### CASE REPORT

# Severe spontaneous intracranial haematoma in a HIV-negative 66-year-old mild haemophiliac. Complete recovery with the use of 1-month factor VIII replacement

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Summary. Intracranial haemorrhage is the most feared manifestation of haemophilia and is usually seen in severe forms. We report herein the case of a 66-year-old HIV-negative patient with mild haemophilia (factor VIII: 7%) who presented with a spontaneous and massive intracranial haematoma causing hemiplegia and aphasia. We discuss the management of this peculiar situation emphasizing

the need for rapid and adapted FVIII replacement. A complete recovery was obtained using this strategy combined with initial resuscitation measures and subsequent physical therapy.

**Keywords:** factor VIII, intracranial haemorrhage, mild haemophilia A

Intracranial haemorrhage (ICH) is the most serious type of bleeding in haemophiliacs [1]. This complication, mainly seen among severe forms and in the young, may occur spontaneously or after every kind of head trauma and must be suspected within the context of unexplained headache, vomiting or any neurological sign. Our present case-report illustrates the possible occurrence of such a complication in an elderly, non-severe haemophiliac without any context of head trauma and underlines the need for rapid and adequate factor VIII replacement in order to have optimal chances of recovery.

## Case report

A 66-year old man with mild haemophilia A (FVIII levels between 5 and 7%) presented on 23 April 2002 with a sudden aphasia associated with severe headache. The past medical history included a prostatectomy performed in 1989 and a haemophilic pseudotumour operated in 2001 (both under FVIII replacement). The patient was HIV-negative but was

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chronically infected by the hepatitis C virus. He was unresponsive to DDAVP. He did not take any medication. At admission, the physical examination revealed a normal level of conscience, a right motor hemiparesia and a complete aphasia. The systolic blood pressure was 140/80 mmHg. A large left temporo-parietal haematoma associated with cerebral oedema and an intraventricular haemorrhage was seen in the CT scan (Fig. 1). The FVIII level was 7%, the prothrombin time 60% and the platelet count  $189 \times 10^9 \,\mathrm{l}^{-1}$ . No signs of disseminated intravascular coagulation were found. No anti-FVIII antibodies were detectable. Liver biology tests were within the normal limits. No aspirin or NSAIDs had been taken recently. No recent episode of head trauma had occurred. The patient, admitted in the intensive care unit of the neurosurgery department, was immediately treated using anti-oedematous measures and recombinant FVIII (Recombinate<sup>®</sup>, Baxter, Maurepas, France). The initial scheme was 2000 units every 8-h during the first 11 days (first dose given within 2 h of admission), 1500 units every 8 h during the next 5 days and 1000 units every 8 h for the last 16 days. These regimens were based on the daily FVIII levels with the aim of exceeding the 60% threshold. This strategy maintained the FVIII level at a mean value of 90% during the 4-week replacement (extremes: 68-140). Cerebral lesions



Fig. 1. Cranial CT scan at admission showing a large haematoma of the left hemisphere and an intraventricular haemorrhage.

were stable in the second CT scan performed 4 days after admission. The patient was transferred to the physical medicine unit on day 21. On day 21, the hemiparesis had disappeared and the recovery of dysphasia was ongoing. Intensive sessions of language re-education and physical therapy were performed. He returned home on 31 May with a slight dysphonia and expressive dysphasia, and recovered fully within a few months. The inquiry did not reveal any aetiology explaining the occurrence of this severe haemorrhagic event although cerebral arteriography was not performed given the age of the patient. A CT scan performed 4 months after the episode was considered as normal with only a discrete hypodense sequelae.

### Discussion

ICH is the most life-threatening bleeding manifestation of haemophilia [1], accounting for 29% of deaths in HIV-negative individuals [2]. This event is observed in haemophilia A patients in the vast majority of cases [1,3,4] (except for the German Society of Thrombosis and Haemostasis study [5]) and predominantly in severe deficiency (about 85%) [3]. In the Greek series, the incidence of fatal ICH in HIV-negative haemophiliacs was 0.4 per 1000 patient years in mild forms and about 1.6 in moderate and severe forms [2]. Frequencies of 2–12% are reported [1,3,6,7]. More than 70% of patients are less than 20 years [3]. Distribution of anatomical sites (i.e. subarachnoid, subdural or intracerebral)

varies according to different studies [3,4,7]. Before the availability of clotting factor concentrates and CT-scan imaging, this complication was lethal in more than two-thirds of cases vs. 12.5-56% in modern series [1,3,4,7]. ICH is usually traumarelated [3,5] even in apparently insignificant challenges but spontaneous episodes are also frequent [4]. During the last two decades, the proportion of cases has appeared to increase [7]. This fact could be explained by the haemophiliac population aging while the impact of HIV infection is debated (precise mechanisms undetermined so far) [3,6]. The risk also seems augmented in patients with inhibitors [1] although this correlation is not found in all studies [3]. A recent epidemiological study performed in the USA isolated the following factors as independently associated with ICH: deficiency severity [odds ratio (OR): 2, P : 0.05], age (more than 51 vs. 6–10 years; OR: 3.7, P: 0.02), presence of an inhibitor (OR: 3.5, P < 0.001), HIV seropositivity (in whites only) (OR: 4, P < 0.001) [7]. In the Greek haemophiliac population studied by Koumbarelis et al. [2], the mortality by ICH was five times higher in HIV-positive patients (5.5 per 1000 patient years) whatever the deficiency severity.

Considering the therapy policy, factor injections should be administered as early as possible in the initial management and long periods of daily replacement are warranted [3,4]. Operation is recommended in some studies when no improvement is noted within a few hours [1]. More than half of patients suffer from psychoneurological sequelae, the major problems being seizure disorders, mental retardation or motor impairment [3–5]. Severity of sequelae in the young was correlated to age at bleeding, neonates demonstrating the least outcome [5]. Late recurrences are possible which explain the prolonged prophylaxis policy proposed by some teams.

Our case is noteworthy on several points. Because the occurrence of ICH is rarely reported among mild haemophiliacs [2], no clear guidelines for management have emerged as in severe cases. Such patients are, in fact, in intermediate clinical position between severe deficient cases and individuals with normal haemostasis. The important issue explaining, in part, the good outcome, besides the use of specific resuscitation measures and physical therapy, was the rapid replacement instituted with FVIII in order to struggle against the haemorrhagic phenomenon. Hence, one must not forget that factor infusions are urgently required in mild haemophiliacs facing severe haemorrhagic challenges. The replacement scheme must be individualized and adapted every day according to FVIII assays. Because the neurological recovery was good, although progressive, no surgical strategy was adopted and the replacement period was limited to 4 weeks considering the regular discussions with the neurosurgery and reanimation teams. Common predisposing factors such as trauma, HIV, inhibitor against FVIII, previous known high blood pressure or cerebrovascular disorder were absent here.

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### References

1 Martinowitz U, Heim M, Tadmor R *et al.* Intracranial hemorrhage in patients with hemophilia. *Neurosurgery* 1986; 18: 538–41.

- 2 Koumbarelis E, Rosendaal FR, Gialeraki A *et al.* Epidemiology of haemophilia in Greece: an overview. *Thromb Haemost* 1994; 72: 808–13.
- 3 De Tezanos Pinto M, Fernandez J, Perez Bianco PR. Update of 156 episodes of central nervous system bleeding in hemophiliacs. *Haemostasis* 1992; 22: 259–67.
- 4 Bentancor N, Lavalle E, Vila VM, Johnston E, Borovich B. Intracranial hemorrhage in hemophiliacs. Study of 10 episodes. *Sangre (Barcelona)* 1992; 37: 43–6.
- 5 Klinge J, Auberger K, Auerswald G, Brackmann HH, Mauz-Korholz C, Kreuz W. Prevalence and outcome of intracranial haemorrhage in haemophiliacs. A survey of the paediatric group of the German Society of Thrombosis and Haemostasis (GTH). Eur J Pediatr 1999; 158 (Suppl. 3): \$162-5.
- 6 Nelson MD Jr, Maeder MA, Usner D *et al*. Prevalence and incidence of intracranial haemorrhage in a population of children with haemophilia. The Hemophilia Growth and Development Study. *Haemophilia* 1999; 5: 306–12.
- 7 Nuss R, Soucie JM, Evatt B. Changes in the occurrence of and risk factors for hemophilia-associated intracranial hemorrhage. *Am J Hematol* 2001; **68**: 37–42.