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Full Length Case Report

DRESS SYNDROME CAUSED BY PHENOBARBITAL: DESCRIPTION OF TWO CASES IN NEUROLOGY DEPARTMENT AT FANN NATIONAL TEACHING HOSPITAL, DAKAR

***Marième Soda Diop-Sène, Ousmane Cisse, Soumaila Boubacar, El Hadji Makhtar Ba, Ibrahima M Diallo, Patrice Ntenga, Adjaratou Dieynaba Sow, Anna Modji Basse, Ngor Side Diagne, Maouly Fall, Moustapha Ndiaye, Amadou Gallo DIOP, Mouhamadou Mansour Ndiaye**

Department of Neurology, Fann National Teaching Hospital, 5035 Dakar, Senegal

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ABSTRACT

Drug reaction with eosinophilia and systemic symptoms (DRESS) or drug hypersensitivity syndrome, or even drug-induced hypersensitivity syndrome (DIHS) is a rare and often unknown reactions. It has been used for the first time in 1996 by Bocquet and characterised by demonstrations at type of generalized rash of hyperthermia, polyadenopathy, breach united or it's including a hepatic cytolysis, of hypereosinophilia, of acute renal failure. Here, we report two cases of DRESS syndrome after a traitmeent by Phenobarbital. They are a man aged 26 and a woman of 32 years who are patients known epileptics whose man presented a DRESS Syndrome three weeks after the beginning of Phenobarbital taken while the woman developed her symptomatology after two weeks of taking the treatment. The 26-year-old patient had a hepatocellular insufficiency associated with lung damage. The 32-year-old patient had not other complications but was in an array of severe dehydration. We had carried the biological tests and medical imaging for the assessment of extension. HIV status was negative in our two patients. Two patients after a stop of Phenobarbital benefited each symptomatic treatment and a prescription of sodium valproate. Evolution was marked in the two patients by a sharp decline of the hypereosinophilia and other biological markers. However, a few episodes of generalized seizures were noted following the change of Phenobarbital. Dress syndrome must be discussed in any patient taking phenobarbital and presents cutaneous signs because early treatment is necessary to avoid complications and improves the prognosis.

Key words: Phenobarbital, Dress syndrome, Dakar

INTRODUCTION

The syndrome drug reaction with eosinophilia and systemic symptoms (DRESS) or drug hypersensitivity syndrome, or even drug-induced hypersensitivitysyndrome (DIHS) is a rare and often unknown reaction (Rabenkogo *et al*., 2015). "Drug hypersensitivity syndrome" refers to a drug reaction specific acute serious and potentially fatal (Roujeau, 1994; Moubachir *et al*., 2013). It has been used for the first time in 1996 by Bocquet *et al*. (1966) characterised by demonstrations at type of generalized rash of hyperthermia, polyadenopathy, visceral attack including a hepatic cytolysis, of hypereosinophilie, of acute renal failure (Sparsa *et al*., 2008). It may be secondary to the antiepileptic, carbamazepine is often offending molecule (Sparsa *et al*., 2008). We report two (2) cases of DRESS Syndrome related to Phenobarbital and show through these two cases that the Dress syndrome is a reality under-diagnosed in our regions.

Corresponding author: Marième Soda Diop-Sène
Department of Neurology, Fann National Teaching Hospital, 5035 Dakar, Senegal.

Clinical case 1

It was of 26 years epileptic patient known who takes the phenobarbital 100 mg/day since august 2016, no other disease has been reported. We received him at the department of Neurology at Fann University Hospital three weeks after the start of taking Phenobarbital. Interrogation revealed a concept of fever associated with skin lesions without other particular context and the patient not taking any other medication. Clinical examination has objectified erythemato-squamous lesions extended with mucous membranes mouth and eye damage, jaundice cytolytic, severe extracellular dehydration, cervical, axillary and inguinal lymphadenopathy. In front of this clinical aspects, we performed a paraclinical emergency assessment of blood electrolytes (unremarkable) renal stock was a urea to 0.24 meq/l, a creatinine to 0.72 and a clearance to 94,56. A blood count showed a Leukocytosis 19.040/mm3 associated with a 2050/mm3 hypereosinophilia. Her CRP (Protein C reactive) was 92. On the liver plan noted the ASAT (aspartate amino transferase) at 505 (11 times the normal), of the ALAT (alanine amino transferase) at 687 (17 times the normal), the gamma GT to 587 (12 times normal), the PAL (alkaline phosphatase) at 526 (2 times normal), total

bilirubin at 292 (29 times normal), the direct bilirubin to 184 (61 times normal), hepatocellular with RT (Rate of Prothrombin) at 31.8% failure and INR (International Normalised Ratio) at 2.8. Retroviral serology was negative and hepatitis B antigen. The chest x-ray contrast to one carried out after the first crisis was an interstitial syndrome. Dress syndrome diagnosis decided to: a rash broadcasts; Fever, Lymphadenopathy, a hypereosinophilia and Hepatic impairment by syndrome of cytolysis. About therapeutic after cessation of phenobarbital, the patient received a rehydration plan A of WHO (World Health Organization) . The following drugs were administered to him Omeprazole 20 mg /day, steroid 60 mg 3 /day, Sodium Chloride 600 mg /day, Spiralide 3millions 3 drops /day. Finally the sodium valproate 1000 per day on his release from the hospital. The balance achieved at 10 days of hospitalization showed a leukocytosis at11,000 /mm3 with Eosinophilia in 520 /mm3, a rate of prothrombin at 40.8%, of the ASAT at 281,6 (6 times normal), of the ALAT at 339,6 (8 times the normal). Evolution was marked by the occurrence of tonic-clonic seizures to J16 of hospitalization with biting tongue and loss of urine what had motivated the injectable valium turning in an emergency then the relay by sodium valproate 1000 mg per day.

Clinical case 2

It was a woman of 32 years with history epileptic under phenobarbital 100 mg/day for may 2016. After two weeks of taking phenobarbital the patient had a fever associated with skin lesions. Clinical examination was objectified a buccal enantheme, without other skin basic associated lesions, moderate extracellular dehydration, neck and inguinal lymphadenopathy, edema of the face with itchy lesions farms. The rest of the clinical examination was normal before these signs we had advocated the judgment of phenobarbital. Performed additional tests were objectified: a leukocytosis at 15.300 white blood cell with eosinophilia in 1850 /mm3, a rate of prothrombin at 68.8%, a blood lab found a lack of particularity outside a sodium 132 meq/l. The kidney was normal. There had been a rehydration following the plan c of the WHO. There were also a biological inflammatory syndrome with a CRP at 128. Hepatic noted an absence of anomalies of the transaminases, gamma GT, bilirubin, direct bilirubin had not been assayed. Retroviral (HIV) serology was negative and Antigen of the hepatitis B too . The chest x-ray was normal. Dress syndrome diagnosis was held before: The time to onset of lesions 2 weeks after the start of treatment with Phenobarbital, Disseminates a rash, Fever, Lymphadenopathy, and hypereosinophilia; On the treatment plan we had set up outpatient treatment with: Omeprazole 20 mg/day, Corticoid 60 m/day and Sodium Chloride 600 mg/day evolution was marked by the appearance of generalized seizures what had motivated the introduction of sodium valproate. The evolution after 1 month revealed white blood cells at 9,300/mm3 with Eosinophilia in 450 /mm3, a rate of PR at 70.8% , the ASAT at 21, ALAT at 34. Clinically there is a lack of notable features.

DISCUSSION

Drug rash with hypereosinophilia and systemic symptoms (DRESS) syndrome is a serious drug hypersensitivity syndrome associating rash, hypereosinophilia. This table, later than the conventional drug reactions appears two to six weeks after the start of administration of the drug responsible (François, 2015) which has been observed in two patients. The incubation period may be reduced in the event of new introduction (Descamps *et al*., 2010) done phenobarbital out of the list of possible causes (Oliveira, 2005; Patrice Cacoub *et al*., 2011). Indeed the first case of a Dress syndrome was reported in 1953 (MacGeachy, 1953) and the responsible molecule was phenobarbital, but it was in 1996 that the terminology of "Dress syndrome" was used for the first time by Bocquet *et al*. (1996). in total 44 drugs have caused 172 cases between January 1997 and may 2009 including 3 cases by phenobarbital (Cacoub *et al*., 2011). Usually incriminated medicines are anticonvulsants (Carbamazepine, Diphenylhydantoin, valproic acid), allopurinol, antibiotics (sulfonamides, Minocycline) and antiretrovirals (Efavirenz1) (Bocquet *et al*., 1966). The annual incidence of DRESS syndrome was estimated at 0.9 per 100,000 population (Muller *et al*., 2003). A personal or family of Dress history and an African-American are the factors of risk (Atadokpede, 2011). The discovery of two cases secondary to phenobarbital in 3 months raises the question of the lack of diagnosis of this illness in our african sub Saharan context, because on the one hand this molecule (phenobarbital) is the most widely used antiepileptic in our regions (Dadah *et al*., 2014) and on the other hand Dress syndrome was rarely reported in Senegalese literature with only 2 cases on a cohort of 70 drug reactions reported by Diop *et al*. (2013).

The pathophysiology of this condition remains little coonue, but involves the reactivation of the herpes virus (HHV-6, HHV-7, EBV and CMV), against which the body up a strong immune response. The guilty drugs can not only affect epigenetic control mechanisms but also induce a response of antiviral t (Atadokpede *et al*., 2011). Other mechanisms indicate a role for immunogenetiques susceptibility factors and for the reactivation of herpes human virus (HHVs), mainly HHV-6. Account means limits of our patients these explorations had not been made. Dress syndrome diagnosis is progressively codified (Rabenkogo *et al*., 2015) and is based on clinico-biological criteria described (Moubachir *et al*., 2013). Our patients fulfilled these requirements. The liver was the internal body most often affected with essentially an increase in transaminases approximately 10 times (1.5-54) and 9 times (1.5-160) normal (Rabenkogo *et al*., 2015). What has been the case with one of our patients with a hepatic cytolysis, in addition, a cholestaes and an interstitial syndrome confirmed by chest x-ray. Outside of phenobarbital, the medications that may be responsible for Dress syndrome had not been found in our patient that allowed us to make this diagnosis Dress syndrome secondary to phenobarbital. Despite the presence of bad prognosis for one of our patients to know a liver damage, evolution has been satisfactory in our two patients. Indeed a 10% death rate has been reported before this disease whose main cause was liver damage (Atadokpede, 2011). Only under corticosteroid therapy associated with symptomatic treatment has been effective unlike the recommendations of (Descamps *et al*., 2010) who advocated the combination corticosteroid and immunoglobulin.

Conclusion

Dress Syndrome is a nosological entity to know refer to any patient under phenobarbital that presents cutaneous signs because early treatment to avoid complications and improves

the prognosis. In addition, patients need to be aware on the mode of installation of the signs and their characteristics.

Conflict of interest: the authors have no conflict of interest in relation to this article

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