nesium subsequently stabilised at the lower end of the reference range (figure), and no further intravenous magnesium replacement was required.

Comment

Calcium and magnesium share a transport system in the gut, and both 1-α-hydroxycholecalciferol and 1,25 dihydroxycholecalciferol have been successfully used in the treatment of hypomagnesaemia associated with the short bowel syndrome.[2] A recent report describes the use of 1-α-cholecalciferol in a patient with the short bowel syndrome in whom, the authors claim, renal tubular absorption of magnesium was increased.[3]

In our case oral magnesium supplements in high doses were associated with diarrhoea, and 1-α-hydroxycholecalciferol enhanced magnesium absorption and possibly reduced urinary losses. The figure shows that normal serum magnesium concentrations were maintained after the administration of 1-α-cholecalciferol, with resolution of symptoms. Two 24 hour collections obtained while the patient was taking 1-α-cholecalciferol contained 5 and 8 mmol magnesium (figure), suggesting that any effect of 1-α-cholecalciferol on renal magnesium conservation was minimal.

The role of vitamin D in the renal handling of magnesium is unclear. Levine *et al* found a diminution of magnesium tubular reabsorption in vitamin D deficient rats given 1,25 dihydroxycholecalciferol,[4] and Burnatowska *et al* showed an increased fractional excretion of magnesium in hamsters from which thyroid and parathyroid glands had been removed.[5] Fukumoto *et al*, however, described a decrease in fractional excretion of magnesium in a hypomagnesaemic patient with the short bowel syndrome who was given large doses of 1-α-cholecalciferol.[3] In their patient, as in our case, the serum concentration of 1,25 dihydroxy-cholecalciferol was abnormally low, and this was felt to contribute to impaired renal resorption of magnesium.

More work is required on the effect of 1-α-cholecalciferol on renal magnesium handling, but the case reported here suggests that this drug may be useful in the management of hypomagnesaemia induced by cyclosporin.

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1 Thompson CB, June CH, Sullied KM, Themes ED. Association between cyclosporin neurotoxicity and hypomagnesaemia. *Lancet* 1984; ii:1116–20.
2 Selby PL, Peacock M, Bambach CP. Hypomagnesaemia after small bowel resection: treatment with 1-alpha hydroxylated vitamin D metabolites. *Br J Surg* 1984;71:334–7.
3 Fukumoto S, Matsumoto T, Tanaka Y, Harada S, Ogata E. Renal magnesium wasting in a patient with short bowel syndrome with magnesium deficiency: effect of one alpha hydroxyvitamin D3 treatment. *J Clin Endocrinol Metab* 1988;**65**:1301–4.
4 Levine BS, Brautbur N, Walling MW, Lee DBN, Coburn JW. Effects of vitamin D and diet magnesium on magnesium metabolism. *J Physiol* 1980;**239**:E515–23.
5 Burnatowska MA, Harris CA, Suttyon RAL, Seely JF. Effects of vitamin D on renal handling of calcium, magnesium and phosphate in the hamster. *Kidney Int* 1985;**27**: 864–9.

Parathyroid hormone related peptide in ovarian carcinoma

Hypercalcaemia is one of the commonest paraneoplastic syndromes encountered clinically, being associated with an estimated 10–20% of all solid tumours. Many factors contribute to this syndrome of humoral hypercalcaemia of malignancy (HHM), including cytokines and prostaglandins of the E series.[1] Recently, a peptide structurally and immunologically distinct from parathyroid hormone (PTH), but with parathyroid hormone bioactivity, has been implicated in the pathogenesis of HHM and has been termed parathyroid hormone related peptide or PTHrP.[2]

Hypercalcaemia is associated with ovarian carcinoma frequently enough for the ovary not to be ignored as a primary tumour site in women presenting with clinically unexplainable hypercalcaemia.[3] We therefore felt it would be of interest to examine a number of ovarian carcinomas for the presence of PTHrP.

Immunocytochemistry was performed using an antibody raised against the first 34 amino acids of PTHrP (kindly donated by Drs GV Segre and H Jüppner, Boston, Massachusetts, USA) and standard indirect immunocytochemical techniques. Two cases of ovarian carcinoma associated with hypercalcaemia (one small cell and one non-small cell type, supplied by Dr GR Dickersin, Boston) were found to contain PTHrP. PTHrP was present throughout the cytoplasm of the tumour cells but was absent from inflammatory and stromal cells and areas of tumour necrosis. The immunoreactivity was completely abolished when the antibody was pre-incubated with PTHrP (1–34) overnight. Two cases of serous cystadenocarcinoma and two cases of mucinous cystadenocarcinoma of the ovary (from patients who were normocalcaemic) were found to be negative for PTHrP.

Normal adult ovary does not produce PTHrP, but the peptide has been detected in the human fetal gonad.[4] This is the first report of the presence of PTHrP in a hypercalcaemic ovarian carcinoma. While the pathophysiological role of PTHrP is yet to be elucidated, one possibility is that in addition to it inducing hypercalcaemia it may stimulate the growth of tumours in an autocrine manner.[5] It may also regulate the fetal calcium balance.[4]

The widespread presence of PTHrP in lung, renal cell, and squamous cell carcinomas and its presence in small cell ovarian carcinoma, as reported here, suggests that PTHrP is a common manifestation of the transformed cell.

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1 Mundy GR, Ibbotson KJ, D'Souza SM, Simpson EL, Jacobs JW, Martin TJ. The hypercalcemia of cancer. Clinical implications and pathogenic mechanisms. *N Engl J Med* 1984;**310**:1718–27.
2 Orloff JJ, Wu TL, Stewart AF. Parathyroid hormone like proteins: Biochemical responses and receptor Interactions. *Endocrine Reviews* 1989;**10**:476–95.
3 Dickersin GR, Klein IW, Scully RE. Small cell carcinoma of the ovary with hypercalcemia: A report of eleven cases. *Cancer* 1982;**49**:188–97.
4 Burton PBJ, Moniz C, Quirke P, *et al*. Parathyroid hormone related peptide in the human fetal uro-genital tract. *Mol Cel Endocrinol* 1990;**69**:13–17.
5 Burton PBJ, Moniz C, Knight DE. Parathyroid hormone related peptide can function as an autocrine growth factor in human renal cell carcinoma. *Biochem Biophys Res Comm* 1990;**67**:1134–8.

Prorenin in ovarian cyst fluid

Aspartic proteinase renin is secreted by the kidneys and, as the initial enzyme in the renin/angiotensin cascade, it is important in the regulation of blood pressure and fluid homeostasis. Recently, high concentrations of the zymogen prorenin have been shown in female reproductive organs.[1] The concentrations of prorenin in follicular fluid collected from women undergoing in vitro fertilisation are at least 10 times higher than those in plasma.[2] Immunohistochemical staining has shown that the prorenin is present in the theca cells lining the follicles from where it is, presumably, secreted into the fluid.[3] As only very low concentrations of active renin are found in the ovary, it has been postulated that ovarian prorenin may be biologically active without any necessity for prior removal of the propart sequence.[1] The role of ovarian prorenin is still unclear but it probably operates through the formation of angiotensin II (AII). Studies with the AII antagonist, saralasin, have indicated a direct role for AII in ovulation,[4] and, in addition to its effects on steroidogenesis, the vasoconstrictor and angiogenic properties may be important for follicular growth.

Cysts are commonly derived from the ovarian follicles and frequently contain a large volume of liquid. It was thus considered of interest to determine whether this fluid might also contain a high concentration of prorenin. The fluid from six ovarian cysts removed at laparotomy was collected, stored at −20°C, and assayed for prorenin by the trypsin-activation method of McIntyre *et al*.[5] Renin activity was estimated by measuring the rate of angiotensin I (AI) production from human angiotensinogen.[6]

Prorenin was detected in the fluid from four of the cysts assayed—three of follicular origin and one from a mucinous cystadenoma—with two others being virtually negative (table). The concentration of active renin detected in all of the fluids was very low (less than 5% of total) and may have been due to partial activation of the prorenin during collection. This predominance of prorenin over renin is in keeping with previous results for normal ovarian follicular fluid.[1,2]

Concentrations of prorenin in ovarian cyst fluid

Age	*Diagnosis*	*Prorenin (ng AI/ml/h)*
18	Follicular cyst	41
29	Follicular cyst	9
42	Follicular cyst	24
44	Mucinous cystadenoma	15
32	Serous cystadenofibroma (16 weeks pregnant)	1
83	Serous cystadenofibroma	0