

Sudden Respiratory Failure in a Patient with Cushing's Syndrome

Sara Lemoinne¹, Jean- Luc Baudel¹, Arnaud Galbois¹, Georges Offenstadt^{1,2} and Eric Maury^{*,1,2}

¹Réanimation Médicale, Université Pierre et Marie Curie-Paris 6, France

²INSERM, UMR-S 707; APHP, Hôpital Saint Antoine, F-75012, Paris, France

Abstract: A 79 year-old patient with prostate cancer related Cushing's syndrome was referred to ICU for acute respiratory distress occurring two days after introduction of mifepristone. *Pneumocystis jirovecii* pneumonia was diagnosed. Despite anti pneumocystis therapy and supportive treatment, the patient died of multiple organ failure. The relationship between mifepristone and Cushing's syndrome and potential implications are discussed.

Keywords: Acute respiratory failure, *Pneumocystis jirovecii*, steroids, Cushing's syndrome.

Cushing's syndrome is a classical but rare disease resulting from exposure to excessive concentrations of glucocorticoid. When surgery is not feasible medical therapy should be discussed. A 79 year-old man was admitted to intensive care unit for acute respiratory distress. He had been treated for prostate cancer for 12 years, with radiotherapy and hormonotherapy. The last prostate-specific antigen (PSA) level was (0, 24 ng/ml) while pelvis MRI disclosed irregular prostate consistent with radiotherapy after-effects without any sign of recurrence of malignancy. He was referred 3 months before to the general ward because of depression, severe systemic hypertension, hypokalaemia and diabetes mellitus. Endogenous hypercortisolism was diagnosed. Static and dynamic analysis: [plasma cortisol level at 8 am : 1564 nmol/l (normal<200 nmol/l), 24h urinary free cortisol excretion: 20200 nmol/24h (normal <270 nmol/24h), no suppression of plasma cortisol with low dose of dexamethasone, adrenocorticotrophic hormone (ACTH) : 145 ng/l.(normal<50 ng/l)] were in favour of an ACTH dependent Cushing's syndrome. Considering normal pituitary MRI, final diagnosis was paraneoplastic Cushing's syndrome. CT scan imaging of the thorax (Fig. 1), abdomen and pelvis disclosed bilateral adrenal hyperplasia but did not show any thoracic or pancreatic tumours which are the most common tumours responsible for ectopic ACTH secretion.

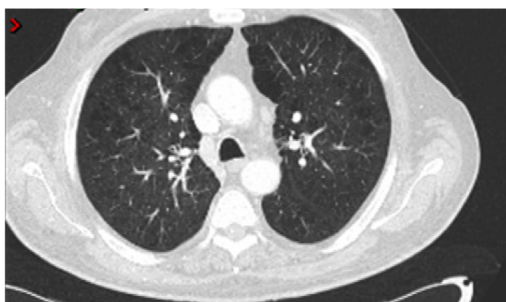


Fig. (1). CT scan of the thorax before pneumoniae, searching for a chest tumor secreting ACTH.

The patient was given mifepristone (a potent glucocorticoid receptor antagonist [1]). On the second day of this treatment, the patient complained of shortness of breath and cough. Temperature was 38,6°C, respiratory rate was 35/minute, blood pressure was 120/72 mmHg. Physical examination was unmodified except for bilateral crackles. Arterial blood gases on room air were: pH=7.38, PaO₂=37 mmHg, PaCO₂=40 mmHg, HCO₃=28 mmol/L. Chest X-ray and CT scan showed bilateral interstitial infiltrates (Fig. 2). The white cell count was 4750/mm³, lymphocyte count was 630/mm³, (CD4:29/mm³). Screening for HIV was negative. The patient was admitted to intensive care unit. A fiberoptic bronchoscopy was performed. Examination of the bronchoalveolar lavage disclosed no bacterial strain but *Pneumocystis jirovecii* was detected by immunofluorescence. Despite supplemental oxygen the patient had to be intubated and placed on mechanical ventilation. Intravenous sulfamethoxazole and trimethoprim 100 mg/kg/24h and 20 mg/kg/24h respectively and methylprednisolone 240 mg daily during 3 days were begun. Mifepristone was stopped. Despite this treatment and supportive care, respiratory status did not improve. The patient developed *P. aeruginosa* pneumonia, multiple organ failure occurred finally died eleven days after ICU admission.

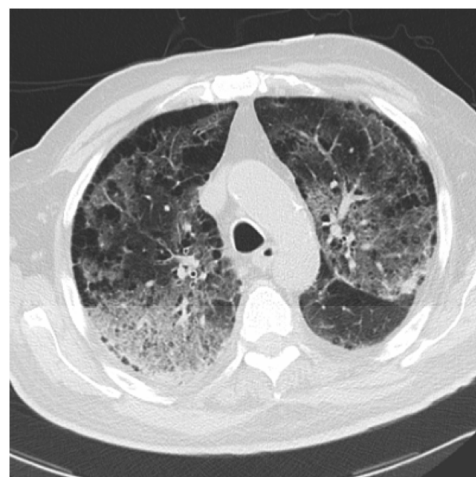


Fig. (2). CT scan of the thorax performed two days after the acute respiratory distress onset.

*Address correspondence to this author at the Service de Réanimation Médicale, Hôpital Saint-Antoine, Assistance Publique-Hôpitaux de Paris, 184 rue du Faubourg Saint-Antoine, 75571 Cedex 12, Paris, France; Tel: 33 (1) 49 28 23 18; Fax: 33 (1) 49 28 21 45; E-mail: eric.maury@sat.ap-hop-paris.fr

The post-mortem examination did not found any other malignancy than prostate cancer.

Pneumocystis jiroveci pneumonia has previously been reported in patients with Cushing's syndrome [2]. Asymptomatic carriage of pulmonary *Pneumocystis jiroveci* has been observed in animals following long term corticoid treatment. This suggests a potential interest for primary prophylaxis towards *Pneumocystis jiroveci* in these patients.

The second remarkable issue of this case is that *Pneumocystis jiroveci* pneumonia seems to have been abruptly triggered by mifepristone treatment. *Pneumocystis jiroveci* pneumonia has already been reported in patients with Cushing's syndrome following therapy using mifepristone [3] or other cortisol lowering agents [4], and sometimes could occur in such abrupt and severe presentation [5, 6]. It can be hypothesized that mifepristone suddenly suppressed the anti-inflammatory glucocorticoids effects and restored the immune system similarly to what has been observed in AIDS patients starting on HAART [7]. Clinicians should be aware of this potential complication in patients with Cushing's syndrome.

REFERENCES

- [1] Johansen S, Allolio B. Mifepristone (RU 486) in Cushing's syndrome. *Eur J Endocrinol* 2007; 157: 561-9.
- [2] Graham BS, Tucker WS. Opportunistic infections in endogenous Cushing's syndrome. *Ann Intern Med* 1984; 101: 334-8.
- [3] Oosterhuis JK, van den Berg G, Monteban-Kooistra WE, et al. Life-threatening *Pneumocystis jiroveci* pneumoniae following treatment of severe Cushing's syndrome. *Neth J Med* 2007; 65: 215-7.
- [4] Keenan N, Dhillon WS, Williams GR, Todd JF. Unexpected shortness of breath in a patient Cushing's syndrome. *Lancet* 2006; 367: 446.
- [5] Kim DS, Park SK, Choi WH, et al. *Pneumocystis carinii* pneumonia associated with a rapid reduction of cortisol level in a patient with ectopic ACTH syndrome treated by octreotide and ketoconazole. *Exp Clin Endocrinol Diabetes* 2000; 108: 146-50.
- [6] McQuillen DP, Hesketh PJ, Sugar AM. *Pneumocystis carinii* pneumonia complicating somatostatin therapy of Cushing's syndrome in a patient with metastatic pancreatic islet cell carcinoma and Zollinger-Ellison syndrome. *Am J Gastroenterol* 1991; 86: 512-4.
- [7] Wu AK, Cheng VC, Tang BS, et al. The unmasking of *Pneumocystis jiroveci* pneumoniae during reversal of immunosuppression: case reports and literature review. *BMC Infect Dis* 2004; 4: 57.

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