



Original Article

A Study on Hypercalcaemia in Patients with Bronchial Carcinoma: At a Tertiary Level Hospital

I Mahmood¹, M K Rahman², M A Haque², M M R Khan², M M H Chowdhury²,
A Iqbal³, A R M S Ekram⁴, M H Rashid⁵, M J Alam⁶

Abstract

Bronchial carcinomas often present with some paraneoplastic features which may present even before the offending tumor has been detected. Hypercalcaemia is one of the most common paraneoplastic symptoms. In this prospective cohort study attempts has been made to demonstrate the incidence and pattern of hypercalcaemia in bronchial cancers. The study was undertaken at the Medicine Department of Rajshahi Medical College Hospital, Rajshahi in between July, 2009 to December 2009. In this study hypercalcaemia was found in 30.76% cases with anorexia, dyspepsia, nausea, polyuria, polydipsia and constipation being most common features related to it.

TAJ 2009; 22(2): 245-247

Introduction

Hypercalcaemia is common in patients with bronchial carcinoma and some other malignancies. They may be the presenting finding or the first sign of bronchial carcinoma or its recurrence. There are three main mechanisms of hypercalcaemia in malignancy:

- PTH-rP related hypercalcaemia
- Osteolytic metastases
- Tumor production of calcitriol

Most common cancers associated with hypercalcaemia are *breast cancer, lung cancer, and multiple myeloma*. To assess the incidence and pattern of hypercalcaemia in patients with bronchial carcinoma. Serum calcium level was estimated.

Material and Methods

A prospective cohort study on 52 confirmed (by ultra sonogram guided fine needle aspiration cytology) bronchial carcinoma patients admitted from July, 2009 to December 2009 in Medicine Department of Rajshahi Medical College Hospital was carried out. The clinical and biochemical parameters recorded were: age, sex, underlying medical illness and serum calcium levels. The localization of the tumors was done by chest x-ray and ultra sonogram. The clinical presentation of hypercalcaemia, if any was noted. Hypercalcaemia was defined as a serum calcium level exceeding 10.5 mg/100 ml.

Results

Among the subjects 51(98.07%) were male and 1(1.93%) were female. The only female patient

¹ Associate Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.

² Assistant Professor, Department of Medicine, Rajshahi Medical College, Rajshahi.

³ Indoor Medical Officer, Department of Medicine, Rajshahi Medical College, Rajshahi.

⁴ Professor & Head, Department of Medicine, Rajshahi Medical College, Rajshahi.

⁵ Assistant Professor, Department of Hepatology, Rajshahi Medical College, Rajshahi

⁶ Assistant Professor, Department of Community Medicine, Shaheed Ziaur Rahman Medical College, Bogra.

did not present with hypercalcaemia. All were heavy smokers or ex-smokers. The histological types were 8 (15.38%) small cell carcinoma and 44 (84.62%) non-small carcinoma. All were primary tumors. The mean age was 63.11 ± 10.22 years. The Hypercalcaemia was found in 16 (30.76%) patients. The different histological types associated with PNS were as follows: Hypercalcaemia -all 16 patients (100%) were associated with non small cell carcinoma; 12 (75%) patients with squamous cell carcinoma and 4 (25%) patients with adenocarcinoma. The results are shown in the following tables.

Table 1: Correlation of Hypercalcaemia with Histological Types of Bronchial Carcinoma

Histological type	Incidence in this study	Occurrence of Hypercalcaemia
Squamous cell carcinoma	24(46.15%)	12 (50%)
Adenocarcinoma	15(24.85%)	4 (26.67%)
Small cell carcinoma	8 (15.38%)	-
Large cell carcinoma	5 (9.62%)	-

Table 2: Correlation of Hypercalcaemia with other disease entities

Concomitant disease	Incidence in this study	Occurrence of Hypercalcaemia
Diabetes mellitus	22 (42.30%)	7(31.82%)
Hypertension	14 (26.92%)	3 (21.43%)
COPD	16 (30.76%)	6 (37.5%)

Table 3: Presenting complains of hypercalcaemia

Presenting complains for hypercalcaemia	Incidence
Polyuria and Polydipsia	8(50%)
Renal colic	3(18.75%)
Lethargy	5(31.25%)
Anorexia, Nausea	9(56.25%)
Dyspepsia	9(56.25%)
Peptic ulceration	2(12.5%)
Constipation	11(68.75%)
Depression	1(6.25%)
Drowsiness	2(12.5%)
Impaired Cognition	-

Discussion

The fact that bronchial carcinoma is caused by carcinogens and tumor promoters inhaled through cigarette smoking is fully corroborated in this study where almost 100% patients were either

heavy smokers or ex-smokers. Hypercalcaemia, which is the distant effect of underlying carcinoma can present early, well before the primary lung lesion produces local symptoms and even when the tumor is undetected or very small. The signs and symptoms of hypercalcaemia produced by the bronchial carcinoma can be detected early by clinical and biochemical means. The bigger the tumor, the more florid are the signs and symptoms of hypercalcaemia. The diagnosis of occult tumor associated with hypercalcaemia requires a high degree of suspicion and careful exclusion of other causes of hypercalcaemia, such as; hyperparathyroidism, Familial Hypocalciuric hypercalcaemia, Lithium, Vitamin D toxicity, Thiazide Diuretics, Glucocorticoid deficiency, Thyrotoxicosis, Milk Alkali Syndrome, Paget's disease and other malignancies like breast, multiple myeloma, etc. But still on some occasions the tumor may remain undetected and this will lead to delay in initiation of treatment.

Hypercalcaemia is the commonest PNS of bronchial carcinoma and is most commonly associated with the squamous cell carcinoma type, but can be associated with the other non-small cell bronchial carcinomas, i.e. adenocarcinoma and large cell undifferentiated. Hypercalcaemia is uncommon at presentation but becomes apparent as the tumor progresses. Its pathogenesis is related to hormone production and is called humeral hypercalcaemia of malignancy.

In our study hypercalcaemia was present in 30.76% of the patients, which co-relates well with the other studies. Hypercalcaemia was most common in Squamous cell carcinoma (75%) and to a lesser extent in Adenocarcinoma (25%). It did not show any specific correlation with other concomitant diseases. The most common presenting complains with hypercalcaemia were Polyuria and Polydipsia (50%), Anorexia, Nausea (56.25%), Dyspepsia (56.25%), Constipation (68.75%).

Conclusion

Hypercalcaemia is common in patients with bronchial carcinoma. These patients may clinically present with clinical features related to

hypercalcaemia. It is therefore important to consider the possibility of bronchial carcinoma in smokers who present with signs, symptoms and biochemical evidence of hypercalcaemia and to investigate them thoroughly.

References

1. Mewan A, Moody PM, Sugratan TN, et al. Environmental health. Bull World Health Organ. 2000; 78:1306-15.
2. Ende E : Paraneoplastic syndromes. Am J Hospital Palliate care 2004; 21:85-6.
3. Van Wichest P. Paraneoplastic syndrome. Problems & Importance of early diagnosis and treatment of neoplasms. Med Klin 1971; 66:1461-5.
4. Oura S. Malignancy associated hypercalcemia. Nippon Rinsho 2003;61:1006-9.
5. Van Roh, Cerny T, Jos SR, et al. SIADH in small cell Bronchial Carcinoma, Scheneiz Med Wodensche. 1991;121:1271-82.
6. Bataller, L, Dalmau J. Paraneoplastic neurologic syndromes: approaches to diagnosis and treatment. Semin Neurol 2003;23:214-5.
7. Voltz R Paraneoplastic neurological syndromes: an update on diagnosis, pathogenesis, and therapy. Lancet Neurol 2002;1:294-305.
8. Finster J, Bodenteich A, Drlicek M. Atypical Paraneoplastic syndrome associated with anti-Yo antibodies. Clin Neuropathol 2003;22:137-40.
9. Shams'ili S, Grefkens J, de Leeuw B, et al. Paraneoplastic cerebellar degeneration associated with antineuronal antibodies: analyses of 50 patients. Brain 2003;126:1409-18.
10. Pedersen LM, Milman N. Diagnostic significance of platelet count and other blood analysis in patients with lung cancer. Oncol Rep 2003;10:213-6.
11. Johnson RA, Roodman GD. Hematologic manifestation of malignancy. Dis Mon 1969;35:721-68.
12. Raz I, Shinar E, Polliack A. Pancytopenia with hypercellular bone marrow-a possible paraneoplastic syndrome in carcinoma of the lung: a report of three cases. Am J Hematol 1984;16:403-8.
13. Koistinen P, Kinnula V, Timonen T. Aplastic anaemia as a paraneoplastic syndrome in lung cancer. Eur J Cancer 1990;26:651-3.
14. Bahrain Medical Bulletin, Vol. 27, No. 4, December 2005, A Study of Paraneoplastic Syndrome Patterns in Patients with Bronchogenic Carcinoma. Vurgese Thomas Abraham, MD, MRCP (UK)* Bahl Sunil Radhakrishna, MBBS, MD** Mapkar Osman Abdulwahab, MBBS, MD*
15. SJS July-03 Hypercalcaemia of Malignancy, Grill V, Martin TJ. Hypercalcaemia of malignancy. Rev Endocr Metab Disord. 2000 Nov;1(4):253-63. Mundy GR, Guise TA. Hypercalcaemia of malignancy. Am J Med. 1997 Aug;103(2):134-45. Major P, et al. Zoledronic acid is superior to pamidronate in the treatment of hypercalcaemia of malignancy: a pooled analysis of two randomized, controlled clinical trials. J Clin Oncol. 2001 Jan 15;19(2):558-67

All correspondence to:

I Mahmood

Associate Professor

Department of Medicine

Rajshahi Medical College, Rajshahi