she appeared chronically ill looking, pale, lethargic, febrile at 37.80c, with left cervical lymphadenopathy measuring 2x3cm in diameter. Abdominal examination revealed tenderness more marked at the left flank, massive ascites and multiple nodular masses of varying sizes, involving the left hypochodrium, right and left iliac fossae, with the largest measuring about 10x8cm in diameter. Routine blood count showed a haematocrit of 21%, white blood cell count of 11.5 x 109/L and platelet count of 300 x 109/L. The erythrocyte sedimentation rate was raised at 90mm/hour. The serum urea (27.7mmol/l), creatinine (400μmol/l), phosphate (3.2mmol/l), uric acid (551mmol/l) were raised; while serum calcium (2.1mmol/l) and albumin (33g/dl) were low. She was transferred to the Obstetrics and Gynaecology ward on account of an initial finding of a positive serum and urinary beta human chorionic gonado trophin (HCG) test, taken on two different occasions. Abdomino-pelvic ultra sound scan revealed multiple para-aortic and mesenteric lymph nodes, splenomegaly, and bilateral ovarian masses demonstrating the same echogenicty as the spleen; there was no evidence of intra-uterine or ectopic pregnancy. Fine needle aspiration of the splenic and ovarian masses under ultra sound guidance and biopsy of the cervical node were obtained, and the result was consistent with a high grade Non-Hodgkin lymphoma (figures 1-3). The patient was subsequently referred to the Haematology unit. In view of the rapid nature of her condition and evidence of pre-treatment

tumour lysis syndrome, she was commenced on aggressive intravenous hydration and allopurinol for 24hr prior to commencement of chemotherapy following appropriate counseling. She received two cycles of chemotherapy using CHOP regimen. Her peripheral lymphadenopathy resolved after two courses of chemotherapy and the β-hCG became negative; however, abdomino-pelvic USS showed only minimal change in the spleen size and intra-abdominal masses. She defaulted follow up thereafter, possible due to financial constrain.

Discussion: β-hCG is a growth factor which consists of a 92 amino acid alpha subunit and a 145 amino acid beta subunit, and shares mutual evolutionary sequences with transforming growth factor (TGF) (4). It is primarily produced by placental syncytiotrophoblast cells during pregnancy. The differential diagnosis of a raised level in the absence of a viable pregnancy include ectopic pregnancy, gestational trophoblastic disease and paraneoplastic syndrome in several solid tumours (5,6). Reported rates of β-hCG production by non-gestational cancers varies, higher rates have been reported in cancers of the pancreas (7), lungs (8) and kidney (9). Lower rates have been reported with some GI malignancies (10) and oro-pharynx (11). The lymphomas are less likely to express β-hCG.

The exact mechanism of action of β-hCG is not clear. It is speculated to exert its effect both in an autocrine and paracrine fashion. It stimulates advanced cancer cells to produce invasion proteases, such as, collagenases and metalloproteinases, leading to metastases (4). Also, it may inhibit apoptosis of malignant cells by interfering with the function of TGF by binding to a component of its receptor complex. This interaction prevents the growth factor from interacting with other receptor molecules, thereby inhibiting its ability to induce apoptosis (7). This may explain why malignancies associated with raised level of β-hCG are associated with an aggressive course and poor prognosis (4).

The significance of raised level of β-hCG varies depending on the type of cancers. In pancreatic cancer, it was associated with an aggressive course and poor outcome (7). It's an independent prognostic marker in cancer of the oro-pharynx, and it is use to identify high risk patients (11). In renal cell carcinoma, a prognostic value of β-hCG was observed, even with normal values exceeding the median value (9). Reports about raise level of β-hCG are rare in the NHL. Maxim et al reported three cases of positive β-hCG tests in women of non-childbearing potential due to diffuse large B cell NHL. Two of the patient had advance disease and had relapsed from their initial treatment (3). Similarly, raised level was reported in a young patient with anaplastic large cell lymphoma involving the groin, who responded poorly to chemotherapy (12); and in two elderly men with diffuse high grade testicular NHL(13). It is speculated that the lymphomateous cells express β-hCG as a result of chromosomal translocation or aberration involving the gene encoding β-hCG (2).

The HCG test was first developed in the 1950s by a renowned oncologist, who found raised levels in patients with various types of cancers even before signs or symptoms develop (14).The test is based on a theory that cancer is related to a misplaced trophoblast cell which has become malignant, and consequently secretes β-hCG. Therefore, a measure of the amount of β-hCG in blood or urine is also a measure of the severity of the malignancy - the higher the number, the greater the severity of the cancer (14). Ectopic expression of β-hCG is now a recognized phenomenon, however, the mechanism of β-hCG production by tumor cells is still poorly understood and the action is at best speculative. Studies have shown that its production by non-gestational tumors indicates a poorer prognosis; it is not clear whether it should be widely used as a prognostic marker and routinely measured in the patient's serum and urine. (8).

Given the rare reports of raised level in NHLs patients, the prognostic significance of its elevation remains to be investigated, as does the usefulness of β-hCG as a tumor marker for early detection of recurrences and for monitoring the therapy of patients with β-hCG NHL. A report of a 30yr survivor of advanced NHL who claimed to have used the β-hCG to monitor his response and progress during chemotherapy is encouraging (15). He used the β-hCG test as a reliable means of assessing his improvement throughout the treatment phase. The initial high β-hCG level prior to commencement of chemotherapy had dropped in parallel with both clinical and laboratory evidence of improvement. However larger studies are needed to ascertain and replicate such finding.

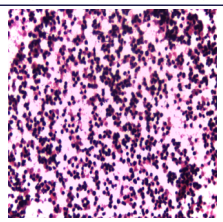

Figure 1: Splenic aspirate

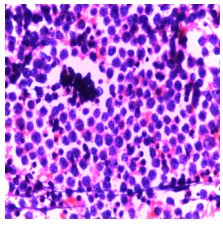

Figure 2: Ovarian aspirate:

Figure 1-2: The smears are cellular and show clusters and scattered atypical lymphoid cells having large hyperchromatic nuclei with coarse chromatin and 1-2 nucleoli and scanty amphophilic cytoplasm. There are scattered lymphocytes in the background, with haemorrhage in the ovarian aspirate

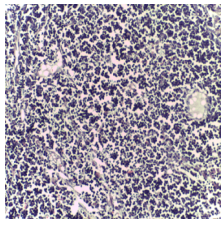

Figure 3: Cervical node biopsy x 20X . Section shows fragment of lymph node tissue whose architecture has been effaced by a diffuse lymphoid cell population composed of medium to large atypical lymphoid cells with hyperchromatic nuclei and some with prominent nucleoli. Mitotic figures are apparent with some abnormal forms

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