Severe acute hepatitis induced by a DRESS syndrome to piroxicam

The DRESS syndrome or Drug Rash with Eosinophilia and Systemic Symptoms is an acute, not specific, severe drug-induced hypersensitivity syndrome, described for the first time in 1966 by Bocquet and al (1). Aim: to report the first case published of a DRESS syndrome associated with severe acute hepatitis and an auto-immune hemolytic anemia induced by the piroxicam.

Case report

A 45-year-old woman was admitted with five days history of high fever, generalised maculo-papular rash, jaundice and cervical lymph node enlargement. On physical examination, she presented flank pain. We noted the absence of hepatic encephalopathy and hepatosplenomegaly. She was given piroxicam 20 mg a day for intense polyarthralgy. Twelve days later, she was admitted in our department. Blood tests showed a marked impairment in liver function with cytolysis activity (aspartate transaminase (AST): 828UI/l (Normal < 40 UI/l) , alanine transaminase (ALT) :479UI/l (N< 60 UI/l)) , cholestasis (alkaline phosphates (AP) : 204 (N < 125 UI/l), gamma glutamyl transferase (GGT) : 197 (N < 64 UI/l) , total bilirubin: 95 μmol/l (direct: 58 μmol/l)) and liver insufficiency (prothrombin time : 45% and factor V: 40%). Her white cell count was 11600/mm3, with 10% eosinophils (1870/mm3) and her hemoglobin level was 9g/dl. The anemia was an auto-immune hemolytic anemia (reticulocytes: 170000/mm3) with a positive direct Coombs'test (IgG-C 3b).

A biological inflammatory syndrome (VS: 50mm, CRP: 190 mg/l) and a polyclonal hyper gamma-globulinemia at 21 g / l (N: 7.5-16g/l) were also noted. The rate of the IgE was 1940 UI / ml (N < 160 UI / ml). The ferritinemia was 46000 μg / ml (N: 8-120 μg/l). Hepatitis B and C, cytomegalovirus, Epstein-Barr virus and Herpes virus serology were negative. Auto-antibody screening revealed positive antinuclear antibodies (ANA) (homogeneous, 1/320) and native DNA (ELISA). Anti-smooth muscle antibodies, anti-mitochondrial, anti-SSA, anti-SSB and anti-cardiolipin antibodies were negative. Ultrasonography showed a hepato-splenomegaly without portal hypertension. The chest radiography was normal. Percutaneous liver biopsy was not performed because of deranged hemostasis. 24-hour urine protein test was negative. Sterna bone marrow aspiration didn't show hemophagocytosis. DRESS syndrome was suspected and the piroxicam was stopped. Four days after her admission, despite spontaneous improvement of liver tests (TP: 55 % and ALT: 5 x N), her hemoglobin level decreased to 6g/dl. Oral prednisolone (1mg/kg/daily) for hemolytic anemia was administered. Fever and rash gradually resolved and hemoglobin levels started to improve. Afterwards, the serum ALT level and pro-thrombin time progressively normalized and complete resolution of all symptoms was achieved 2 months after discontinuation of the peroxicam. Prednisone was completely tapered in Marsh 2010. ANA tests were negative twice. Two years after prednisone discontinuation, the liver function is completely normalized without recurrence of the symptoms. Her hemoglobin level is also normal.

Table 1: Diagnostic criteria of DRESS syndrome according to Bocquet and al (1)

Diagnostic criteria
• drug-induced skin eruption
• blood disturbance
o Hypereosinophilia : eosinophilia > 1,5x109/l
o Or atypical lymphocytes
• systemic abnormalities
o enlarged lymph nodes > 2 cm diameter
o Or hepatitis (transaminases > 2 N)
o Or interstitial nephropathy
o Or interstitial lung disease
o Or carditis

**DRESS syndrome: association of three criteria, one of each category*

Conclusion

The DRESS syndrome is a rare pathology but must be promptly recognised in case of any symptom arising after the introduction of a new drug especially in case of fever, of flu-like syndrome or of associated skin manifestations.

DRESS syndrome continues to carry a high mortality rate of about 10% (1). Liver involvement is the most frequent. In our knowledge, no case of DRESS syndrome induced by the piroxicam has been published until this day. Some cases of systemic involvement induced by piroxicam (interstitial eosinophilia lung disease, glomerulonephritis, hepatitis with hemolytic anemia) have been reported (2-4). Some of them were probably DRESS syndrome but data are insufficient concerning skin lesion and blood hypereosinophilia, the articles were written before the introduction of the term DRESS syndrome. The second originality of our case report is the association of an auto-immune hemolysis anemia to the DRESS syndrome. Only two cases of hemolytic anemia secondary to the piroxicam, were reported in the literature (2, 5) The DRESS syndrome is a rare pathology but must be promptly recognized. The prognosis depends on the precocity of its care which essentially consists on prompt withdrawal of the suspected drug.

References

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