Vertical Evolution[#]

Dictyostella[*] forage around
Singly, and virtually unbound.
Yet during a genuine drought.
The value of such freedom is in doubt,
For their future would not look bright
Unless they dutifully unite!
Thereupon starts a CAMP surge
And a hundred Thousand cells converge.
As, their will, this molecule bends
And, their multiplicity it ends.
Now they are strongly urged to unite,
To love each other rather that fight,
To show exemplary altruism
And to abandon idolism!
Many amoebae thus apoptose
To raise the living with no applause.
From lowly underground heathen
To multicellular slugs in 'heaven'!

[*]Plural of Dictyostelium, a species of amoebae

[#]It is unusual for Saudi Medical Journal to publish such material. It is customary to reserve this section for scientic material only.

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Primary Hyperparathyroidism

Sir,

I read the interesting article of "Primary Hyperparathyroidism and Pregnancy" by Dr. Mona A. Fouda, but I think there are some other valuable points worth mentioning. For example, the parathyroid adenoma of women can be asyptomatic during pregnancy and with the evaluation of a symptomatic infant after delivery (including hypocalcemia and tetany), the diagnosis of adenoma being confirmed.[1,2]

Other complications for the fetus include; increase intrauterine fetal growth retardation, spontaneous abortion and stillbirth.[3] In addition, to maternal complaints described by Dr. Fouda, the patient may present herself with symptoms of toxemia of pregnancy, so differentiation between pre-eclamsia and the hyperparathyroidism should be kept in mind, due to similar symptomatic and clinical findings.[4,5] Some authors explained that the mother presented herself first with the symptoms and signs of acute pancreatitis (including vomiting, nausea and abdominal pain). So the evaluation of the parthyroid glands for a co-existence of parathyroid adenoma during pregnancy should be considered in acute pancreatitis.[6] Consequently, determination of calcium serum concentration of every trimester of pregnancy and regular intervals after delivery and also serial ultrasound evaluation of the fetal growth are recommended.[3,4] And finally, about the mortality of this co-existence, some authors believe that this is related to delayed resection of parathyroid adenoma.[6]

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Sir,

I read with interest the recent article "primary hyperparathyroidism and pregnancy.[7] The author has successfully alerted the readers to the coexistence of primary hyperparathyroidism and pregnancy that is a very rare and an easily overlooked situation. Hereby, I would like to elaborate important points about calcium-phosphate relationship and certain pitfalls in their interpretation from chemical pathological point of view.

1. It is worth stating that for diagnosing primary hyperparathyroidism there is nearly always hypercalcemia with occasionally serum calcium is only raised intermittently.[8] However an increase in circulating PTH is usually, but not always, present and is not a consistent finding and so the results of PTH assay must be interpreted with caution. In the presence of hypercalcemia due to causes other than primary hyperparathyroidism, PTH production from the parathyroid glands should be suppressed to below normal range (i.e. undetectable).[8] A PTH concentration even in the normal range in association with hypercalcemia is considered, therefore, inappropriate and suggests autonomous PTH secretion.[9] Thus, primary hyperparathyroidism can be defined as a disturbance of parathyroid where circulating level of PTH is high or even inappropriately normal for the prevailing high concentration of plasma calcium (cf ADH secretion and hypo-osmolality in SIADH, insulin secretion and hypoglycemia in insulinoma).[10] The identification of the laboratory contribution in the diagnosis of primary hyperparathyroidism is of paramount importance as nowadays, only about 20% of these patients have urolithiasis, and radiographically detectable bone disease is rare.[11] 2. An important diagnostic criterion for diagnosing primary hyperparathyroidism is the deranged state of phosphate which the author didn't make use of. The paradoxical relationship between serum calcium and phosphate (hypercalcemia with hypophosphataemia) occurs almost exclusively (in the absence of renal impairment) in primary hyperparathyroidism.[12] This occurs due to the phosphaturic effect of PTH on renal tubules. Hence, a low (or even low-normal serum phosphate) with hypercalcemia are considered to be diagnostic for primary hyperparathyroidism. Furthermore, tests based on the renal response to excess PTH particularly concerning its phosphaturic effect are considered to be a further diagnostic prove.[13] This can be elicited by careful assessment of the renal handling of phosphate. Measurement of 24 hours urine phosphate excretion, as such, is of limited value because of its variability and low specificity. It is, therefore, not surprising for the 24 hour urine phosphate to be low in the reported three cases (which is against the sounder physiological principles of excess PTH). Phosphate excretion was 3.0 mmol/day in patient 1, 15.2 mmol/day in patient 2 and 11.4 mmol/day in patient 3 (reference range 13-42 mmol/day).

An improvement in the validity of the phosphaturic effect of PTH on the kidney can be achieved by measurement of the indices of tubular reabsorption of phosphate.[12] Although these tests have been replaced by the newer PTH immunoassay, however, their usefulness may still be considered in district hospitals using the commonly available simple data before further referral. These tests include the following:[13] a. Ratio of phosphate clearance of creatinine clearance (Cp/Ccr) which gives the proportion of phosphate filtered at the glomeruli, which has been reabsorbed in the tubules. Normally the ratio is <0.15 and is often raised in primary hyperparathyroidism. This is calculated as follows: Cp/Ccr = urine phosphate X serum creatinine, divided by serum phosphate X urine creatinine b. Percentage tubular reabsorbed phosphate (TRP) where: TRP = (1 – Cp/Ccr) X 100. With normal range being 84-95% and it is usually decreased in primary hyperparathyroidism. c. Phosphate excretion index (PEI) which allows for changes in Cp and Cp/Ccr which can result from changes in serum phosphate and in phosphate intake. PEI is calculated as: PEI = (Cp/Ccr) – (0.05 X serum phosphate in mg/dl) – 0.05 with normal value being – 0.12 to + 0.12 and it is often increased in primary hyperparathyroidism. An additional advantage in using these phosphate reabsorption and excretion indices is that their measurement does not necessitate timed 24-hour urine specimen. Instead, a random urine sample can be used for measuring urine phosphate and creatinine and together with the corresponding values in serum sample, calculation of these parameters can be made. It would, therefore, be advantageous to derive these indices in the reported three cases using the available data. Measurement of serum calcium and its interpretation in the light of other commonly available results (biochemical bone profile) including: serum phosphate, alkaline phosphatase, albumin (for correcting calcium), urea (for excluding renal impairment) and bicarbonate (for detecting any associated metabolic acidosis consequent upon inhibition of tubular bicarbonate reabsorption by excess PTH) may be sufficient for diagnosis. This may obviate the need for measurement of PTH, which is of very limited availability, even in the well-equipped hospital laboratory.

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Reply from the author

Sir,

I have received two correspondences from you regarding my manuscript published in your esteemed journal "primary hyperthyroidism and pregnancy".

The first one from Dr. Payam S Pahlavan from Shaheed Beheshi University of Medical Sciences, Tehran, Iran with interesting expansion on the complications that could happen to the mother and the fetus. He confirmed what has been stressed in my manuscript on the need for routine screening for serum calcium level during pregnancy, and early resection of the parathyroid adenoma during pregnancy when feasible.

The second correspondence is from Dr. Waad Allah S. Mula-Abed from College of Medicine, University of Mosul, Mosul, Iraq. With his detailed biochemical analysis of the disturbed relationship between the calcium and phosphoros minerals and the PTH. However, his statement "hence a low or even low normal serum phosphate with hypercalcemia are considered to be diagnostic for primary hyperparathyroidism", is not totally true, since other causes of inappropriately high PTH or PTH-like peptides could account for a similar presentation, e.g. solid tumors, lithium therapy etc. The twenty-four-hour urinary phosphate excretion even though could be of further help is not very diagnostic, and the renal phosphate handling as provided by the equations quoted by Dr. Mula-Abed could be helpful, but since the advent of PTH essays it has been customary to do this since it also helps in the differential diagnosis of hypercalcemia especially the new standard intact PTH essay.

I would like to thank both correspondents for their interest in the manuscript and their valuable comments. With best regards.

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