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Increasing Skin Pigmentation Following Severe Head Trauma: All That Glitters Is Not Gold!

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ABSTRACT

We report the case of a 67-year-old man who was admitted to our Intensive Care Unit because of traumatic brain injury. During his prolonged hospitalization, gradual darkening of the skin all over his body was observed. An excess corticotropin (ACTH) production syndrome was considered. The patient's hormone study showed high levels of ACTH (978 pg/ml) with normal cortisol levels. Extensive clinical and laboratory investigations revealed adenocarcinoma of the colon, which was likely the site of the ectopic ACTH production. This is a very rare manifestation of paraneoplastic syndrome during the course of colon adenocarcinoma. The most important feature of this case report is that this rare syndrome was accidentally discovered, in a patient hospitalized for unrelated reasons, by simple clinical investigation.

LEARNING POINTS

- Careful physical examination can provide valuable information which can lead to the diagnosis of rare and unexpected syndromes.
- Common clinical wisdom says that all signs and symptoms must fit one diagnosis, but in some cases there is more than one diagnosis.

KEYWORDS

ACTH; colon adenocarcinoma; ectopic corticotropin production.

INTRODUCTION

Ectopic production of adrenocorticotropic hormone (ACTH) from colon cancer is very rare. We report the case of a patient with an ACTH-producing adenocarcinoma of the colon who was admitted to hospital for an unrelated reason.

CASE PRESENTATION

A 67-year-old man was admitted to hospital after an accidental fall. On admission, the patient had a Glasgow Coma Scale (GCS) score of 13, a respiratory rate of 20 breaths per minute, blood pressure of 120/80 mmHg and heart rate of 120 beats/min. The rest of his physical examination was unremarkable. A CT scan of the brain revealed a frontal haemorrhagic contusion, frontal skull fracture, traumatic subarachnoid haemorrhage and a small subdural haematoma. Except for a history of unintended weight loss (5–6 kg during the previous year), no other health problems were reported. However, 24 h after admission the patient's mental status deteriorated (GCS: 7) due to

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cerebral oedema and he developed respiratory failure due to aspiration pneumonia (PO2/FiO2: 250). The patient was intubated and transferred to the ICU. A tracheostomy was performed on the 15th day of hospitalization because of a continued need for mechanical ventilation and prolonged coma (GCS: 7). The patient experienced several septic episodes and norepinephrine was administered over a long period. Blood cultures yielded *Enterococcus faecalis*, *Pseudomonas* spp. and *Acinetobacter baumannii*. During this lengthy hospitalization, the attending physician noticed a gradual darkening of the patient's skin all over his body. This observation along with the haemodynamic instability, raised the suspicion of possible adrenal insufficiency. The ACTH was 987 pg/ml (normal range: 9–52 pg/ml) and the cortisol level at 8:00 a.m. was 23 µg/ml (normal range: 5–25 µg/ml), so adrenal insufficiency was ruled out. Another interesting feature was persistent metabolic alkalosis and hypokalaemia. The possibility of a paraneoplastic syndrome was considered. However, chest and abdomen CT scans were negative for neoplastic disease. The adrenals were normal. On the 30th day after admission, the patient passed stools mixed with blood and a colonoscopy was performed. An ulcerated neoplastic mass 5 cm from the anus, extending to 15 cm and partially obstructing the colon was found. The biopsy showed ulcerated adenocarcinoma of the colon, grade II, with signs of chronic inflammation.
An operation was planned but the patient died from refractory septic shock 35 days after admission.

DISCUSSION

The present report describes a case of colon adenocarcinoma-related ACTH production, which is very rare according to our knowledge. All reviewed articles are single case reports. In an extensive related review, Beuschlein and Hammer found only five cases of ectopic production of ACTH originating from colon carcinomas, after reviewing 530 published case reports on ectopic ACTH production[1]. According to their review[1], the four most common causes of ectopic proopiomelanocortin (POMC) production are small cell carcinomas of the lung (27%), bronchial carcinoids (21%), islet cell tumours of the pancreas (16%) and thymic carcinoids (10%).
Current data demonstrate that virtually all tissues produce small amounts of a biologically inactive precursor ACTH molecule, probably POMC[2, 3]. ACTH is produced via the proteolytic conversion of POMC, in the anterior pituitary, by prohormone convertase PC 1/3, along with β-endorphin and β-lipotropin[4]. In physiological conditions, the POMC gene is transcripted using the P3 promoter in non-pituitary tissues, thus generating a shorter mRNA that is not translated. The non-pituitary ACTH-secreting tumours use the pituitary P2 promoter or the P1 promoter, generating a mRNA which is as long as the mRNA produced in the pituitary[5]. Therefore, the ectopic ACTH syndrome represents a cancer-induced amplification of a biological process taking place in the normal cells from which the cancer originates.
The development of hypercortisolism and Cushing's syndrome features in patients with ectopic POMC syndrome varies regarding severity and rapidity of onset[1]. This explains the absence of Cushing's syndrome signs in our patient. Hypercortisolism is occasionally intermittent and this could explain our patient's normal cortisol levels.
As previously noted, neoplasms of the colon are infrequently associated with ACTH production. We must admit that the connection between the colon cancer and the ACTH production in this case report is not well established as we only ruled out other possible causes of ectopic ACTH production through diagnostic imaging. Unfortunately, the cancer was not removed as a post-operative fall in ACTH levels would have been proof of ectopic ACTH production.

CONCLUSION

We believe that the presented case is interesting because of the syndrome's rarity and its accidental identification.

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