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Oral Lichen Planus in Patients with Chronic Hepatitis C – One Year of Observation

Liszaj płaski jamy ustnej u pacjentów z przewlekłym zapaleniem wątroby typu C w obserwacji rocznej

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Abstract

Objectives. The aim of this study was to determine the relationship between the incidence of oral lichen planus (OLP) in patients suffering from chronic hepatitis C treated with interferon alpha (IFN-alfa) and Ribavirin (RBV) and those receiving no treatment.

Material and Methods. The study involved patients treated at the Department of Infectious Diseases Wrocław Medical University, who had a confirmed diagnosis of chronic hepatitis C. The study group consisted of 38 patients out of whom 15 had been treated for 12 months with IFN-alfa + RBV (group I) and group comprised 23 untreated patients (group II). The control group comprised 29 healthy subjects. Both groups of patients were followed up for 12 months and the condition of their oral mucosa was assessed at 0, 3, 6 and 12 month. The assessment included clinical and histopathological examination of the observed lesions.

Results. During 12 months of follow-up the symptoms of OLP were observed in 2 patients from the group I (2/15). In the group II was observed in 1 patient (1/23). In the control group OLP was not observed.

Conclusion. Incidence of OLP in our patients have no connection with chronic hepatitis C and IFN-alfa + RBV therapy (**Dent. Med. Probl. 2003, 40, 2, 233–237**).

Key words: oral lichen planus, chronic hepatitis C.

Streszczenie

Cel pracy. Celem pracy było określenie zależności między częstością pojawiania się *oral lichen planus* (OPL) u pacjentów z przewlekłym zapaleniem wątroby typu C leczonych interferonem alfa (IFN-alfa) i rybawiryną (RBV) i pacjentów nieleczonych, w porównaniu do osób bez patologii wątroby, w obserwacji rocznej.

Materiał i metody. Badaniem objęto pacjentów leczonych w Klinice Chorób Zakaźnych AM we Wrocławiu z potwierdzonym rozpoznaniem przewlekłego zapalenia wątroby typu C. Grupę badaną stanowiło 38 chorych, z których 15 poddano 12-miesięcznej terapii IFN-alfa + RBV oraz 23 nieleczonych pacjentów. Grupę kontrolną stanowiło 29 pacjentów Katedry i Zakładu Chirurgii Stomatologicznej we Wrocławiu bez patologii wątroby. W czasie 12-miesięcznej obserwacji we wszystkich grupach pacjentów oceniono stan błony śluzowej jamy ustnej w 0, 3, 6, 12 miesiącu. Ocena oparta była na badaniu klinicznym i histopatologicznym stwierdzanych zmian.

Wyniki. W grupie badanej objawy OLP stwierdzono u 2 pacjentów (2/15) w czasie 12-miesięcznej obserwacji. W grupie nieleczonych OLP obserwowano u 1 pacjenta (1/23). W grupie kontrolnej u żadnego z badanych pacjentów nie stwierdzono OLP przez cały czas prowadzenia obserwacji.

Wnioski. Nie wykazano jednoznacznie by 12-miesięczna terapia IFN-alfa + RBV miała istotny wpływ na częstość występowania OLP u zakażonych HCV w 12-miesięcznej obserwacji (**Dent. Med. Probl. 2003, 40, 2, 233–237**).

Słowa kluczowe: liszaj płaski jamy ustnej, przewlekłe zapalenie wątroby typu C.

Since hepatitis C virus (HCV) was discovered in 1989 until nowadays HCV infections have presented an extremely significant clinical and epidemiological problem [1–3]. The number of patients diagnosed with chronic HCV increases year by year. It has been estimated that HCV infected patients all over the world account for 170–300 mln people [2, 3]. In Poland the incidence of infections ranges from 0.2 to 1.4% of the population, what means that about 600 000 Polish people suffer from HCV [4]. The infections are usually diagnosed on routine check-up (e.g. in blood donors) or in patients who developed complications associated with advanced damage to the hepatic parenchyma. The fact that HCV infection produces few or no symptoms in as many as 70–80% of patients contributes to the clinical complexity of the disease [5]. Clinical observations of acute hepatitis due to HCV infection are rare. Thus endeavors are being undertaken constantly to search for extrahepatic symptoms which might point to HCV infection and enable early diagnosis and treatment. More and more numerous reports point to an association between HCV infection and oral lichen planus (OLP).

The aim of the work was to determine the prevalence of OLP in patients suffering from hepatitis C who were treated with immunomodulating and antiviral agents (interferon alpha + ribavirin) as well as in untreated patients suffering from chronic hepatitis C in comparison to the control group of subjects who were free from hepatic pathology.

Material and Methods

The study involved patients treated at the Department of Infectious Diseases, Wrocław Medical University with clinically, biochemically, serologically and molecularly confirmed HCV infection, in whom chronic hepatitis C was diagnosed on the basis of thick-needle biopsy according to Menginje and histopathological evaluation according to Child. All the patients gave their informed consent for the observation. Patients with hepatitis C were divided into two study groups.

Group I – patients suffering from chronic hepatitis C treated with immunomodulating– interferon alpha (IFN-alpha) and antiviral – ribavirin (RBV) agents; (15 patients, mean age 35.4 years);

Group II – patients suffering from chronic hepatitis C who did not receive any treatment (23 patients, mean age 44.7 years).

The control group recruited from patients at the Department of Oral Surgery Wrocław Medical

University who did not have any hepatic pathology (29 subjects, mean age 41.2 years).

The observations continued for 12 months. The examinations were carried out at 0, 3, 6 and 12 months. The condition of oral mucosa was estimated for OLP type lesions, which were confirmed by clinical (Schiller's iodine test) and histopathological examination.

The incidence of OLP in the study groups and in the control group was analyzed statistically by means of Fisher's test.

Results

The primary examination in one of the patients from group II (1/23) revealed OLP within the buccal and gingival oral mucosa (reticular form) which persisted without any clinical symptoms until the end of the observation period (Fig. 1). Neither the patients from group I nor from the control group revealed OLP on primary examination. After 3 months no new cases of OLP were observed in neither of the groups. However after 6 months one patients from group I (1/15) treated by means of combination therapy, who had been diagnosed with Delbanco disease (ectopic sebaceous glands) at the beginning of the observation, developed burning sensation of the oral mucosa on the right cheek. The sample taken for histopathological evaluation revealed ectopic sebaceous glands and lymphocytic infiltrations into the epithelial interstitium consistent with OLP (Fig. 2). The lesion persisted until the end of the observation period (follicular form). The examination carried out after 12 months of combination therapy revealed OLP on the buccal mucosa (reticular form) in another patient from group I (2/15) (Fig. 3).

OLP was ultimately observed in 3 patients (3/38, i.e. 7.89%) out of both groups followed for one year. Out of these, group I patients suffering from chronic hepatitis C, treated with IFN-alpha + RBV revealed two cases (2/15) which appeared during combination therapy, and in the patients suffering from chronic hepatitis C awaiting treatment – in one case (1/23) and it was not associated with any clinical symptoms throughout the whole follow up. Among patients on combination therapy who developed OLP, the symptoms did not aggravate, what might have necessitated the treatment to be discontinued. None of the patients developed erosive form of OLP. In the control group, without liver pathology, no lesions suggestive of OLP were observed throughout the whole follow-up.

On statistical analysis by means of Fisher's test, the comparison of groups: control vs. I + II



Fig. 1. OLP – reticular form – in a patient with chronic hepatitis due to HCV infection, who is awaiting treatment

Ryc. 1. OLP – postać siateczkowa – u chorego na przewlekłe zapalenie wątroby, związane z zakażeniem HCV, oczekującego na leczenie



Fig. 3. OLP – reticular form – in a patient with chronic hepatitis due to HCV infection treated with IFN+RBV in the 12th month of follow-up

Ryc. 3. OLP – postać siateczkowa – u chorego na przewlekłe zapalenie wątroby związane z zakażeniem HCV leczonego IFN+RBV w obserwacji w 12. miesiącu

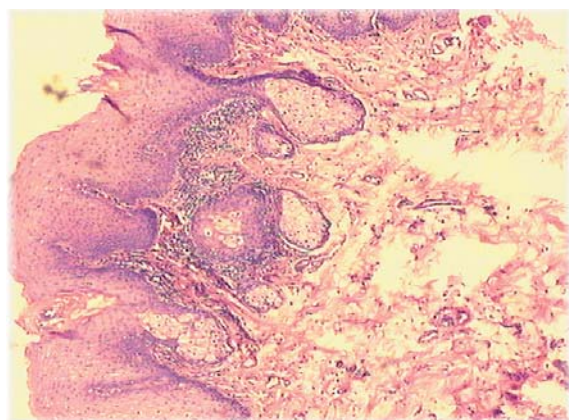


Fig. 2. Histopathological picture of OLP (lymphocytic infiltration in the epithelial stroma) and Delbanco's disease (ectopic sebaceous glands) in a patient suffering from chronic hepatitis due to HCV infection treated with IFN+RBV in the 6th month of follow-up

Ryc. 2. Obraz histopatologiczny OLP (nacieki limfocytarne w podścielisku nabłonka) i choroby Delbanco (ektopowe gruczoły łojowe) u chorego na przewlekłe zapalenie związane z zakażeniem HCV leczonego IFN+RBV w obserwacji w 6. miesiącu

($p = 0.252$) and group I vs. group II ($p = 0.550$) did not indicate any significant statistical differences in the prevalence of OLP.

Discussion

The prevalence of OLP in various populations has been estimated in epidemiological studies to range from 0.1 to 2% [6, 7]. The etiology of OLP morbidity has not been explained yet, the role of numerous toxic agents (including medicaments),

stress, genetic (HLA antigens: HLA-B8, HLA-B16), immunological (e.g. in the course of graft vs. host disease – GvHD) or viral effects has been suggested [8, 9].

Numerous reports, especially from Japan and Italy suggest a relation between HCV infection and OLP [10, 11]. The pathomechanism of OLP is unclear and what's more, it seems to point to the role of immunogenetic status of the host and not directly of the virus and its genotype. Thus the search for associations between OLP and chronic viral hepatitis seems justified. In their studies from 1991, Rebory and his colleagues [12] were among the first to suggest an association between LP and chronic liver diseases (CLD). They evaluated a group of 50 patients with LP, but without a history of liver disease. They revealed the presence of HBV infection markers in 11 patients (22%) and anti-HCV antibodies in 2 (4%). However in a group of 43 patients with LP suffering from chronic liver diseases, HBV infection markers were found in 15 patients (35%) and HCV in 19 out of 29 investigated patients (65%), 3 patients being infected both with HBV and HCV. Bagan et al. [13] analyzed 3 groups of patients. In the first group of 505 patients with confirmed HCV infection, OLP was diagnosed in 3.36%. In the second group of 100 patients with histologically confirmed OLP, HCV infection was confirmed by means of ELISA 2 test in 23% of patients and in the control group of 100 healthy volunteers, HCV genetic material was discovered in 5% and OLP was diagnosed in 1% of the subjects.

However, the studies from Scotland, Germany and Poland contradicts the above findings. Grote

et al. [14] diagnosed OLP in 3 cases (2.4%) out of 127 investigated patients with HCV infection, out of 17 patients with HBV infection there were no cases of OLP, while in the group of 21 patients with confirmed OLP there was one case of HCV infection and none of HBV infection.

Pawlotsky and his colleagues in France out of 61 patients with chronic hepatitis C found 3 cases (5%) of LP [15]. Their findings are similar to ours, in which in patients suffering from chronic hepatitis due to HCV infection (total 38 cases), OLP was found in 3 (7.89%) cases. However our observation extended over 12 months' period; the above-mentioned authors did not follow their patients for such a long period, neither did they monitor the effect of combination therapy on the occurrence of OLP.

At present the question about etiopathogenetic association between OLP and chronic liver diseases associated with HCV infection remains unanswered. Our own as well as other authors' observations seem to indicate that OLP may

accompany chronic HCV infections. The relation reveals geographical variability, what may be associated with various dominating genotypes of virus C over the given area. This affects biological changeability of HCV as well as determines the effectiveness of the response to antiviral therapy.

The results of our observations indicate the necessity for constant monitoring of patients suffering from chronic hepatitis due to HCV infection for OLP, especially those treated with IFN. This is the more important as some authors have described cases of aggravation of OLP symptoms in the course of IFN therapy, what in some cases has necessitated the decision to discontinue the treatment. Such situation did not take place in our patients and all of them terminated the treatment according to the protocol. Moreover, in cases in which the therapy was discontinued due to aggravation of OLP symptoms, the erosive form of the disease was diagnosed, which did not occur in our patients.

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