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POST-TRANSFUSIONAL HEPATITIS: NATURAL HISTORY AND EVOLUTION*[1]

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Medicine evolves, like many other sciences, in surges of discovery, breaking through periods of relative stagnation. Some of our questions find definite answers in new knowledge. Others, however, are but far from solved, and the tentative brings with it more puzzle, the source of profounder enigmas.

The knowledge about post-transfusional hepatitis follows a similar course. Since the description by Lurman, in 1885, of a surge of "catarrhal jaundice" that infected almost two hundred shipyard workers in Bremen, Germany, by a smallpox vaccine made of human linfblood, that parenteral transmission was suspected. However it was only in the 1940's, when a viral etiology for hepatitis was almost certain, that the first reports on blood transmission appeared. At this time it was demonstrated, by work with human volunteers, the existence of two types of viral hepatitis. One was called "catarrhal" or epidemic jaundice or hepatitis A, already described by Hippocrates; another was described as serum hepatitis or homologous serum hepatitis (hepatitis B). There were marked distinctions between them: Hepatitis A had a short incubation period, oral-fecal route, food-handler related, appearing in outbreaks; the second had a long incubation period, and was transmitted by parenteral inoculation.

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In 1955 laboratory tests were developed that detected enzime levels, making possible the diagnosis of hepatitis with or without jaundice. This allowed also for a better understanding of the pathophysiology of the disease.

A period of few added knowledge ensued, until 1963 when Blumberg discovered an antigenic molecule in the blood of a native of Australia (Australia antigen - AgAu). At first erroneously related to leukemia and Down syndrome, it was in 1966 considered definitely related to hepatitis B virus. A year later, Krugman and cols confirmed previous studies, showing that Hepatitis A and B viruses were diverse, from the immunological point of view.

From the 1970's on, serologic tests were introduced that allowed the certain diagnosis of Hepatitis A and B. The prospect that the problem of post-transfusional hepatitis was solved, gave way to the frustating discovery that another type of transfusional hepatitis existed: even after selection of blood donors by HBV serum marker, a third type of hepatitis could occur, that was called, by exclusion (and by the absence of serum markers) non A, non B Hepatitis. Since then, studies from many countries allowed some general conclusions:

a) Clinically, non A, non B Hepatitis is somewhat similar to Hepatitis B, but incubation period is shorter, signs and simptons are less florid, and there is a low incidence of jaundice. Time of incubation is usually 7 to 8 weeks, and there is a fluctuating pattern in the aminotransferase levels - episodic rises alternating with periods of normality, not seen in other types of viral hepatitis.

b) Post-transfusional hepatitis is seen in 7 to 10% of receptors, when given by volunteer donors, and in 17 to 35% when originated from paid donors.

c) Since the introduction of the Hepatitis B surface antigen (HBsAg) for the selection of donors, the incidence of non A, non B Hepatitis in receptors is of 90 to 95%, and the incidence of Hepatitis B is 5 to 10% (relative).

d) The risk of post-transfusional hepatitis is 3 to 7% for one blood unit and 10 to 12% for more than one.

e) The great majority (3/4) of people with non A, non B Hepatitis are assymptomatic, even when in chronicity.

f) Chronic hepatitis occurs in 50% of the cases of non A, non B transfusional hepatitis, and in 10% after hepatitis B.

g) Structural charges associated with cirrhosis are seen in 20% of patients with non A, non B chronic hepatitis, and in 1% of all patients having acute post-transfusional hepatitis, after 10 years from the acute phase.

This knowledge and the possibility that, like in Hepatitis B, non A, non B chronic hepatitis could be related to hepatocelular carcinoma, gave rise to studies in the search of tests to detect potential carriers of non A non B Hepatitis among

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blood donors. Many reports demonstrated the valour of exclusion of donors among those who had elevated serum levels of ALT or were positive for HBc antibody. Much debate was held on the question of the sensibility, predictive value and the ethics of applying those tests to donors. The inclusion of the tests was favoured by many laboratories in most parts of the world.

The report of the identification of the virus implicated in non A non B Hepatitis (or at least one of them) appears in 1989, and it is called Hepatitis C virus. Radioimunoassay and ELISA methods to detect the correspondent antibodies were then developed. It was soon discovered, however, that this antibody appears usually 15 weeks after the hepatitis, (limits of 4/32 weeks), with the implication that the test may not identify all infected donors. FDA alerts that the selection for anti-HCV may not lower the ammount of virus, but may substantially decrease the concentration of antibodies, in the production of blood derivatives.

The failure of anti-HCV to safely identify infected donors stimulated the investigation of the virus RNA, using experimentally infected chimpanzees. A positive correlation was seen between the presence of HCV-RNA and infectiveness of blood samples, and it was shown that infected patients could remain positive for as long as 9 years.

As could be seen in this brief historic review, the knowledge about the natural history of post-transfusional hepatitis shows a sequence of enigma solutions, followed in sequence by bigger and profounder ones. Blumberg searched in the greek mithology a comparison for this "Deadelus" effect of the viral hepatitis.