Hypercalcemia of malignancy

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الخلاصة:

ان ارتفاع مستوى الكالسيوم في الدم يعتبر من اغلب الاضطرابات الايضية المصاحبة لامراض السرطان والمهددة للحياة. تحدث بنسبة 10-20% من مجموع مرضى السرطان،الاورام الصلبة (مثل سرطان الرئة والثدي) وكذلك سرطانات الدم (ورم نخاع العظم المتعدد) غالبا ما تكون مصحوبة بارتفاع نسبة الكالسيوم في الدم.

تهدف الدراسة لمعرفة نسبة ارتفاع مستوى الكالسيوم في الدم في انواع السرطانات المختلفة،تضمنت الدراسة (130) مريض (67) نساء (63) رجال كانوا مصابين بامراض السرطان المختلفة والمشخصة بالفحص السريري والخلوي،الكل خضعوا لدراسة منظورة تم فيها اخذ عينات من مصل الدم بدون استخدام الضاغط (تورنيكا) في وضع الاستلقاء لغرض قياس مستوى الكالسيوم الكلي في مصل الدم،اظهرت النتائج ان (7) فقط من المرضى المصابين بمختلف امراض السرطان يعانون من ارتفاع مستوى الكالسيوم بالدم (3) مصابين بسرطان الثدي (1) لكل من سرطان الدم ،الغدد اللمفاوية، الرئة والجهاز الهضمي،لقد اظهرت الدراسة ان سرطان الثدي يعتبر من اغلب السرطانات المصحوبة بارتفاع مستوى الكالسيوم بالدم وهذا ما يبرهن ارتفاع نسبة الكالسيوم لدى النساء اكثر من الرجال.

Abstract:

Hypercalcemia is the most common life threatening metabolic disorder associated with neoplastic diseases, occurring in an estimated 10-20% of all persons with cancer. Solid tumors (such as lung or breast cancer) as well as hematological malignancies (particularly multiple myeloma) are frequently associated with hypercalcemia.

Our study aims to detect the incidence of hypercalcemia in variable malignancies,130 patients, 67 female and 63 male who are presented to surgical and medical wards as a proved cases of malignancies by histopathological and/ or cytological examination were included in a prospective study in which serum was obtained with out use of tourniquet in supine position to measure total serum calcium, from all patients collected there were only 7 having hypercalcemia, 3 out of them were having breast cancer, 1 lung cancer, 1lymphoma, 1leukaemia and 1GIT cancer, thus from this study we concluded that the breast cancer is the most common tumor associated with hypercalcemia and this can accuse hypercalcemia in female more than male .

Keywords: Hypercalcemia , metabolic disorder , neoplastic diseases.

Introduction:

Calcium absorption and regulation involve a complex interplay between multiple organ systems and regulatory hormones. [(1)]The three predominant sources and targets for regulation are the bones, renal filtration and reabsorption, and intestinal absorption.

The major regulators of calcium levels are parathyroid hormone (PTH) and vitamin D, which target the bones, intestine, and kidneys to increase serum calcium.

Calcitonin, a more minor player in regulation, decreases serum calcium by its effects on bone and kidney. Cyclically, high levels of the active form of vitamin D by decreasing the activity of renal 1ά-hydroxylase

The kidney serves as the rapid regulator of calcium fluxes but has limited capacity to handle large swings in the serum calcium levels. Sixty –five percent of the calcium filtered through the glomeruli is reabsorbed in the proximal tubule a process linked to sodium reabsorption. Although dependent on concentration and voltage, this process is independent of PTH. From 20-25% of filtered calcium

is reabsorbed in the ascending 105 is reabsorbed under in the influence of PTH and vitamin D in the distal tubule.

The bones serve as a reservoir, storing 99% of the body's calcium. Bony remodeling can engineer large, but slower, alterations in the serum calcium by a slow change in the balance between ectoblastic bone formation and orthoclastic bone resorption. However, deposition and release from hydroxyapatite can also provide slightly faster regulation. The intestine serves as a long-term homeostatic mechanism for calcium. Although the major source of calcium is dietary, seven eighths of dietary calcium is excreted unabsorbed in feces. Absorption occurs primarily in the ileum and jejunum by means of active transport and facilitated diffusion. [2] Half the plasma calcium is ionized and freely diffusible while 10% is bound to citrate and phosphate but able to diffuse into cells. The remaining 40% is plasma protein bound and not diffusible into cells. In the setting of calcium increase in a person with normal regulatory mechanisms, the hypocalcaemia suppresses the secretion of PTH. This plays a prominent role in calcium maintenance, however, only in the narrow range of serum calcium levels from 2.1 -2.6 mmo1/1.

Levels above or below this range are relatively ineffective at further stimulating or suppressing PTH and rely on direct exchange of calcium between bone and extracellular fluid. [3,4] Although early diagnosis followed by hydration and treatment with agents that decrease serum calcium concentration (hypocalcaemic drugs) can produce symptomatic improvements within a few days, diagnosis may be insidious at onset and can be confused with those of many malignant and nonmalignant diseases. It should be emphasized however, that diagnosis and timely interventions are not only lifesaving in the short term, but also may enhance the patient's compliance with primary and supportive treatments and may improve quality of life.

When a patient has a refractory, widely disseminated malignancy for which specific therapy is no longer being pursued. the patient may want to consider with holding their whishes regarding end –of- life issues, this may represent a preferred timing and /or mode of death (as compared to a more prolonged death from advancing metastatic diseases). This option is best considered long before the onset of severe hypocalcaemia or other metabolic abnormalities that impair cognition, so that the patient may be involved in the decision making.

Mechanisms of Cancer-Associated Hypercalcemia

The fundamental case of cancer –induced hypercalcemia is increased bone resorption of calcium mobilization into the extracellular fluid and secondarily, inadequate renal calcium clearance. Two types of cancer-induced hypercalcemia have been described: osteolytic and humoral hypercalcemia. Osteolytic hypercalcemia is due to direct bone destruction by primary or metastatic tumor. Humoral hypercalcemia is mediated by circulating factors secreted by malignant cells without evidence of bone disease. [5, 6] It is now believed that hypercalcemia is due to the release of factors by malignant cell that ultimately cause calcium resorption from bone. [7] One such factor is a PTH-like protein known as parathyroid hormone- related protein or peptide (PTHrP). PTHrP is a primitive protein that appears to have important roles in calcium transport and developmental biology. It shares partial amino acid sequence and conformational homology with normal PTH, binds with the same receptors on skeletal and renal target tissues, and affect calcium and phosphate homeostasis as does PTH.[6,8,9] Increased blood levels of PTHrP have been found in patients with solid tumors, but not in patient with hematologic

malignancies who develop hypercalcemia.(7)

Circulating growth factors may also mediate hypercalcemia. Potential mediators include transforming growth factor (TGF) alpha and beta, interleukin-1, tumor necrosis factors (NTF) alpha and beta, and interleukin-6. (10)

Aim of the Study:

To detect the prevalence of hypercalcemia in patient with different malignancies.

Patients and methods:

A prospective study conducted on 130 patients having malignancies regardless their grade and stage over the period between Jan 2004 2005 in al najaf hospital and from Nuclear medicine hospital which is the center for malignancies in Baghdad all were proved to have cancer by histopathological and \ or cytological studies and we include in the data the age ,sex.

2ml of blood was taken without use of tourniquet in supine position and centrifuged and serum was isolated and calcium level was measured by using radioimmunoassay by spectrophotometry 80samples were tested in AL Hakeem laboratory and 50 samples were tested in nuclear hospital

Results:

During the period between Jan 2004 _Jan 2005 130 patients of different malignancies we collected patients, ages ranged from (1-70) years

Table (1) distribution of malignancy with sex

Type of malignancy	female	Male	Total
Ca.breast	16	-	16
Lymphoma	18	9	27
Leukaemia	10	19	29
Ca. bladder	6	8	14
Ovarian tumour	3	-	3
Renal carcinoma	2	-	2
Thyroid carcinoma	2	-	2
Lung cancers	-	8	8
Ca .prostate	-	3	3
G.I.T cancer	10	16	26
Total	67	63	130

Table (1) shows the female malignancies were 67 (51.5%) males malignancies were 63 (48.5%) the most common malignant tumor in the females was Lymphoma while in the males it was leukemia which is also the highest malignancy in both sex.

Table (2) illustrates distribution of malignancy according to the result of serum calcium level

Malignant diseases	Normal calcium	Hyper calcaemia	Total
Ca.breast	13	3(18.75%)	16
Lymphoma	26	1(3.7%)	27
Leukaemia	28	1(3.4%)	29
Ca. bladder	14	-	14
Ovarian tumour	3	-	3
Renal carcinoma	2	-	2
Thyroid carcinoma	2	-	2
Lung cancers	7	1(12.5%)	8
Ca .prostate	3	-	3
G.I.T cancer	25	1(3.8%)	26
Total	123(94.6%)	7(5.4%)	130

Table (2) shows the highest incidence of hypocalcaemia of malignancy occurred in breast patients (18.75%).

Table (3) sex distribution in relation to serum calcium level

Sex	Serum calcium level		Total
	Normal	hypocalcaemia	
Male	61	2(3%)	63
Female	63	5(7%)	67
total	123	7	130

Table (3) show the prevalence of hypocalcaemia of malignancy was higher in females 7% than the males 3%

Table (4) age distribution in relation to serum calcium level

Age \year	Serum calcium level		Total
	Normal	hypocalcaemia	
1-10	3(2.4%)	-	3
11-20	11(9%)	-	11
21-30	14(11%)	-	14
31-40	16(13%)	1(14%)	17
41-50	19(15%)	3(42.8%)	22
51-60	30(24.3)	2(28.5%)	32
>60	30(24.3%)	1(14%)	31
total	123(94.6%)	7(5.4%)	130

Table (4) shows the incidence of hypocalcaemia of malignancy found to be highest in the middle and old age group with a peak incidence in the age group 41-50 years (42.8%).

Table (5) incidence of hypercalcaemia

Serum calcium level	No . of patients	Percentage
Normal	123	94.6%
Hypercalcalcamia	7	5.4%

Table (5) shows the incidence of hypercalcemia of malignancy found to be 5.4%

Discussion:

Our study done on patients with carcinomas the type of tumor regardless its stage and grade only could be included as there was difficulty in obtaining this information from patients who were only having biopsy or F.N.A.C.

The results showed that the age of patients presented in this study range between (1-70 years) with commonest age incidence of malignancy between (51-60 years) the most common malignant tumor in our study was leukemia .

Over all 130 patients tested for serum calcium level only 7 were associated with hypercalcemia and highest incidence of hypercalcemia occurred in breast cancer (18.75%).

Hypercalcemia was more common in female which could be due to the high prevalence of hypercalcemia in breast cancer patients.

The prevalence of hypercalcemia had been compared in different age groups of patients, the highest prevalence of hypercalcemia (42.8%) were found in the age group (41-50).

In our study the prevalence of hypercalcemia were not significantly ($p>0.05$) more common in female (7.4%) than male (3%) .

In comparison with other study the prevalence of hypercalcemia was 3% in females while in males was 1% [11]

Out of 16 breast cancer in our study only 3(18.75%) had hypercalcemia out of 27 lymphoma 1(3.7%) ,29 leukemia 1(3.4%)

,8 lung cancer 1(12.5%) ,26 GIT cancer 1(3.8%)

In comparison with Lang _Kummar study [12] the prevalence of breast cancer was 25.7%, Lymphoma 4.3%, leukemia 4.3%, lung cancer 27.3%, GIT cancer 4.1%

Will show the prevalence of breast was high in the two studies , but it was higher in Lang _Kummar study while the lunge cancer in Lang _Kummar study ,the results were similar to our study .

This variation of the prevalence with each malignant type many depend on the numbers of the patients included our study.

In our study the prevalence of hypercalcemia of malignancy was found to be 5.4% and this similar the incidence in the Warrell RP Jr [7]

Conclusion:

From this study we concluded that the breast cancer is the most common tumor associated with hypercalcemia and this can accuse hypercalcemia in female more than male.

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