LETTER TO EDITOR

HCV AND RENAL CELL CARCINOMA: A NEW INSIGHT BETWEEN HCV AND ONCOGENESIS? REPORT OF FIVE CASES

ВЫЯВЛЕНИЕ ВИРУСА ГЕПАТИТА С И РАК ПОЧКИ: СООБЩЕНИЕ О ПЯТИ КЛИНИЧЕСКИХ СЛУЧАЯХ

Sir, more and more evidences in the literature underlined the association between virus infection and oncogenesis. In particular, viral replication is often associated with apoptosis, thus interfering with normal cell cycle pathways [1]. Cheng et al [2] in fact, showed that DNA viruses, as Hepatitis B Virus (HBV), seem to contain oncogenic proteins which could transform normal cells *in vitro* so inducing cancer in animal models. Mechanisms involved seem to be associated with block of apoptosis. In particular, analyses of 23 genes by cDNA microarrays in hepatocellular carcinoma (HCC) of HBV positive patients showed up regulation of mitosis promoting genes compared to their noncancerous tissues. These findings seem to be different from those reported in HCC of HCV positive patients [3]. HCV, in fact, appears to have a different mechanism of liver carcinogenesis involving NS4B protein and alteration induces in association with *Ha–ras* gene activity [3]. Another possible mechanism involved seems to be the inactivation or induced mutation of tumor suppressor gene *p53* [4]. Yet, all pathways involved between HCV and HCC are not clearly understood. HCV, in fact, is RNA virus which is not integrated in genome of infected hepatocytes. Its replication is maintained also when HCC is detectable [4]. Virus attachement to target cells is related to the engagement of a viral envelope glycoprotein, glycoprotein E2, to CD81, a tetraspanin superfamily member [5].

Interestingly, in fact, E2 engagement of CD81 also influences cell proliferation and aggregation and this activity seem to be common also toward other type of cells [5]. However, oncogenic activity of HCV toward HCC has been showed in lot of reports [6, 7]. Moreover, HCV chronic infection is also associated with other type of cancer of lymphohaemopoietic tissue, in particular B–cell lymphoproliferative disorders [8].

Furthermore, Bruno and colleagues [9] showed increased incidence of second primary malignancies in patients affected by chronic HCV infection and HCC. Common sites of the second primary malignancies were kidney, breast and lymphohaemopoietic tissue.

In this field we can report five cases of renal cell carcinoma (RCC) occurring in patients affected by chronic HCV infection. All patients presented aminotransferases levels lightly increased and in particular one of them presented normal levels of aminotransferases in the last 12 months before the newly cancer diagnosis was performed. All the patients showed positivity for HCV antibodies and for presence of HCV–RNA in blood. We observed these five cases in the last five years in which we performed liver care of HCV infection in 60 patients affected by HCV chronic infection in different stages of disease (no liver test abnormalities, chronic infection, cirrhosis, HCC). We did not find second primary malignancies in these five patients nor in patients with developed HCC. Our data seem to be a particular clinical observation associated to those described above.

Moreover, interestingly, Aoki et al [10] described another particular presentation of RCC: RCC producing α–fetoprotein. This is a very rare condition, that amount ten cases reported by the authors [10]. The patient affected was not positive nor for HCV antibodies nor for HCV RNA: are we looking for an occult HCV infection in this case? This question can be interesting because often haematological and kidney malignancies are sensible to the treatment with α–interferon and/or γ–interferon, the most common treatment of chronic HCV infection [11].

We can summarize that HCV is a virus which could induce different clinical diseases besides liver diseases. The virus is able to induce damages due to capacity to bind a tetraspanin superfamily member, CD81. This capacity could induce penetration of virus and related damages also to other type of cells. These data are associated with oncogenic properties of HCV. So, the ability of HCV to promote other types of cancer should be further investigated both in fundamental and clinical research.

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Abbreviations used: HBV — hepatitis B virus; HCC — hepatocellular carcinoma; HCV — hepatitis C virus; RCC — renal cell carcinoma.

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