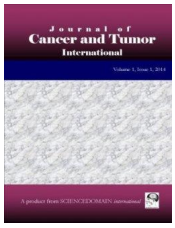

Journal of Cancer and Tumor International
2(1): 37-40, 2015, Article no.JCTI.2015.005

SCIENCEDOMAIN *international*
www.sciencedomain.org

Ectopic Adrenocorticotropin Production in a Patient with Lung Cancer: A Case Report

P. Prodduturvar[1], N. Bongu[1], S. Nauman[2] and S. Mehra[3*]

[1]Department of Internal Medicine, Vidant Medical Center, Greenville, NC, United States.
[2]Eastern Nephrology Associates, Greenville, NC, United States.
[3]Department of Cardiovascular Sciences, East Carolina University, Greenville, NC, United States.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JCTI/2015/16817
Editor(s):
(1) Jeng-Shing Wang, Antai Medical Care Cooperation Antai Tian-Sheng Memorial Hospital, Taiwan and Internal Medicine Department, Taipei Medical University, Taiwan.
Reviewers:
(1) A. Papazafiropoulou, Medicine and Diabetes Center, Tzaneio General Hospital of Piraeus, Greece.
(2) Abrão Rapoport, São Paulo Unversity, São Paulo, Brazil.
(3) I. M. Sechenov First Moscow State Medical University, Russia.
(4) Jelena Stojsic, University of Belgrade, Serbia.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=1040&id=43&aid=8832

Case Study

Received 14th February 2015
Accepted 27th March 2015
Published 15th April 2015

ABSTRACT

Various malignancies have been associated with ectopic adrenocorticotropin hormone production causing paraneoplastic Cushing's syndrome. The most common culprits are small cell lung carcinoma, carcinoid tumors and medullary cancer of the thyroid. Early suspicion and appropriate work up can help diagnose and manage the excessive adrenocorticoid state.

Keywords: Ectopic, adrenocorticotropic; Cushings; small cell cancer; paraneoplastic; metabolic alkalosis.

1. BACKGROUND

Ectopic adrenocorticotropin (ACTH) production causing paraneoplastic Cushing's syndrome has been associated with various malignancies such as small cell lung carcinoma, carcinoid tumors and medullary carcinoma of thyroid [1-4]. We present a rare case of a 61 year old male with

**Corresponding author: Email: mehras@ecu.edu;*

paraneoplastic Cushing's syndrome in association with adenocarcinoma of the lung.

2. CASE PRESENTATION

A sixty one year old male with past medical history significant for 40 pack per year tobacco abuse and alcoholism presented to our institution after sustaining an accidental fall. He had a previous admission at our institution for shortness of breath 3 months ago and at that time his work up led to a computed tomography (CT) scan of his chest, which revealed a 6.6 x 8.2 cm right lower lobe lung mass. He left the hospital against medical advice. On his present admission his blood pressure was elevated at 160/88 mm of mercury, heart rate 90 per minute, respiratory rate 20 per minute and oral temperature 37.1 degrees Celsius. Physical examination revealed an ill appearing male who appeared older than his stated age, with diminished breath sounds bilaterally and bibasilar crackles on chest auscultation. His heart sounds were regular with no murmurs or rubs heard. His abdomen was distended, non- tender, with positive fluid thrill. His upper extremities were remarkable for clubbing and had pitting edema up to thighs in his lower extremities.

His laboratory studies showed serum sodium 144 meq/L, serum potassium 2.4 meq/L, serum chloride 92 meq/L, serum bicarbonate >40 meq/L, serum blood urea nitrogen 21 mg/dl, serum creatinine 0.67 mg/dl, serum glucose 143 mg/dl, serum calcium 8.3 mg/dl and serum magnesium 1.8 mg/dl. His coagulation profile was within normal limits. His blood work 3 months ago had revealed serum sodium of 136 meq/L, serum potassium 4.1 meq/L, serum chloride 106 meq/L, serum bicarbonate 23 meq/L, serum blood urea nitrogen 8 mg/dl, serum creatinine 0.63 mg/dl and serum glucose 104 mg/dl. His urine was clear with pH 7.0, 3 + glucose and trace protein with random urinary chloride 99 meq/L and urine potassium 44.4 meq/L. His 24-hour urine free cortisol level was elevated at 8925.6 mcg/24 hr (normal- 4.0-50.0 mcg/24 hr). His serum hormone analysis showed elevated ACTH level of 731 g/ml (normal reference range: 6 to 50 g/ml).

He had a repeat CT scan of his chest, abdomen and pelvis (Figs. 1-2) that showed progression of his lung mass, with multiple enlarged mediastinal lymph nodes with multiple lesions throughout the liver. The largest lesion was in the central aspect of the liver measuring 6.1 x 8.1 cm. Also noted were multiple bony lesions and bilateral adrenal lesions. The biopsy of his liver mass showed metastatic adenocarcinoma (Figs. 3-4), consistent with lung primary, positive for CK7 and TTF1 and negative for CK20 and CDX2.

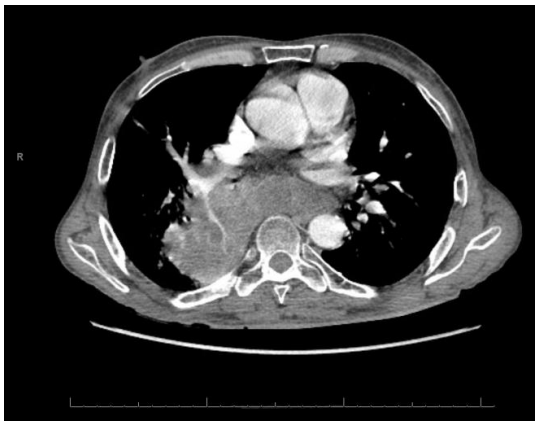

Fig. 1. CT scan of the chest showinglung mass, with multiple enlarged mediastinal lymph nodes

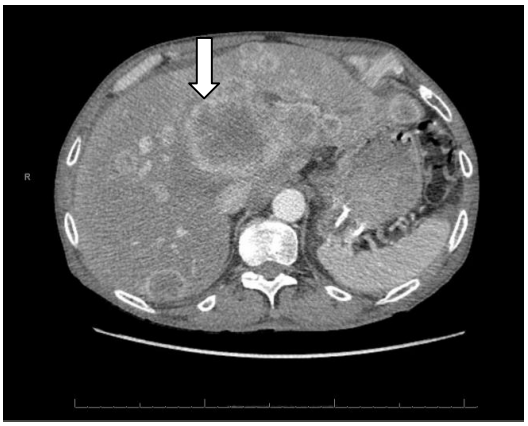

Fig. 2. CT scan of the chest and abdomen showing multiple liver lesions

Patient also had magnetic resonance imaging of his brain, which did not reveal any pituitary lesions. His transthoracic echocardiogram showed normal left ventricular systolic function with no significant valvular abnormalities.

The constellation of findings, including blood chemistry with severe hypokalemia and metabolic alkalosis, presence of anasarca, hypertension and hyperglycemia along with elevated serum ACTH and urine free cortisol with a diagnosis of adenocarcinoma of the lung was consistent with ectopic ACTH Cushing's

syndrome [5]. He was started on Ketoconazole and spironolactone, which led to normalization of his serum potassium and metabolic alkalosis [6]. However his general condition continued to deteriorate. Eventually palliative care team was consulted and because of lack of social support with no family, poor functional status, poor prognosis and patient choice, he was transferred to inpatient hospice. He died 2 months later. Although his ectopic Cushing's syndrome was detected promptly and managed appropriately his prognosis was poor because of his metastatic adenocarcinoma of the lung.

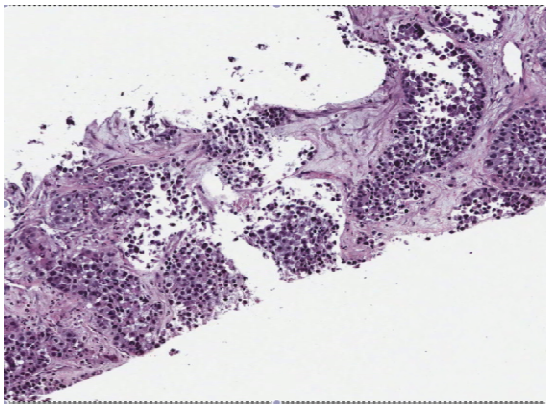

Fig. 3. H and E stained tissue of the liver core biopsy shows an infiltrate of malignant cells

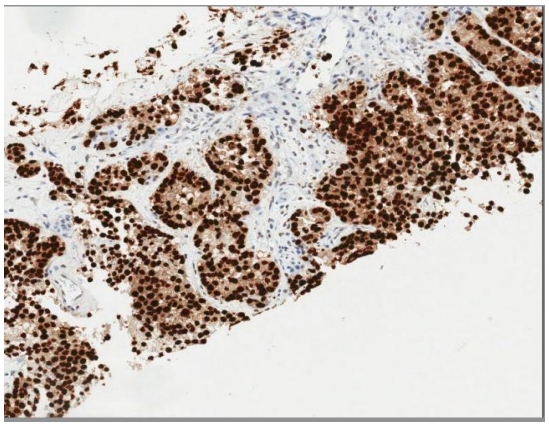

Fig. 4. TTF1 shows strong positivity, consistent. with a metastatic adenocarcinoma of lung primary

3. DISCUSSION

Ectopic ACTH production with paraneoplastic Cushing's syndrome associated with adenocarcinoma of the lung is very rare. To the best of our knowledge, we have come across very few cases associated with non-small carcinoma of lung [7-10]. The treatment of the ectopic ACTH syndrome is surgical excision of the tumor if feasible, thereby removing the source of ACTH. Unfortunately, most if not all of the metastatic cancers cannot be treated by surgical excision. For these patients, hypercortisolism can be controlled with medications like ketoconazole, metyrapone and etomidate [6,11]. Our patient was treated with ketoconazole. Most patients with overt metastases at the time of presentation die from the cancer within one to years, although patients with indolent tumors may survive for many years.

Aldosterone producing adenomas, bilateral idiopathic hyperaldosteronism and ectopic aldosterone-producing tumors could present with similar picture and should be included in the differential diagnosis [12-13].

4. CONCLUSION

Persistent hypokalemia and metabolic alkalosis in a patient with Lung cancer should prompt consideration for diagnosis of ectopic ACTH secretion and paraneoplastic Cushing's syndrome. Although most commonly seen with small cell lung carcinoma and other neuroendocrine tumors, clinicians should consider this diagnosis in patients with adenocarcinoma of lung and treat accordingly to improve the outcome of patients.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Shepherd FA, Laskey J, Evans WK, Goss PE, Johansen E, Khamsi F. Cushing's syndrome associated with ectopic corticotropin production and small-cell lung cancer. J Clin Oncol. 1992;10:21-27.
2. Delisle L, Boyer MJ, Warr D, et al. Ectopic corticotropin syndrome and small-cell

carcinoma of the lung. Clinical features, outcome, and complications. Arch Intern Med. 1993;153:746-752
3. Gandhi L, Johnson BE. Paraneoplastic syndromes associated with small cell lung cancer. J Natl Compr Canc Netw. 2006;4:631-638.
4. Amer KM, Ibrahim NB, et al. Lung carcinoid related Cushing's syndrome: Report of three cases and review of the literature. Postgrad Med J. 2001;77(909):464-7.
5. Singer W, Kovacs K, Ryan N, Horvath E. Ectopic ACTH syndrome: clinicopathological correlations. J Clin Pathol. 1978;31:591-598.
6. Winquist EW, Laskey J, Crump M, Khamsi F, Shepherd FA. Ketoconazole in the management of paraneoplastic Cushing's syndrome secondary to ectopic adrenocorticotropin production. J Clin Oncol. 1995;13:157-164.
7. Yoh K, Kubota K, et al. Cushing's Sydnrome associated with Adenocarcinoma of the Lung. Lung. Internal Medicine. 2003;42(9):831-833.
8. Myers EA, Hardman JM, Worsham GF, Eil C. Adenocarcinoma of the lung causing ectopic adrenocorticotropic hormone syndrome. Arch Intern Med. 1982;142: 1387-1389.
9. Tsukioka T, Inoue K, et al. A resected case of adrenocorticotropic hormone-producing lung adenocarcinoma. The Journal of the Japanese Association for Chest Surgery. 2006;20(5):756.
10. 10.Boon ES, Leers MP, Tjwa MK. Ectopic Cushing's syndrome in a patient with squamous cell carcinoma of the lung due to CRF-like production. Monaldi Arch Chest Dis. 1994;49:19-21.
11. Verhelst JA, Trainer PJ, Howlett TA, et al. Short and long-term responses to metyrapone in the medical management of 91 patients with Cushing's syndrome. Clin Endocrinol (Oxf). 1991;35:169-178.
12. Mattsson C, Young WF Jr. Primary aldosteronism: Diagnostic and treatment strategies. Nat Clin Pract Nephrol. 2006;2:198.
13. Young WF. Primary aldosteronism: Renaissance of a syndrome. Clin Endocrinol (Oxf). 2007;66:607.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=1040&id=43&aid=8832