# Hypocalcemia After Commencing Cetuximab in a Patient With Oesophageal Cancer at Baze University Hospital, Abuja.

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#### Abstract

Currently, there is increasing use of epidermal growth factor receptor (EGFR) monoclonal antibodies in the management of cases with advanced cancers. These medications are found to be associated with complications, including dyselectrolytaemia. Cetuximab, an EGFR monoclonal antibody is known to cause electrolyte abnormalities, including hypomagnesemia, hypokalemia, and hypocalcemia. We report a female patient admitted to our Hospital with advanced oesophageal cancer who developed symptomatic hypocalcemia after commencing cetuximab. Hypocalcaemia was confirmed by measurement of serum total calcium level. Monitoring of electrolyte levels before and after commencement of cetuximab is therefore recommended for early identification of any derangement.

Key words: Hypocalcemia, Cetuximab, Oesophageal Cancer.

### Introduction

Hypocalcaemia is a fatal electrolyte disorder defined as corrected serum total calcium levels <2.12 mmol/L (8.5 mg/dl).<sup>1</sup> Hypocalcaemia can be lifethreatening if not promptly identified and appropriately treated. The cause of hypocalcaemia varies widely and is highly dependent on the interaction between parathyroid hormone, phosphorus, vitamin D and bone metabolism. The clinical manifestations of hypocalcaemia can range from asymptomatic at mild deficiency to life-threatening symptoms like seizures, heart failure, psychiatric manifestations etc.<sup>2</sup>

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Hypocalcaemia may occasionally develop in the course of treatment with drugs used in everyday clinical practice; including antiepileptics, aminoglycosides, proton pump inhibitors, and chemotherapeutic drugs.<sup>3,4</sup> Hypocalcemia associated with drug treatment can be easily missed in hospitalized patients as a consequence of coexistence of multiple factors which may contribute to low serum calcium levels.Cetuximab, an epidermal growth factor receptor (EGFR) monoclonal antibody, is usually utilized in combination with chemotherapy for the management of metastatic or recurrent colorectal cancer, head and neck cancers as well as esophageal cancer.<sup>5,6,7</sup> it is known to cause electrolyte abnormalities, including hypomagnesemia, hypokalemia, and hypocalcemia.<sup>6</sup>

We present the case of a patient who developed symptomatic hypocalcaemia with hypomagnesaemia after Cetuximab treatment for advanced oesophageal adenocarcinoma.

### **Case Presentation**

A 64 year old female patient was referred to our hospital with chief complaint of epigastric pain, dysphagia and progressive weight loss. A diagnosis of advanced oesophageal adenocarcinoma was made for which she has had three cycles of chemotherapy (cisplatin and paclitaxel) as well as other palliative treatment from the referral hospital

An endoscopic gastro-oesophageal biopsy was performed on the  $18^{th}$  of August 2023, which confirmed the histopathological diagnosis of advanced a d e n o c a r c i n o m a of the o e s o p h a g u s. Immunohistochemistry result revealed that the tumour is CK7 positive suggesting an oesophageal origin. Carcinoembryonic antigen was slightely elevated and serum electrolyte levels were essentially normal except for moderate hypokalaemia, which was corrected with KCL infusion.

Patient received first course of cetuximab (a chimeric EGFR monoclonal antibody) on the  $24^{th}$  of October 2023. A single dose of 400mg in 1 litre of normal saline was administered; five days later she developed twitching of the muscles of the upper limbs, muscle cramps, and irritability with personality

changes. An urgent examination of blood electrolyte was performed. Serum calcium level was 1.80 mmol/L and magnesium of 0.7mmol/L. Intravenous calcium was administered 2g of 10% calcium gluconate in Normal saline 12 hourly. She experienced significant clinical improvement with complete resolution of hypocalcemia symptoms 3 days after, with corrected calcium of 2.2mmol/L. She was subsequently maintained on oral calcium, magnesium and vitamin D supplementation. The second course of cetuximab was administered on the 18<sup>th</sup> of November 2023; she developed similar hypocalcaemia symptoms four days later with measured albumin-corrected calcium of 1.74mmol/L, which was immediately corrected with intravenous calcium gluconate infusion.

## Discussion

Oesophageal cancer has become the 8th most common cancer type and the 6th leading cause of cancer mortality with over 400, 000 deaths annually worldwide.<sup>7</sup>

Cetuximab, a monoclonal antibody of EGFR, could improve outcomes when given in combination with chemotherapy/radiotherapy in several tumors, including advanced colorectal adenocarcinomas, squamous-cell head and neck cancer as well as esophageal cancer.<sup>7</sup> Lu et al. argued that cetuximab could improve clinical therapeutic effects, prolong survival time, and reduce therapeutic side effects in the treatment of intermediate and advanced esophageal cancer.<sup>8</sup>

Cetuximab induced hypomagnesaemia may be related to its inhibition on the EGFR receptors highly expressed in the ascending limb of the Loop of Henle, leading to impaired renal resorption of magnesium via the transient receptor potential melastatin subtype6 (TRPM6) ion channel. PTH suppression in severe hypomagnesaemia may be mediated by an increase in G-alpha subunit activation of the calcium-sensing receptor, leading to severe hypocalcaemia.<sup>5</sup> Yamashiro K and coworkers demonstrated that electrolyte abnormalities developed in 58.3% of patients undergoing cetuximab therapy, with the incidence of hypokalemia, hypomagnesemia, and hypocalcemia documented as 25.0%, 29.2%, and 25.0%, respectively.<sup>6</sup> Similarly, Wang Q and coworkers in a pooled analysis of 25 randomized clinical trials demonstrated that the incidence of hypomagnesemia related to anti-EGFR monoclonal antibodies was 34.0 % and that for hypokalemia and hypocalcemia were 14.5% and 16.8%, respectively.<sup>9</sup>

## Conclusion

We have presented a case of hypocalcemia diagnosed after the commencement of cetuximab therapy in a patient with advanced oesophageal adenocarcinoma. Drug-induced hypocalcemia in

clinical practice is not an uncommon condition, but very few serious cases have been reported. It is essential to recognize the clinical signs of hypocalcemia as well as monitor serum calcium levels, even in unlikely cases, and to promptly initiate the appropriate management if it occurs.

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