

MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

April 23, 1970

HYPERCALCEMIA OF MALIGNANCY

Case 1, [REDACTED] - Hypercalcemia associated with nonendocrine tumor

A 45 y/o [REDACTED] male [REDACTED] was admitted to [REDACTED] with a chief complaint of chest pain. He had experienced excellent health until 4 months prior to admission when he noted intermittent, sharp severe pain in the right hip that worsened with motion. He also noted a bilateral lower chest pain that was intensified by deep breathing and coughing. Both pains progressed until 3 weeks prior to admission the patient was unable to walk. The patient described a 20 to 30 pound weight loss with a good appetite. A productive cough occasionally tinged with blood and an occasional blood-streaked stool were present. At the time of admission, he had constipation for one week. He denied chills, fever or night sweats but admitted to smoking one package of cigarettes daily for more than 25 years. The review of systems revealed polyuria and polydipsia present for approximately one month.

The salient features on physical examination included a left-sided ptosis and anisocoria, right greater than left in a chronically ill wasted Negro male in moderately severe pain. Cervical and supraclavicular hard fixed nontender nodes were especially prominent on the left. Modest clubbing of the digits was present and muscle wasting was remarkable.

Laboratory examination on the day following admission revealed a serum calcium determination of 19.4 mg% which was confirmed. Patient was treated with intravenous saline infusions, diuretics, and hydrocortisone intravenously initially. In addition he was placed on INH and Pyridoxine therapy. On the second hospital day he was begun on a program of Prednisone 100 mg daily and 1 molar sodium phosphate solution 25 cc every 6 hours (3.1 gm phosphorus daily). During the remainder of his hospital course a lymph node biopsy was reported showing epidermoid carcinoma and despite a brisk diuresis the patient was noted on one occasion to be in pulmonary edema. Digitalization was carried out cautiously and hypokalemia was treated. Although diarrhea developed, sodium phosphate therapy was continued in order to keep the serum calcium in a tolerable range. Despite these efforts the patient progressively deteriorated and was found without vital signs on the tenth hospital day.

Lab Work	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
Ca		19.4	18	15.3	15.0	15.0
Phos		4.8	4.8		7.4	7.3
BUN	66		87	71	59	96
Cr	1.8		1.4	2.6	2.7	3.5
Alk phos		23.5		16.0		

At post-mortem examination a poorly differentiated squamous cell carcinoma originating from the right upper lobe bronchus was found involving nodes with lymphangitic spread and blood vessel on occasion. Calcification was seen in the lung, kidney and heart. One metastatic tumor focus was found in the vertebral column.

Case 2, [REDACTED] - Carcinoma of the breast with induced hypercalcemic syndrome

A 53 y/o woman presented herself to [REDACTED] in [REDACTED] 1, 1964 at which time an infiltrating duct cell carcinoma of the left breast was diagnosed. A left radical mastectomy was performed at that time and subsequently the patient received radiotherapy to the left chest wall and left axilla. For the ensuing three years the patient was asymptomatic until five days prior to her next admission when she developed pain in her left hip and x-rays revealed a subtrochanteric fracture of the left femur.

The pertinent findings on physical examination were palpable lymph nodes in the left axilla and supraclavicular area along with erythematous nodules in the old mastectomy incision. A lateral bowing deformity of the left proximal femur was present and a bone survey revealed pathological fractures of the left femur and right inferior pubic ramus. Evidence of metastatic disease was noted in the skull, thoracic spine and left clavicle. At this time the serum calcium was 9.1 mg%, the serum phosphorus 2.9 mg%, and the alkaline phosphatase 5.5 Bodansky units. The fracture was treated with open reduction and insertion of a Jewett nail. Following an uneventful postoperative course the patient was begun on 5 mg of Halotestin 3 times daily which was shortly thereafter increased to 10 mg t.i.d.

During the ensuing course, the patient was noted to have developed further lymph node enlargement three months following discharge. Six months later she was seen in the emergency room with severe pain, mild disorientation and confusion which necessitated her being placed in a nursing home. Within one month the patient was readmitted to [REDACTED] because of the development of generalized grand mal seizures and loss of consciousness. The deep tendon reflexes were reduced in the left leg. A positive Babinski sign was present on the right. On the day following admission the serum calcium determination was recorded as 16.8 mg%. At this point the patient was treated with 100 mg of Solu-Medrol intravenously and 40 mg of intravenous Furosemide were given every 6 hours. Intravenous saline was administered to keep up with the diuresis which amounted to approximately 4 liters daily. Within two days the patient was noted to have become more alert at a time when her serum calcium was 13.6 mg%. However she experienced repeated hypotensive episodes and expired three days later.

The post-mortem examination revealed multiple chest nodules of tumor which also involved axillary and inguinal lymph nodes. New bone formation existing outside the old periosteum was noted. There was invasion of the brain by tumor emanating from the skull.

Case 3, [REDACTED] - Carcinoma of the breast: Treatment with sodium phosphate

A 68 y/o woman was admitted to [REDACTED] because of an abscess of her upper left arm. Two months previously carcinoma of the left breast had been diagnosed for which patient underwent a radical mastectomy. The patient's postoperative course was unremarkable and she was discharged on the eighth postoperative day. One month following discharge a dull aching pain began in her right hip and became progressively more severe until ambulation was no longer possible. Physical examination at the time of admission showed considerable mental deterioration. There was evidence of marked weight loss. Subcutaneous nodules were palpable in the left chest wall, cervical region, and upper abdomen. The abscess was seen to arise from the surgical incision.

Laboratory studies revealed a blood urea nitrogen of 28 mgs. per 100 ml., serum calcium 9.5 mgm. per 100 ml., serum phosphorous 5.5 mgs. per 100 ml., and alkaline phosphatase of 49 Bodansky units per 100 ml. Roentgenograms showed a pathological fracture of the right hip and evidence of osteoblastic lesions in the pelvis.

The abscess was incised and drained. A course of external radiation was given to the right hip region (1520 Roentgens) and in addition oral estrogen therapy was begun (Estinyl 0.5 mgs. bid). During the next three days the patient developed episodes of severe nausea and vomiting. Isotonic saline was given intravenously to replenish an extracellular fluid volume deficit. She remained responsive but confused. On the fourth day following estrogen therapy her BUN had risen to 39 mgs. per 100 ml. and the serum calcium was 18 mgs. per 100 ml. On the following day the patient became obtunded; the serum calcium was 22 mgs. per 100 ml. She was treated over the next 14 hours with two liters of intravenous isotonic sodium phosphate (17 gms. per liter). During this period her urine output remained satisfactory (greater than 100 ml. per hour). After four hours the serum calcium had fallen to 16.2 mgs. per 100 ml. and by the 9th hour to 11.5 mgs. per 100 ml. The total urinary calcium excretion was 375 mgs. After 10 hours of treatment the patient's clinical state had failed to improve, despite the falling serum calcium concentration. Shortly thereafter her respirations became shallow and irregular. She expired four hours later in respiratory arrest. Resuscitative measures were without avail.

The findings at autopsy revealed residual carcinoma to be present in the left axilla, pleura, lymph nodes, and multiple sections of bone from both femurs, the right ileum, and the vertebral column. There were extensive metastatic calcifications in the heart, kidneys, liver, spleen, and pancreas. The parathyroids were normal.

Case 4, [REDACTED] - Acute leukemia: Treatment with sodium sulfate

A 65 y/o woman was admitted to [REDACTED] because of progressing lethargy and stupor. The patient had been in good health until four weeks prior to admission when she developed fever and a non-productive cough. She had improved on treatment with aspirin and penicillin. Three days prior to admission the patient became lethargic and spoke incoherently. At the time of entry into the hospital she was semicomatose.

Physical examination revealed an acutely ill, unresponsive woman. Her pulse was 108 and regular, respirations 28 per minute, and temperature 101.2°. The liver was palpated 2 cms. beneath the right costal margin in the mid-clavicular line. The neurologic examination showed the patient to be responsive to painful stimuli with normal deep tendon reflexes.

Laboratory tests showed 12.4 gms. of hemoglobin per 100 ml. and hematocrit of 39 per cent. Abnormal immature white cells were seen on the peripheral blood smear. The blood urea nitrogen was 27 mgs. per 100 ml., sodium 135 mEq/L, chloride 84 mEq/L, potassium 4.2 mEq/L, and CO₂ combining power 35 mEq/L. The serum protein concentration was 6.4 gms. per 100 ml., of which 3.1 gms. was albumin and 3.3 gms. globulin. Uric acid was 18.2 mgs. per 100 ml. and the serum calcium was 16.5 mgs. per 100 ml. The bone marrow was interpreted as showing acute leukemia of the stem cell type.

During the first four days of hospitalization, the patient was treated with intravenous fluids, penicillin, chloramphenicol and prednisolone (160 mgs. total). The fever and semicoma were unaffected by these measures and the serum calcium remained elevated. Over the next five hours the patient was given intravenously 500 ml. of isotonic sodium sulfate (14.4 gms.). Fourteen hours later the patient was found to be suffering from pulmonary edema. The serum calcium was 12.7 mgs. per 100 ml. Digitalis, intermittent positive pressure breathing, and peritoneal dialysis failed to correct the condition and the patient expired. A final serum calcium value was 12.0 mgs. per 100 ml.

The findings at autopsy revealed leukemic infiltrates in the liver, spleen, lymph nodes, bone marrow, and kidneys. Extensive metastatic calcifications were present in the lungs, heart, kidneys and lymph nodes. In the regions of marked calcification of the lungs, the alveolar septa and capillary walls were entirely calcified. In these areas fibrin strands and edema fluid were present in the alveolar spaces.

Table I - Hypercalcemia in Association with Malignant Disease*

Diagnosis and site of malignancy	No.
Breast	65
Multiple myeloma	5
Kidney	5
Bronchus	4
Malignant lymphoma	4
Oral cavity	3
Uterus	2
Thyroid	2
Breast and ovary	2
Acute lymphatic leukemia	1
Brain (astrocytoma)	1
Testicle	1
Ovary	1
Antrum	1
Esophagus	1
Larynx	1
Pharynx	1
Total	100

* After Warwick et al.

Table II - Symptoms Associated with Hypercalcemia*

Nausea	46	
Vomiting	40	
Anorexia	28	
Constipation	28	74%
Abdominal discomfort	3	
Diarrhea	1	
Dysphagia	1	
Thirst	7	
Nocturia	7	11%
Polyuria	6	
Dry mouth	3	
Drowsiness	8	
Blurred vision	3	
Dizziness	2	
Diplopia	1	
Dysarthria	1	
Lightheadedness	1	10%
Paresthesiae	1	
Restlessness	1	
Depression	1	
Confusion	1	
Weakness	6	
Malaise	4	5%
Fatigue	4	

* After Warwick et al.

Table III - Signs Associated with Hypercalcemia*

Lethargy		
Drowsiness	18	
Stupor		
Disorientation	7	
Apprehension	3	
Confusion	2	
Inattention	1	50%
Incoherence	1	
Confabulation	1	
Depression	1	
Behaviour problem	1	
Incontinence	1	
Muscle weakness	6	
Absent reflexes	5	
Diminished reflexes	4	
Dysarthria	3	
Slowness of movement	2	35%
Miosis	1	
Diplopia	1	
Dysphagia	1	
Babinski response	1	
Urinary retention	1	
Dehydration	9	
Oliguria	2	15%

* After Warwick et al.

Hypercalcemia Associated with Leukemia

Author	Age (Sex)	Type of Leukemia	Highest Ca (Mg/100 cc)	PO ₄ (Mg/100 cc)	Alkaline Phosphatase	Urine Ca (Mg/24 Hr)	BUN (Mg/100 cc)	Bone X-Ray Changes
Myers	---	Acute	11.8	---	---	---	---	Yes
Mawdsley & Holman	20 (M)	Acute lympho- blastic	24.0	Normal	Normal	560	80	Yes
David et al	49 (M)	Chronic lympho- cytic	16.0	3.0	Elevated	---	66	Yes
Kronfield & Reynolds	14 (M)	Acute myelocytic	18.5	4.3	Elevated	183	80	Yes
Green	66 (M)	Chronic lympho- cytic	16.7	4.0	---	---	---	Yes
Knisley	64 (F)	Acute lympho- cytic	15.2	4.4	Elevated	160	58	Yes
Ballard & Marcus	31 (M)	Chronic myelocytic	14.1	5.2	Elevated	---	33	---
Benvenuti et al	40 (M)	Chronic myelocytic	21.5	---	Elevated	---	---	Yes
	58 (F)	Stem cell	18.9	2.8	Normal	---	30	No
Jordan	54 (F)	Acute following chronic lymphocytic	17.0	5.7	Elevated	---	73	No
	17 (M)	Acute lympho- cytic	12.3	5.4	Elevated	---	---	---
Present Case	33 (M)	Acute granulocytic	13.1	4.6	Elevated	845	---	---
	47 (M)	Acute granulocytic	11.9	4.2	Elevated	---	---	---
	56 (F)	Subacute lymphatic	23.8	4.4	Normal	720	---	---
	16 (M)	Acute lymphocytic	11.5	5.8	Elevated	---	---	---
	60 (M)	Chronic lymphatic	12.1	2.0	Elevated	176	---	---
	65 (F)	Stem cell	16.5	3.1	---	---	27	---

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