Intracranial hemorrhage in a HIV patient.
Case report and review of the literature

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Intracranial haemorrhage in a HIV patient: A case report and review of the literature

The authors report on a case of a hemophilic male patient, aged 43, HIV positive, HCV positive, who had an episode of intracerebral hemorrhage after a car accident. Intracranial hemorrhage is the most feared complication of hemophilia, especially among HIV positive, who now are considered to be a group at high risk for bleeding. In this report, it is reviewed available data on clinical and imaging features of ICH and the association between ICH and HIV.

KEY WORDS: Hemophilia, HIV infection, Intracranial haemorrhage.

Introduction

Hemophilia A is a hereditary X-linked recessive disorder in which the clotting ability of the blood is impaired and excessive bleeding results. It is caused by deficiency of coagulation factors. Factor VIII deficiency causes hemophilia type A and factor IX deficiency causes Christmas disease. Severity of symptoms can vary and severe forms become apparent early on. Prolonged bleeding is the hallmark of hemophilia A Mild cases may go unnoticed until later in life when there is excessive bleeding and clotting problems in response to surgery or trauma. Internal bleeding may happen anywhere, and bleeding into joints is common, whereas other sites may also bleed, including CNS. In the past, the plasma concentrates carried the risk of transmitting blood-borne diseases such as hepatitis and AIDS. About 60 percent of

persons with hemophilia who were treated with plasma concentrates in the early 1980s were infected with HIV. However, the risk of transmitting HIV infection through plasma concentrates has been virtually eliminated by today's use of screened and processed blood and a genetically engineered factor VIII (Recombinant).

Case report

A 43-years old male patient with severe type A hemophilia (fv $\pi\pi\pi$<1%) and no known history of inhibitor was admitted to the hospital with vision disturbances and sensory ataxia after a car accident.
He is HCV and HIV seropositive since 1982. He has received combined treatment (peginterferon alpha-2b + rebavirin) for HCV infection with no response, and at the present time the disease has progressed to decompensated cirrhosis. He is on antiretroviral therapy since 1989 and his HIV stage is C3. (CD4.80cells/mm3, HIV RNA 22.990 copies/ml)
He had developed high grade B cell lymphoma in 1997 for which he was treated with chemotherapy (CHOP-6 cycles). He responded well and stayed in remission for 5 years; when he relapsed, he responded well once again to chemotherapy.

Computed tomography revealed a hyperdense lesion in the left parietal lobe, surrounded by large edema, without displacing the midline structures (Fig. 1). After intravenous administration of contract media there was a slight enhancement of the lesion (Fig. 2).

Magnetic resonance imaging showed a hyperintense lesion in the posterior left parietal lobe with surrounding edema on both T1 and T2 weighted images suggestive of subacute intracerebral hemorrhage (Figs. 5 and 6).

After administration of gadolinium (GD) the lesion was slightly enhanced (Fig. 4). FT image with suppression of CSF signal revealed a high signal lesion. In the cortex of the right temporo-occipital lobe there were high signal foci indicative of infracts (Fig. 3).

The patient was treated with recombinant factor VIII and mannitol, leading to gradual improvement of clinical symptoms.
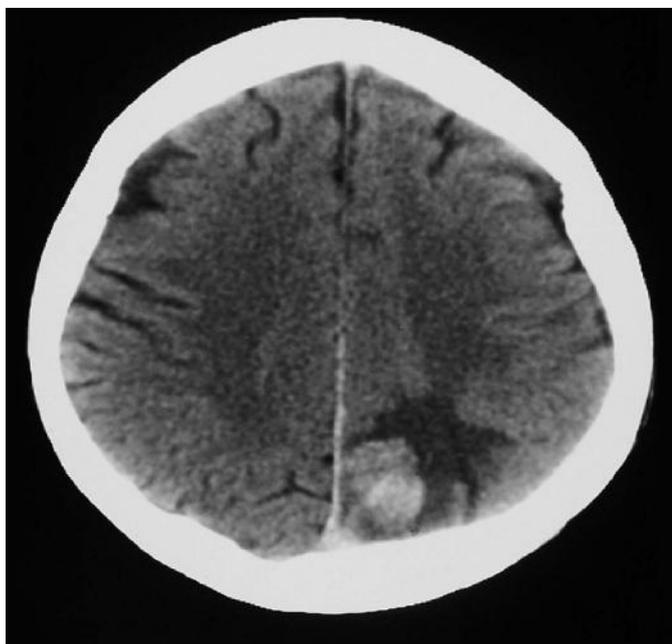
Fig. 1: CT: Hyperdense lesion in left parietal lobe, surrounded by large edema, without displacing the midline structures.
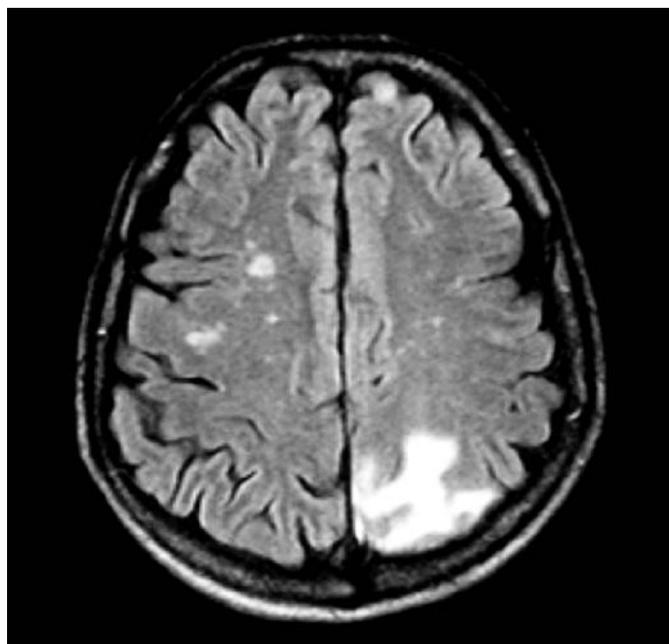
Fig. 3: MRI, FT image with suppression of CSF signal: High signal lesion. Coexistence of hyperintense areas in the cortex of the right temporo-occipital lobe, suggestive of infracts.
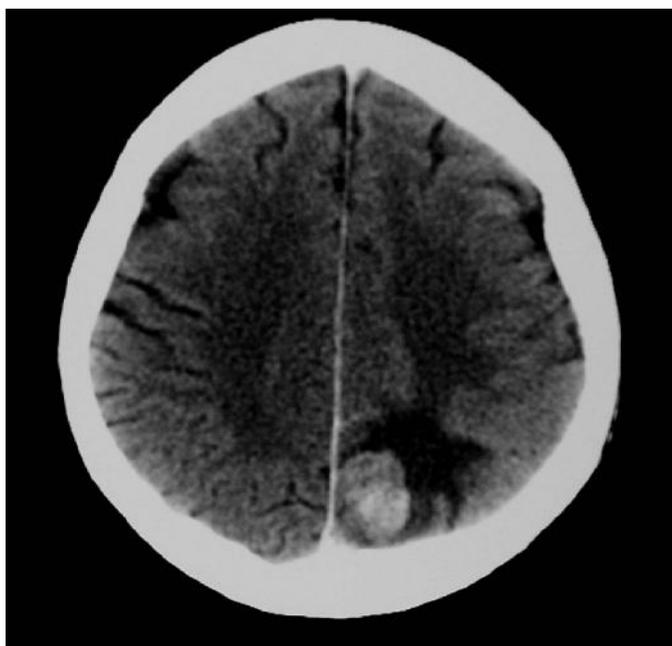
Fig. 2: CT after intravenous administration of contract media: Slight enhancement of the lesion.
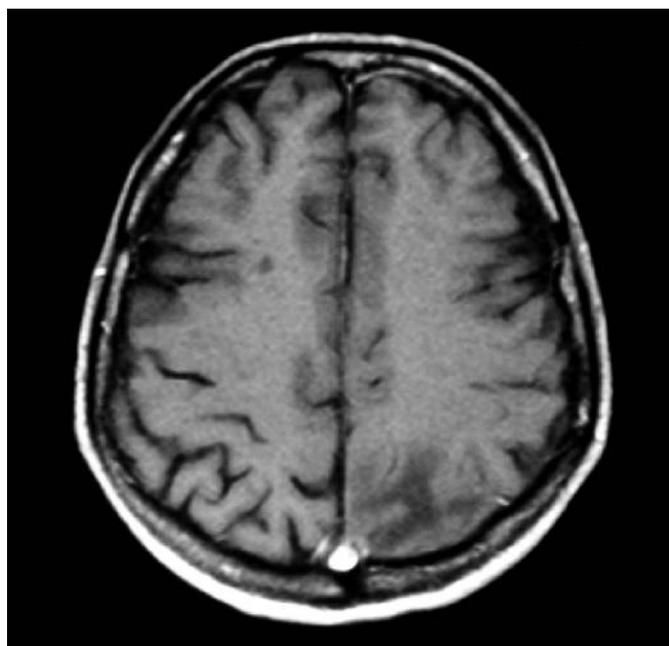
Fig. 4: MRI, T1W1 image, after administration of gadolinium (GD): Slight enhancement of the lesion.
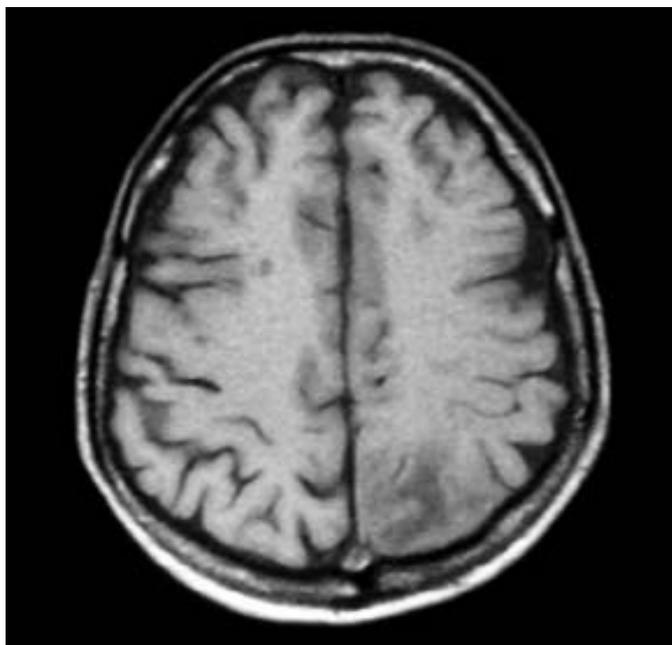
Fig. 5: MRI, TIWI: Hyperintense lesion in the posterior left parietal lobe with surrounding edema.
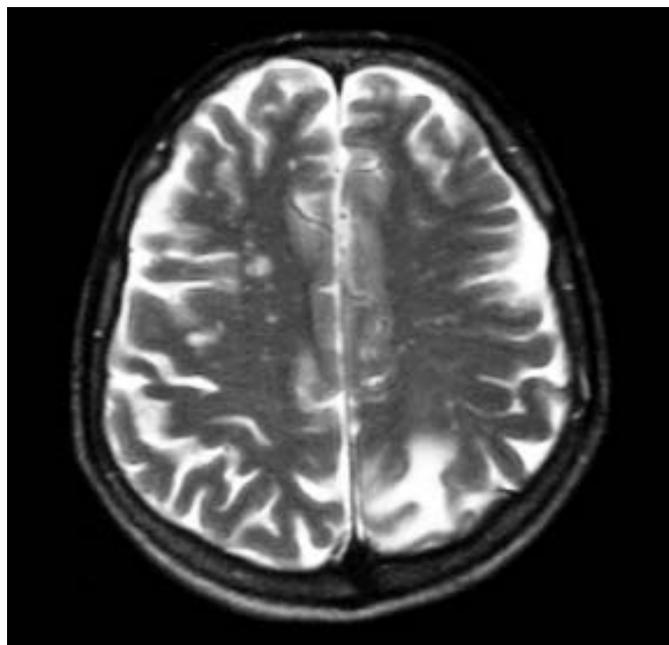
Fig. 6: MRI, T2W1: Hyperintense lesion, indicative of subacute hemorrhage.

Discussion

Hemophilia is characterized by prolonged coagulation times, due to deficiency of coagulation factors, resulting in excessive bleeding either spontaneous or trauma related.

Antracranial hemorrhage (ICH) is the most serious, life-threatening complication of hemophilia and the second leading cause of death of both HIV positive and HIV negative hemophiliacs, second to AIDS [1-4], while those who survive suffer from seizures, decreased intellectual capacity and several sensorimotor and speech disorders [5-8]. The prevalence of ICH in hemophiliacs varies between 4-12% [6,7]. Older age, severe hemophilia and presence of an inhibitor are found to be factors positively associated with ICH [9].

Central nervous system (CNS) hemorrhage may take place at any site. Hematomas may be subdural, epidugral, subarachnoid, intracerebral or intraventricular [9,10]. Clinical symptoms and signs are suggestive of the location of the lesion. Severe sudden headache, nausea, vomiting, seizures, consciousness status alterations and meningism indicate subarachnoid hemorrhage, while focal neurological manifestations imply intracerebral hemorrhage, which when is localized left may also manifests with aphasia, agnosia and apraxia. In our case, the patient presented with sensory ataxia and vision disorders compatible with optic radiation involvement, findings that are suggestive of the lesion being in the parietal lobe, as proved with the imaging examination.

Computed tomography (CT) is the indicated imaging modality for demonstrating intracerebral hemorrhages. The lesion appears as an area of increased attenuation, ranging from 50-90 Hounsfield units, seen immediately from the time of hemorrhage onset, surrounded by a low attenuation ring, which results probably from clot retraction and damage of the blood-brain barrier. After contrast media administration, enhancement occurs peripherally. Subarachnoid hemorrhage is recognized on CT as high attenuation areas anywhere in the subarachnoid space or the basal cisterna, representing the extravasating blood. Subdural bleeding appears as a crescent-shaped hyperdense area; the hematoma is concave toward the hemisphere. Finally, epidural hematomas present as biconvex, hyperdense areas immediately adjacent to the vault [11,12].

The appearance of intracerebral hematomas with magnetic resonance imaging (MRI) depends on the time passed from onset. Acute hematomas may escape detection, since they appear isointense with normal parenchyma on both T1- and T2- weighted images, while subacute hemorrhage presents as area of high signal on both T1- and T2-weighted images. Administration of intravenous gadolinium, after about a week, results in a thin rim of peripheral enhancement. MRI is less sensitive in detecting subarachnoid hemorrhage, which can be recognized by the relatively high signal compared to the low signal of the CSF. Extracerebral hematomas are better demonstrated with MRI; although initially hematomas appear isointense and become progressively hyperintense on T1-weighted images, the displacement of the cortex is an indirect sign of extracerebral collection [11].

Since 1982, HIV has been observed to play a role in the occurrence of ICH among hemophilic patients and is considered to be a major risk factor for ICH especially among whites, attributed maybe to genetic susceptibility [7,9]. In the literature it is reported that the incidence of ICH among HIV positive patients is greater than that of HIV negative [7,9]; in some series the ICH cases were even twice as many in HIV positive population than the ICH cases in HIV negative individuals [9]. It is known that the majority of ICH in hemophilic patients occur in the pediatric population, in which trauma and birth related injury are the most important risk factors [7,13]. Since HIV infection, it is observed that intracranial hemorrhagic episodes in hemophilic patients older than 20 years old have increased [7,9]. This age shift happened mainly during and following the HIV epidemic, while it is to mention that the majority of hemophilic patients with ICH are HIV positive.

ICH in HIV positive patients is most often spontaneous [7,9]. The non trauma related ICH among hemophilic patients is probably due to CNS lymphoma, metastatic Kaposi's sarcoma, which is quite rare, and HIV-related thrombocytopenia that occurs frequently among whites [14,15], either immune-mediated or caused by bone marrow suppression by drugs or HIV itself [7,9,16]. Platelet count less than 50.000/Il is a serious risk factor for developing spontaneous hemorrhage at any site including intracranially. In HIV positive patients, primary high grade B cell lymphoma is the most common tumor.

It tends to be multifocal with periventricular spread and necrosis and hemorrhage are common. CT shows a hypo- or hyperdense lesion with ring or nodular enhancement after contrast media administration, while on MRI T1 weighted images appears as low signal lesion, enhancing with gadolinium and on T2 weighted images as an intermediate to high signal lesion. Edema and mass effect are variable [11].

Although it is reported a small number of ICH cases in patients under continuous prophylaxis [9], further studies need to be conducted so that there will be sufficient data to assess the effect of this form of therapy.

Hemophilic HIV positive patients who experience ICH unfortunately have a poor survival [4]; nevertheless in our case there was gradual clinical improvement after treated with recombinant VIII factor and mannitol. It is worth mentioning that our patient suffers from cirrhosis due to HCV, not responding to antiretroviral therapy with pegintron and rebavirin. Liver failure and cirrhosis result in the decreased production of coagulation factors, especially of II and VII and the in the reduction of platelets due to hypersplenism, respectively. Thus, there was an additional aggravating factor that may have had an influence on coagulation mechanism except from hemophilia and HIV related decreased number of platelets. Moreover, the patient is under antiretroviral therapy with protease inhibitors, which have been found to be associated with increased bleeding tendency in cas-

es of hereditary disorders, poorly responding to factors replacement therapy. Fortunately, this bleeding tendency seems to subside with time [17,18].

We believe that the absence of coagulation factor inhibitors and the prompt replacement of VIII factor, which appears to be the most important aspect of treatment [5,7,19], contributed to his recovery.

In conclusion, intracranial hemorrhage among hemophiliacs is a serious disease. Moreover HIV has become a major risk factor for hemophilic patients. Since treatment regimens are limited, prevention is the most effective approach. Coagulation factor replacement and multidisciplinary team approach may result in decreasing mortality and morbidity.

Riassunto

Si riporta il caso di un paziente di 43 anni affetto da emofilia, HIV ed HCV positivo, il quale ha avuto un episodio di emorragia intracerebrale in seguito ad un incidente stradale. L'emorragia intracranica è la complicanza più temuta nei soggetti affetti da emofilia, specialmente se HIV positivi, i quali ad oggi si considerano un gruppo di malati ad elevato rischio di emorragia. Si procede quindi ad una revisione dei dati disponibili circa il quadro clinico dell'emorragia intracranica (EI) ed i risultati ad essa relativi derivanti dall'uso delle tecniche diagnostiche per immagini, documentando l'associazione tra EI e HIV.

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