Cushing’s Storm Secondary to Ectopic ACTH Secreting Metastatic Breast Cancer

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Objective:
A 31 year old female, with triple negative, high grade invasive right ductal carcinoma treated with chemotherapy, bilateral mastectomy, and radiation presented with acute psychosis. She had not slept for 4 days, was hyperenergetic, easily distracted, impulsive with racing thoughts, pressured speech and was paranoid that her husband was trying to hurt her. On exam she had round, ruddy, hirsute face with acne and her blood pressure was 156/108. Labs showed potassium 1.7 mEq/L, normal range 3.7-5.2 mEq/L, random cortisol >70 mcg/dL (normal range 6-23 mcg/dL), 1mg and 8mg overnight dexamethasone tests showed cortisol <100 mcg/dL (normal range <1.8 mcg/dL). She had elevations in AST to 103 IU/L (normal range 10-34 IU/L), ALT 237 IU/L (normal range 5-37 IU/L), AST 1173 IU/L (normal range 5-52 IU/L), total testosterone 170 ng/dL (normal range 15-70 ng/dL in women), DHEA-S 499 mcg/dL (normal range 45-270 mcg/dL), 17 OH progesterone 1780 ng/dL (normal range <200 ng/dL) and 24 hr urine cortisol (UFC) 14766mcg (normal range 10-100 mcg/24hr). CT abdomen showed a 1.2 cm nodule, thymic neoplasm, and bronchial carcinoid. Core liver biopsy revealed metastatic breast adenocarcinoma chromagranin A, corticotropin releasing hormone, and gastrin levels were normal. Imaging was negative for thyroid nodule, thymic neoplasm, and bronchial carcinoid. Core liver biopsy revealed metastatic breast adenocarcinoma that was negative for neuro endocrine markers CD56, synaptophysin, neuron specific enolase, and chromogranin.

Case Presentation:
CT head showed white matter disease consistent with PRES. She was psychotic and hypertensive despite using mitrapenem with multiple antihipertensives including lisinopril, albuterol, and metoprolol targeting a systolic blood pressure of 110-130. Transaminitis did not allow mifepristone escalation > 300mg/day. Ectopic ACTH Cushing's Syndrome due to Neuroendocrine Carcinoma of the Kidney. Exp Clin Endocrinol Diabetes 2008; 116(9): 515-519.

Discussion:
Ectopic ACTH Cushing's syndrome from breast cancer is extremely rare. The biopsy specimen did not stain for neuroendocrine markers and work up of other etiologies was completely unrevealing. The declining cortisol response requiring methylprednisolone de-escalation following chemo therapeutic intervention strongly suggested breast cancer as the etiology of her Cushing's.

The imaging done for evaluation of her acute psychosis revealed changes consistent with posterior reversible encephalopathy syndrome (PRES) and usual PRES characteristics. The biopsy specimen with Cushing's syndrome has been previously reported only in pediatric patients for which HCTZ and propranolol was used for hypertension management. To the best of our knowledge, this is the first case of adult PRES associated with hypertension from Cushing's ever reported. Initial utilization of intravenous etomidate in the intensive care unit due to bactrim allergy did not prevent PCP pneumonia, but the infection was successfully treated with primaquine. This strategy also avoided needing bilateral adrenalectomy which is reserved for severe Cushing's patients but carries high mortality. Hypercortisolism causes immunosuppression which not only facilitated rapid relapse of her previously treated breast cancer, but also rendered her susceptible to opportunistic infection with pneumocystis jirovecii pneumonia. Pneumocystis pneumonia has a high mortality rate, especially in patients with Cushing's, hence its prophylaxis is essential in the management of severe cases of Cushing's. Bactrim, which is the drug of choice of pneumocystis pneumonia prophylaxis, could not be utilized due to severe sulfa allergy, so dapsone was initiated. Pneumocystis pneumonia management in Cushing's was further complicated because glucocorticoid treatment is used as an adjunctive therapy. Rapidly decreasing circulating cortisol levels resulting from etomidate therapy could have potentially worsened her pneumonia. For this reason, a random cortisol level of 40mcg/dL, was initially targeted. Despite initiation of dapsone, she developed pneumocystis pneumonia, but subsequently was successfully treated with primaquine.

Conclusion:
Ectopic ACTH Cushing's syndrome from breast cancer is extremely rare, presenting with significant morbidity and mortality from opportunistic infections, psychoses, metabolic, and coagulation derangements. This case reports management of Cushing's psychosis resulting from PRES and hypertension with etomidate followed by methylprednisolone and spironolactone transition since mifepristone could not be increased in liver dysfunction. Also, it reports successful management of severe cases of Cushing's. Bactrim, which is the drug of choice of pneumocystis pneumonia prophylaxis, could not be utilized due to severe sulfa allergy, so dapsone was initiated. Pneumocystis pneumonia management in Cushing's was further complicated because glucocorticoid treatment is used as an adjunctive therapy. Rapidly decreasing circulating cortisol levels resulting from etomidate therapy could have potentially worsened her pneumonia. For this reason, a random cortisol level of 40mcg/dL, was initially targeted. Despite initiation of dapsone, she developed pneumocystis pneumonia, but subsequently was successfully treated with primaquine.