

## Cerebral haematoma and diffuse cerebral hemorrhage in the context of chronic viral liver disease with severe metabolic disorder of hemostasis. Observations on a series of 7 cases

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### Abstract

The aim of our study was to describe some characteristics of a series of 7 cases with subdural (4), extradural (1) and intracerebral hemorrhage (2) associated with chronic hepatitis and liver cirrhosis in the context of long-term infection with B and C viruses. We collected data regarding hepatic dysfunction (ALT, AST) and hemostatic disorder (blood platelet count, prothrombin time and Howell test). In conclusion, patients with chronic and cirrhotic liver disease and a severe hemostatic syndrome should be investigated neurosurgically in order to prevent intracerebral hemorrhage and hematoma. An important laboratory alarm signal could be an important decrease of blood platelet count and a prolonged prothrombin time and a pathologic Howell test.

**Key words:** viral chronic hepatitis, hemostasis, intracerebral hemorrhage, liver cirrhosis, subdural hematoma.

### Introduction

Chronic subdural hematoma represents a common condition seen usually in the

later stages of life (12). Epidemiological data suggested that the incidence of chronic subdural hematoma and intracerebral hemorrhage did not decrease between 1980 and 2008. The overall incidence was 24.6‰ per year (95 % confidence interval 19.7–30.7), ranging from 1.8 to 129.6. The incidence values were 15 % lower in women than men (overall incidence ratio 0.85, 95% CI 0.61-1.18). Incidence ratios increased from 0.10 (95% CI 0.06-0.14) for people aged less than 45 years to 9.6 (6.6-13.9) for people older than 85 years. Case fatality is lower in Japan than elsewhere, increases with age, and has not decreased over time (2, 5, 13).

Chronic subdural hematoma is known to have a recurrence rate from 5% to 30%, reported by several studies, but authors did not establish the recurrence criteria, yet. However, one of them could be the low blood platelet count and other signs in the context of liver or spleen disorders such as chronic hepatitis and cirrhosis due to viral infections (10, 14)

Many epidemiological studies tried to identify risk factors for intracerebral hemorrhage, in order to find targets for

preventive and therapeutical strategies. Along with hypertensive vasculopathy and amyloid angiopathy, or warfarin use, authors highlighted that an important risk factor in these cases is the hemorrhagic syndrome in the context of a chronic liver dysfunction (3, 4, 6, 9).

**Material and methods**

Our study included a series of 7 cases admitted County Emergency Hospital of Bacau, Romania, Department of Neurosurgery, with diagnosis of subdural hematoma or intracerebral hemorrhage, between 2011 and 2012. The inclusion criteria contained also hepatitis or cirrhosis due to a chronic viral infection with B or C virus, with a low blood platelets count. The exclusion criterium considered patients without viral liver infections.

The studied series included 5 males (3 from rural and 2 from urban area) and 2 females (both from rural area). The age range was 44 to 69, with a median=54 and an mean age=55.85 years.

We considered clinical diagnosis and certain laboratory investigations such as: ALT and AST (alanine and aspartate aminotransferases), blood glucose level, hemoglobin and blood platelet count, as well as the prothrombin time (Quick-test) and Howell test.

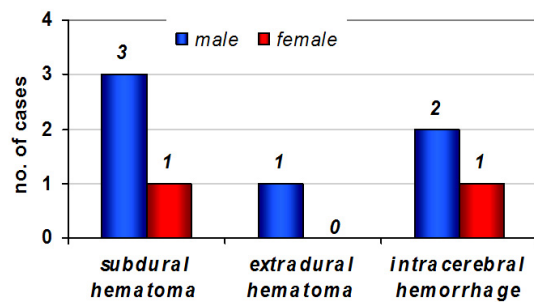
**Results**

1. Clinical features of the studied series. Chronic subdural hematoma was found in 4 patients (3 males and 1 female), one patient with extradural hematoma, and intracerebral hemorrhage in 3 cases (2 males and 1 female) (Figure 1).

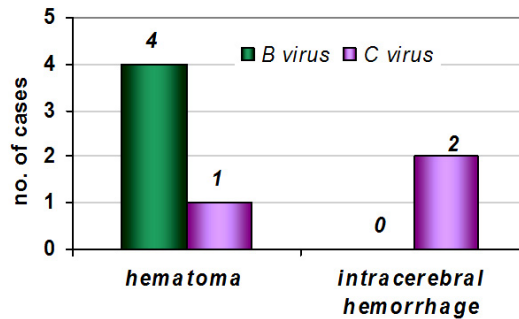
Patients suffering from cirrhosis were 5 (3 males and 2 females) and from chronic

hepatitis – 2 males. Liver disorder was given by B virus in 4 cases (all males) and C virus in 3 patients (1 male and 2 females).

Patients with chronic hematoma also suffered from B virus infection in 4 cases and C virus in 1 case, but intracerebral hemorrhage was observed only in patients with C virus (1 male and 1 female) (Figure 2).



**Figure 1** Distribution of cases by type of lesions and sex



**Figure 2** Distribution of cases by type of lesions and type of liver viral infection

2. Laboratory characteristics. Liver disorder was highlighted by the ALT levels which ranged between a minimum of 15 UI (female, subdural hematoma, chronic hepatitis with C virus) and a maximum of 73 UI (female, intracerebral hemorrhage, liver cirrhosis with C virus). Besides, AST levels ranged between a minimum of 29 UI (male, intracerebral hemorrhage, chronic hepatitis with C virus) and a maximum of 56 (the same patient for maximum of ALT).

Blood glucose levels over 120 mg/dl defined 4 males (all of them with hematoma) and 1 female (with intracerebral hemorrhage), with a maximum of 147 in a patient also suffering from diabetes mellitus type-1.

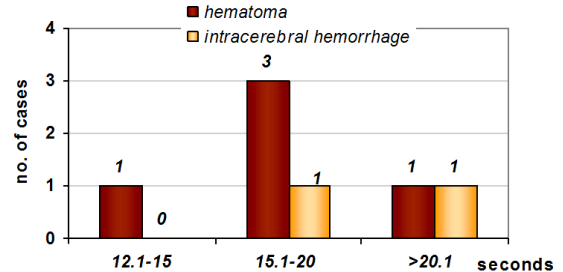
Hemoglobin levels ranged between a pathological minimum of 9.4 g/dl (male, subdural hematoma, liver cirrhosis due to B virus infection) and a normal maximum of 13.9 (female, intracerebral hemorrhage, liver cirrhosis with C virus).

More important in our study context was blood platelet count that could explain a severe hemostatic syndrome in these patients. A minimum of blood platelet count (48,000/ $\mu$ L) registered in the same male patient with a minimum of hemoglobin, and a maximum (91,000/ $\mu$ L) in the same female patient with normal glucose level.

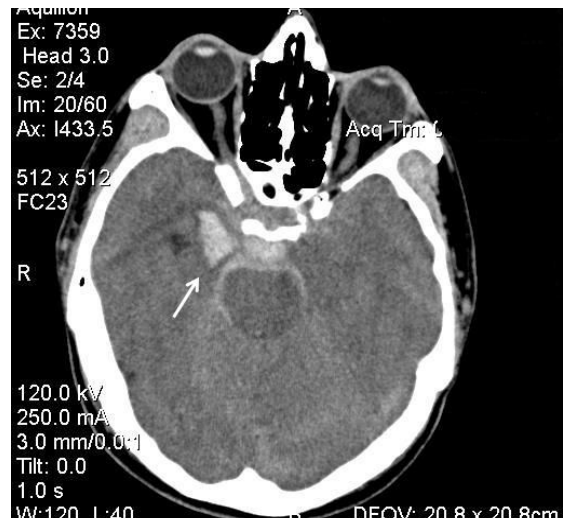
We also took into account the prothrombin time (Quick-test) and Howell test. The Quick-test maximum value in the studied series was of 21.5 sec. in a male case (the same patient with the lowest platelet count), followed by a value of 20.5 sec. found in a female patient with intracerebral hemorrhage and C viral liver cirrhosis (Figure 3). The Howell test values oscillated between the normal limits (70-140 sec.) in all patients.

Evolution. All 7 patients recovered completely after surgical intervention and no death was noticed.

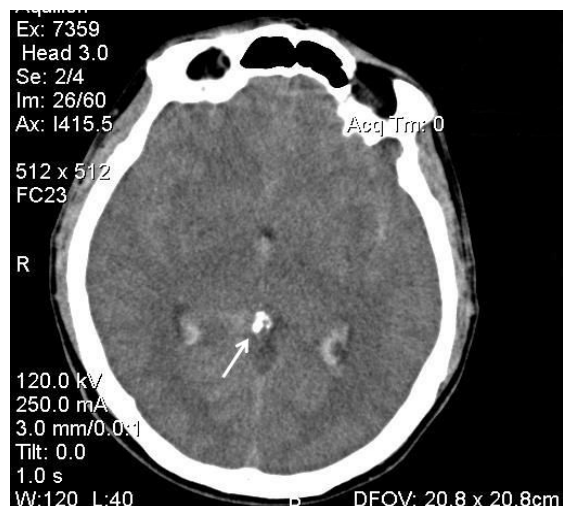
Some radiographic features are presented in Figure 4 and Figure 5 seen below.



**Figure 3** Distribution of cases by type of lesions and sex



**Figure 4** Blood present in the prepontine cisterns, Willis polygon and sylvian valleys (arrow) (male, 63 years old, chronic hepatitis with B virus infection)



**Figure 5** Paracavernos hemorrhagic collection (arrow) (female, 61 years old, liver cirrhosis with C virus infection)

## Discussions

Akioka et al. (1) reported a series of 6 patients with acute spontaneous subdural hematoma, surgically treated between 1994 and 2003. For our study, the most important features of this series was mean age of 53.0 years (range 32-82), and the fact that medical history included hepatitis C. Surgical intervention showed that the bleeding points were identified as ruptures of cortical arteries located near the sylvian fissure. The post-operative evolution showed that one patient completely recovered, one had a moderate deficit, two had severe deficits, one fell into a vegetative state, and one died. Authors highlighted that an early surgical intervention is required for a good outcome.

Other research performed by Hoya et al. (7) on patients with chronic liver disease and their risk of intracerebral hemorrhage noticed that the fatality was lower in this group than in the control group (without liver dysfunction). Authors concluded that the hemostatic disorders seemed to be related to site of hemorrhage, but not to life prognosis in patients with liver disorders and evolution was worsened by non-neurological complications.

In a study performed on 4515 hospitalized cirrhotic patients, between 1997 and 2006, Huang et al. (8) analyzed the risk of spontaneous intracerebral hemorrhage focused on 36 cases with no history of stroke, head injuries, or cerebral arteriovenous malformations. Authors noticed the patients' features, the etiology (virus-related cirrhosis - 0.3%, combined virus- and alcohol-related cirrhosis - 3%) and severity of cirrhosis, as well as hematoma location and prognosis. They concluded that spontaneous intracerebral hemorrhage occurred especially in young

males with mild-to-moderate liver cirrhosis, the etiology of liver dysfunction was related to the incidence of hemorrhage, and not to patients' outcome, but severity of liver cirrhosis was associated with patients' evolution but not with the incidence of hemorrhage.

A cohort study included data collected from the National Health Insurance of Taiwan and performed by Lai et al. (11) during the year 1999 noticed that intracerebral hemorrhage developed in 1.3% of patients with liver cirrhosis, with an adjusted hazard ratio of 1.62 (95% CI, 0.85 to 3.10) for patients with liver cirrhosis to develop intracerebral hemorrhage compared with patients without liver cirrhosis. Authors concluded that patients suffering from liver cirrhosis had a similar incidence rate of intracerebral hemorrhage with a trend of increased risk for intracerebral hemorrhage compared with the control group.

## Conclusions

Patients with chronic and cirrhotic liver disease and a severe hemostatic syndrome should investigate imaginatively at the cranial-cerebral level, when any "soft" neurological signs occur, in order to diagnose intracerebral hemorrhage and hematoma as soon as possible. An important laboratory alarm signal could consider an important decrease of blood platelet count and a prolonged prothrombin time and a pathologic Howell test.

Chronic liver dysfunctions in the context of a long-term infection with B and C viruses represent important risk factors for neurosurgical conditions such as subdural hematoma and intracerebral hemorrhage.

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