Hypercalcemia of Malignancy

Causes:
- most common is production of parathyroid hormone-related peptide (PT-HRP).
- less often related to increased gastrointestinal absorption of calcium or ectopic production of PTH itself.

Clinical Features:
- often difficult to distinguish from underlying malignancy
- lethargy, anorexia, nausea, vomiting, thirst, polydipsia, constipation, dehydration.
- cognitive difficulties, confusion, obtundation, and coma may occur

Important to correct serum calcium for serum albumin (calcium is partially protein bound).

Corrected serum calcium = measured serum calcium + (40 - measured serum albumin x 0.02)

Hypercalcemia = corrected Ca++ > 2.60 mmol/L

Treatment:
If pt. is mildly-moderately hypercalcemic and minimally symptomatic-
- rehydrate pt. with Normal Saline hypodermoclysis at 100 cc/hr or IV at 100-120 cc/hr.
- recheck serum calcium in 24-48 hours- if pt. remains hypercalcemic, consider administration of a bisphosphonate (see below).

If pt. is severely hypercalcemic i.e. corrected serum Ca++ > 3.0 mmol/L and/or is very symptomatic-
- firstly, rehydrate pt. with Normal Saline hypodermoclysis at 100 cc/hr or IV at 100-120 cc/hr.
- administer one of two bisphosphonates (Pamidronate or Clodronate) at the same time hydration is commenced or following correction of pre-existing pre-renal failure with Normal Saline hydration.

Subcutaneous administration of Calcitonin 100-200 units tid x 3-6 doses can be considered as an intermediate step between rehydration and administration of a bisphosphonate if pt. is severely symptomatic or if there is a need to lower the serum calcium quickly.
- recheck the pt's serum calcium in 3-4 days following bisphosphonate administration.

Bisphosphonates:
- effective treatment of hypercalcemia of malignancy
- two most commonly used and proven effective bisphosphonates are Pamidronate and Clodronate.

Renal failure is a relative contraindication to use of bisphosphonates, therefore, check electrolytes, urea and creatinine prior to administration. If pre-renal failure in present, rehydrate pt. with NS prior to use.

Pamidronate - duration of effect approx. 28 days
- unlike Clodronate, cannot be given subcutaneously
- is approx. 3 times as expensive as Clodronate
Dosage: Pamidronate 60-90 mgm (if renal function is preserved, than 90 mgm recommended) IV in 500-1000 cc NS or D5W to run over 4-6 hrs.

Clodronate - duration of effect approx. 14 days
- can be administered subcutaneously permitting home administration
- subcutaneous site should be observed for swelling or redness which is not common
Dosage: Clodronate 1500 mgm subcutaneously or IV in 500-1000 cc NS or D5W to run over 4-6 hrs.

Resistant Hypercalcemia:
- despite prior treatment with fluid hydration, calcitonin, and/or one of the above listed bisphosphonates, some pts. will develop recurrent hypercalcemia which only temporarily responds i.e. days or does not respond at all to treatment.
In this situation, it is often worthwhile to trial the other of the two recommended bisphosphonates that has not previously been used i.e. the hypercalcemia may respond to the other bisphosphonate. Another option for patients with resistant hypercalcemia not responding to pamidronate or clodronate is a trial of a new bisphosphonate, zoledronic acid which is administered intravenously.
- if the above measures prove unsuccessful, consider consulting a Palliative Care Physician

REMEMBER: For referrals, questions, or telephone consultations call 780-496-1300 weekdays and weekends.
Palliative Care Tips are now available on our Website: www.palliative.org