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Case Report

A Rare Cause of Severe Metabolic Alkalosis in the Emergency Room

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Abstract

Severe metabolic alkalosis in the context of the discovery of pulmonary neoplasia in the emergency room: diagnosis, physiology and treatment options of paraneoplastic Cushing's syndrome.

Keywords: Cushing's syndrome; Hypokalaemia; Metabolic alkalosis; Paraneoplastic

Case

We report the case of a 67-years old woman who presents to the emergency room with suspicion of pneumonia. She has been suffering for ten days from a deterioration of her general condition, with asthenia, increasing dyspnea, cough but no pyrexia or sputum. A chest x-ray taken a few days ago showed a postero-basal infiltrate of the right lung.

Her attending physician started antibiotic therapy with Clarithromycin a few days ago. Despite this, the evolution is unfavorable, and the patent is sent to us for hospital care.

Her medical history has reported arterial hypertension (treated daily with Losartan), hypercholesterolemia, urolithiasis, and heavy active smoking since she was 14 years old.

The hemodynamic and ventilatory parameters are marked by a slight hypoventilation and arterial hypertension. Oxygen saturation is moderately reduced (82% in ambient air) and the patient does not have a fever. The clinical examination reveals a puffy face and an accentuated skin coloration of the upper half body. The abdomen is plethoric but not painful. The lower limbs are unremarkable.

The blood test shows hyperleukocytosis (21600/), severe hypokalaemia (1.5mmol / L), greatly increased bicarbonates (64mmol / L), moderate renal failure (urea 116mg / dL - creatinine 1.59mg / dL), disrupted enzymology (LDH 974 IU / L - CPK 944 IU / L), NT-pro BNP at 13233pg / mL and TSH at 0.02mU / L.

The ECG (Figure 1) carried out in the emergency room shows a regular sinus rhythm with signs of severe hypokalaemia (increase in QT space, disappearance of T wave, outline of a U wave, ST segment in S italic lying down).

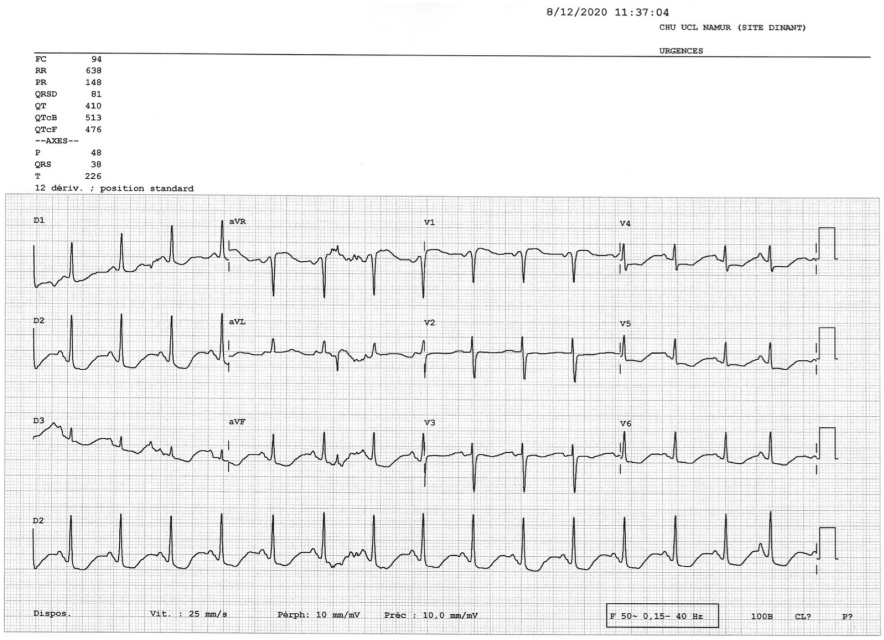

Figure 1: ECG at entrance.

An analysis of the arterial blood is then carried out, highlighting a severe metabolic alkalosis (pH 7.73) with mild hypoxemia (PaO2 44 mmHg / 5.85 kPa) and hypercapnia (PaCO2 62 mmHg / 8.25 kPa), bicarbonates 82 mmol / L, lactates 3.7 mmol / L and a severe hypokalaemia at 1.2 mmol / L.

Analysis of the urinary spot reveals almost no losses of sodium and potassium, probably linked to the high potassium depletion already present.

An emergency thoraco-abdominal CT scan (Figure 2) reveals a right hilar mass associated with mediastinal lymphadenopathy and retro obstructive atelectasis. In addition, an image of intrahepatic dissemination is observed. The adrenal glands are unremarkable.

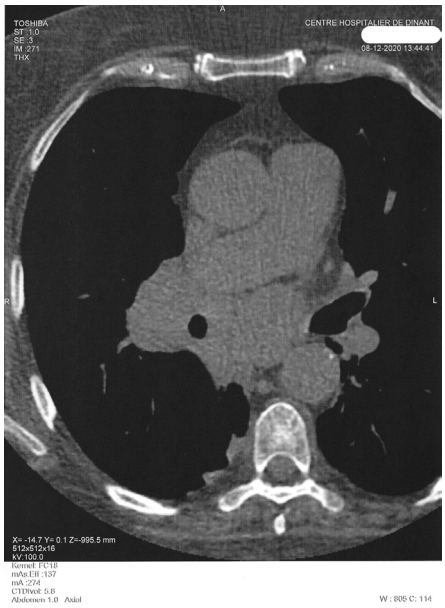

Figure 2: Right hilar mass.

A small cell bronchial carcinoma is then suspected, which will be quickly confirmed by pathological analysis following a bronchial fibroscopy performed the next day. This cancer will be staged cT2 N2 M1c (i.e. stage IV-B).

A paraneoplastic Cushing's syndrome is also demonstrated, with a blood level of ACTH at 90.50 pmol/L (standard < 10pmol/L), cortisol (collected at 8 a.m.) above 3393 nmol/L (standard <606 nmol/L) and urinary free cortisol measured at 13145 nmol / L.

The decision was quickly made to start treatment with chemotherapy (Carboplatin-VP16) and immunotherapy (Atezolizumab). The clinical course is rapidly unfavorable, and the patient will die 20 days after her admission to the hospital.

Paraneoplastic Cushing's syndrome

1° Frequency: Paraneoplastic Cushing's syndrome is a real diagnostic and therapeutic challenge. It represents about 10% of Cushing ACTH dependent cases [1]. It is a rare disease, often serious due to the severity of hypercortisolism [2]. It is therefore a minority entity compared to Cushing's disease by corticotropic pituitary adenoma.

2° Physiopathology: Cushing's syndrome is the clinical expression of a permanent and unrestrainable hypersecretion of cortisol (or very rarely of corticotropin-releasing hormone). The precise mechanism that initiates ectopic hormonal synthesis and release during the neoplastic transformation at a specific time point stills remains to be defined [1-4]. The clinical presentation of hypercortilonism linked to ectopic ACTH secretion is sometimes strictly identical to that of Cushing's disease, which makes difficult diagnosis [1-3]. Certain biological arguments, in particular deep hypokalaemia, the intensity of the biological hypercorticism and the very high plasma concentration of ACTH are strongly suggestive of a paraneoplastic Cushing syndrome [5]. The ectopic ACTH syndrome is caused by abnormal expression of the Pro-Opiomelanocortine (POMC) gene product arising from non pituitary tumours in response to ectopic activation of the pituitary-specific promoter of this gene [1,6]. The first description of paraneoplastic Cushing syndrome was reported by Brown in 1928 [7,8].

3° Diagnostic: This ectopic secretion is secondary to neuroendocrine tumors of variable size and location, but the most frequent (8-20%) of which are endocrine tumors of the lung (then come in descending order: thymic tumors, pancreatic carcinomas, medullary thyroid cancers and pheochromocytomas) [6,9]. Tomography imaging of the cervical, thoracic and abdominal regions makes it possible to investigate the areas most often implicated. Sometimes the tumor remains occult (30 to 50% of cases of paraneoplastic cushing syndrome).

The positive diagnosis of ACTH dependent cushing syndrome is based on 24 hour urinary free cortisol measurements and circulating ACTH assay. In Cushing's disease, the hypohyseal adenoma is sensitive to the strong braking test (dexamethasone) and to corticoliberin stimulation (CRH) or Dermopressin test, unlike the ACTH-secreting neuroendocrine tumor which is most often characterized by an autonomy of secretion and therefore by an insensitivity to these different tests [10]. The CRH hypohyseal stimulation test offers the best specificity and sensitivity [8].

3° Clinical: It takes several weeks of corticosteroid impregnation before developing classic Cushing syndrome, which may explain the very limited number of paraneoplastic hypersecretions with clinical expression. This, when it exists, is then usually dominated by weight loss, asthenia, arterial hypertension, proximal amyotrophy and edema. Biological disturbances are inconsistent: hyperglycemia, hypokalaemia, metabolic alkalosis. Paraneoplastic Cushing syndrome, when it exists, seems to be an independent factor of poor prognosis [1,11].

4° Treatments: Given the rarity of endocrine paraneoplastic syndromes, there is a paucity of prospective clinical trials to guide management [1].

Management is based on first identifying the secreting tumor. In the absence of an identifiable tumor, hypercorticism should be treated medically, by inhibiting steroidogenesis [10]. Ketoconazole, an imidazole antifungal, is indicated as a first-line treatment, or Metyrapone (a reversible 11 B-hydroxylase inhibitor), sometimes combined to enhance the control of severe hypercortisolemia [11]. If parenteral therapy is required, then intravenous Etomidate is rapidly effective in almost all case [10]. The curative treatment of the tumor is based on the most complete possible surgical excision with node dissection, which conditions the prognosis in a major way. In patients with ACTH-dependent Cushing's syndrome who underwent a noncurative surgery or for whom surgery was not possible, it is proposed a bilateral adrenalectomy for occult or metastatic ectopic ACTH secretion or as a life preserving emergency treatment in patients with severe ACTH-dependent disease who cannot be promptly controlled by medical therapy [1,10].

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All authors have completed the ICMJE uniform disclosure and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Conflict of Interest

No conflict of interest as conditions mentioned in the above statement. This study was conducted in accordance with the Declaration of Helsinki.

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