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Recurrent hypertensive intracerebral hemorrhage: a case series from a single institution in Iraq

Tekrarlayan hipertansif intraserebral kanama: Irak'ta tek bir kurumdan vaka serisi

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Abstract
Hypertensive intracerebral hemorrhage (ICH) is usually once in a life event. We aimed to explore the pattern of hemorrhage and outcome of recurrent hypertensive ICH. This prospective, consecutive, case series was conducted at the Sulaimaniya general teaching hospital, Iraq, from June 2008 to April 2012. Survived patients with primary hypertensive ICH were followed-up for a variable time; 4 patients only developed a recurrence. All patients underwent serial non-contrast CT brain scanning on the first and second presentations and after variable intervals. The clinical presentations and their outcomes as well as the sites of the hemorrhages were noted. All patients (n=4) were females and their ages ranged from 58 to 72 years. All of the patients had long-standing hypertension and hypercholesterolemia. The first hemorrhages were distributed equally between the right and left sides of the brain while the recurrent ones were more common on the left side. Three out of 4 recurrences developed contra-laterally while only one was ipsilateral to the first hemorrhage; putamenal-putamenal; thalamic-thalamic; cerebellar-cerebellar; and lobar-thalamic. The interval between recurrences ranged from 54 days to 3 years, 8 months, and 2 days. The functional outcome after the first hemorrhage was relatively good in the majority but the second stroke resulted in prominent neurological dysfunction. Recurrent hypertensive ICH was rare among our patients but resulted in profound neurological functional impairment. Contralateral recurrences dominated the pattern. The thalamus was the target for recurrence in 50% of cases.
Keywords: Hemorrhagic stroke; hypertension; recurrent intracerebral hemorrhage

Özet
Hipertansif intraserebral kanama (HIK) genellikle yaşam boyunca bir kez görünür. Çalışmamızda ise tekrarlayan HIK'ın kanama özelliklerini ve prognozunu aydınlatmayı amaçladık. Haziran 2008 ile Nisan 2012 tarihleri arasında Süleymaniye Genel Eğitim ve Araştırma Hastanesi, Irak'ta çalışma prospektif, ardışık vaka serileri ile sürdürülmüştür. Primer HIK sonrası yaşayan hastalar değişken sürelerde izlendi; sadece 4 hastada tekrarlama görüldü. Tüm hastalara ilk ve ikinci başvurularında ve belirli zaman aralıklarında tarama testi olarak kontrastsız bilgisayarlı beyin tomografisi testi uygulandı. Klinik tabloları, prognozları ile beraber kanama bölgeleri kayıt edildi. Dört hastada kadın idi yaşları 58 ve 72 yıl arasında değişmekteydi. Hastaların hepsinde uzun süreli hipertansiyon ve hiperkolesterolemi öyküsü vardı. İlk kanama odakları beynin sol ve sağ yanlarına eşit dağılmışken, tekrarlayıcı olanlar daha çok sol yandaydı. Üçünün tekrarlayıcı atağı kontro-lateral iken sadece birinin ipsilateral kanama idi; putamenal-putamenal, talamik-talamik, serebellar-serebellar ve lobar-talamik. Tekrarlar arası süre 54 gün ile 3 yıl arasındaydı. Çoğu hastada ilk kanama sonrası fonksiyonel düzelme daha iyiydi ama ikinci inme belirgin nörolojik hasar ile sonuçlandı. Tekrarlayan HIK nadir olmasına rağmen belirgin nörolojik fonksiyonel bozulma ile sonuçlanır. Baskın olan şekil kontro-lateral olandır. Vakaların yarısında talamus hedef organdır.
Anahtar kelimeler: Kanamalı inme, hipertansiyon, tekrarlayan intraserebral kanama

Introduction

Intracerebral hemorrhage (ICH) is one of the devastating subcategories of stroke, comprises approximately 10-15% of all strokes combined, and ranks second to ischemic stroke. Although the list of etiologies behind spontaneous non-traumatic ICH is long, chronic long-standing hypertension by far is the commonest cause and accounts for at least 50% of the cases. It is considered a one-time event and patients rarely rebleed at the same or at another site (1,2).

Materials and methods

This prospective, consecutive, case series was conducted at the department of neurology, Sulaimaniya general teaching hospital, Iraq, from June 2008 to April 2012. All patients with a diagnosis of primary spontaneous ICH who survived the initial event were followed-up at variable intervals and recurrences were noted. To be enrolled in the study, patients should have a documented long-term hypertension before their first stroke (two readings or more of a systolic blood pressure of ≥ 160 mmHg and/or diastolic blood pressure of ≥ 90 mmHg; with or without treatment); have no past history of ischemic stroke (old, recent, or in-between the hemorrhages); and hold no other etiology (or etiologies) for ICH before and during the enrollment. Patients were excluded from the study if they had an etiology other than hypertension, developed a new risk factor for ICH after the first event, or developed an ischemic stroke in-between the hemorrhages. Patients who were lost or died during the follow-up period were excluded from the study.

Patients were examined, managed, and followed-up by a neurologist and neurology interns. All patients underwent routine blood testing (including prothrombin time and activated thromboplastin time), a 12-lead resting ECG examination, and transthoracic echocardiography within 24 hours of admission. An urgent non-contrast CT brain scanning was done at the time of Acute&Emergency department admission and after a variable interval (in both presentations). Cranial magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) were done in all cases after 6 weeks of the first hemorrhage, searching for

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vascular anomalies; we have no facilities for doing conventional cerebral angiography.

Results

Tables 1 and 2 display the various patients' characteristics, dates and sites of the hemorrhages, and their clinical presentations and outcomes.

From June 2008 to December 2010, a total of 169 patients with a hypertensive ICH ware admitted to our neurology department; this defines the period of patients' enrolment, after they had developed their first ICH; the study was stopped in April 2012 when patient 4 developed her recurrent ICH. One hundred and four patients survived their stroke and were discharged home; all patients were scheduled on a regular follow-up and rehabilitation program. Several patients were lost during this follow-up period and many died, as well, and 57 patients remained in the study.

Of those 57 patients, 4 (7%) patients only developed another hypertensive ICH (Figure 1) and all of them were females, hypertensive, and hypercholesterolemic. The site of the first hemorrhage was different among the 4 consecutive patients (lobar; putamenal; cerebellar; and thalamic) respectively, but the thalamus was the target of recurrence in 2 patients only. Three out of the 4 recurrences developed contralaterally on the counterpart anatomical area; putamen-putamen; cerebellum-cerebellum; and thalamus-thalamus. None of the 4 hemorrhages recurred on the previous (first hemorrhagic) site. The time interval between the first and the second hemorrhages was very diverse (Table 1) and ranged from 54 days to 3 years, 8 months, and 2 days. The functional outcome of the first hemorrhage was relatively good but the recurrent ones had resulted in profound neurological dysfunction.

Table 1. Patients' ages and dates and sites of their intracerebral hematomas.

Patient's Number	Age	Duration of hypertension	Date of the first hemorrhage*	Site of the first hematoma	Date of the second hemorrhage*	Site of the second hematoma
1	72	18 Years	28/12/2009	Left lobar Occipital	14/07/2010	Left Thalamus
2	68	9 Years	02/11/2010	Right Putamen	07/04/2011	Left Putamen
3	60	12 Years	30/10/2010	Right Cerebellum	24/12/2010	Left Cerebellar
4	58	8 Years	12/06/2008	Left Thalamus	14/02/2012	Right Thalamus

Table 2. Clinical presentation, CT brain scanning findings, and outcome after the first and second hemorrhages (n=4).

No.	First Presentation	First CT Brain	Outcome*	Second Presentation	Second CT Brain	Outcome§
1	Sudden severe headache, drowsiness, right homonymous hemianopia	Left lobar, occipital hemorrhage	Return to pre-stroke activities; visual defect persisted; independent	Dense right-sided hemiparesis and hemianesthesia as well as drowsiness	Left thalamic hemorrhage	Motor dysphasia; right-hemianesthesia; grade 3 spastic pyramidal weakness; can stand and walk with major assistance
2	Grade zero left-sided flaccid weakness	Right putamenal hemorrhage	Dense left-sided spastic pyramidal weakness; dependent	Grade zero right-sided flaccid weakness	Left putamenal hemorrhage	Spastic quadriplegia; no speech output; bed-ridden
3	Severe headache, vomiting, and instability of stance and gait	Right deep cerebellar hemorrhage	Return to pre-stroke activities; mild left-sided cerebellar signs; independent	Drowsiness, dysarthria, inability to sit unaided, and vomiting	Left deep cerebellar hemorrhage	Scanning dysarthria; ataxic gait but needs minor assistance; semi-dependent
4	Right-sided hemianesthesia and grade 2 flaccid weakness	Left thalamic hemorrhage	Grade 4 right-sided pyramidal weakness; moderate hemianesthesia; independent	Progressive obtundation, left-sided grade zero flaccid weakness	Right thalamic hemorrhage	Motor dysphasia; can stand and walk but with major assistance; dependent

Discussion

Chronic hypertension doubles the risk of developing ICH. Longstanding hypertension results in a necrotizing type of arteriopathy with fibrinoid necrosis and lipohyalinosis (which involves arteries smaller than 300 μ in diameter); both processes eventually end up in the formation of Charcot-Bouchard micro-aneurysms. The rupture of these microaneurysms results in ICH (1,2).

Weisberg and colleagues (3) found that the commonest sites of hypertensive ICH are (in order of decreasing frequency) the putamen; the central subcortical white matter of the temporal, parietal or frontal lobes (so-called lobar hemorrhages); the thalamus; deep cerebellar nuclei; and the basis pontis.

The pertinent literature provides conflicting percentages about the precise incidence of recurrent hypertensive ICH. Douglas and Haerer (4) analyzed 35 survivors of hypertensive ICH and found no recurrences. On the other hand, Richardson (5) concluded that this type of recurrence affects at least 14% of his studied population. However, the available medical literature mentions a

range of 1.8 to 6% (6-9). This diverse and wide range of incidences are best explained by Marquardsen (10) who stated that "survivors from hemorrhage are too few to justify any statements concerning the risk of recurrence in this type of stroke." Our number was 7%, which is somewhat consistent with the aforementioned studies.

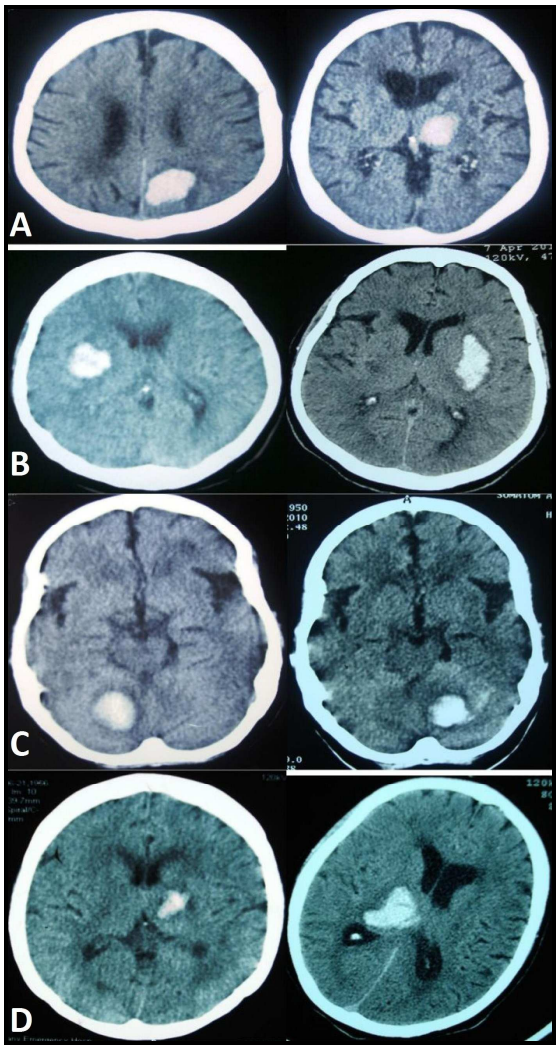

Figure 1. Non-contrast CT brain scanning of patients 1(A), 2(B), 3(C), and 4(D) respectively. All of these scans were done at the time of Acute&Emergency department visit. The scans on the left side represent the first hemorrhagic stroke while the right slices are the recurrent ones. Note that in patients 2, 3, and 4 the hemorrhages had recurred on the contralateral anatomical counterpart area.

In Neau et al (11) series, most patients who sustained a recurrent bleed were females in their 60s while in Chen's paper (12), men marginally outnumbered women and their ages were a little bit younger. However, Hirohata and coworkers (9) found that the ratio of males to females was 8:1 and the average age was 60.5 years. This contrasts with Lee and colleagues (7) opinion who found that the ratio of females to males was 13:1 and that most of the victims were in there mid-fifties. In our series, the victims were the only females and the mean age was 64.5 years.

As for the interval between the attacks (between the first hemorrhage and its recurrent one), the pertinent literature provides a very wide range, from 1 month to 14 years (7,11-13). Our patients' intervals ranged from 54 days to 3 years, 8 months, and 2 days.

Control of blood pressure after the first hemorrhage may prevent ICH recurrences (11) and according to Passero(13), poor control of arterial hypertension was found in 7% of hypertensive patients without rebleeding and in 47% of hypertensive patients with rebleeding. However, in Hirohata series (9), the blood pressure of all cases was normalized or well controlled by antihypertensive agents after the first attack and therefore, he suggested that the mechanism of rebleeding has not been clarified. In our previous report (2), the blood pressure of patient 3 was well controlled after the first hemorrhage; however, she developed another (contralateral) deep cerebellar hemorrhage in less than 2 months. All of our cases seemed to have their blood pressure well controlled after the first hemorrhage, according to the patients' families; this observation is consistent with that of Hirohata et al (9). Patient 1 had a lobar hemorrhage, which in accordance with the patient's age (72 years), points to a cerebral congophilic angiopathic process (cerebral amyloid angiopathy targets the cortical arteries and is more common after the age of 70 years) (14); however, the recurrent bleeding was thalamic and is typical for hypertensive ones (1).

Although we had 4 cases only, the site distribution of the first hemorrhages was equal; lobar; putamen; cerebellar; and thalamic. Two were right-sided and 2 were left-sided. In another word, the putamen and thalamus (so-called ganglionic type) comprised half of the initial sites. This observation goes with published large series (7,15).

The majority of recurrent hemorrhages were lobar-lobar in the reported series of Neau et al (11) and Passero et al (13). However, Lee et al (7) and González-Duarte et al (15) found that the commonest type of recurrence was ganglionic-ganglionic (i.e., putamen and thalamus). The putamen and thalamus, combined, were the target in 3 cases for the recurrent hemorrhage in our series.

The recurrent hemorrhage developed contralaterally in almost all patients and very few patients had a recurrent bleed ipsilaterally, but again, at another (different) site (14). Only 1 out of our 4 cases had a recurrence ipsilaterally; all cases had a recurrent bleed at a different location from the first one. Our observation is consistent with other published series (7,9,11-13,15).

All of our patients recovered functionally to some degree after sustaining their first stroke. However, the second strike resulted in a profound neurological dysfunction and dependency in all patients but patient 3 (with the cerebellar hemorrhages), but none of our patients died during follow-up. The outcome was poor with prominent neurological and cognitive dysfunctions

as reported by other studies (11,15); at least one third of patients died after their second bleeding, early in the follow-up period.

In conclusion, although the number of our cases was very small, our paper has set a new line of research in our institution and this case series, to the best of our knowledge, is the first one addressing this subject in Iraqi patients (all patients were Kurdish in ethnicity, as well).

Limitations

1. No doubt, the number of our cases in this case series was very small. Therefore, the results and outcomes might well have been different if the number of cases was larger. For the same reason, no statistical input was added to the manuscript; observations only were mentioned. Some patients were lost while others died of diverse causes, other than ICH, during the follow-up period. If these groups of patients were added to our data, the outcome might well have been changed considerably.

2. This is a single institutional study addressing Kurdish patients that neither reflects the practice of stroke in the whole of Iraq nor addresses Arab patients (the largest ethnic group in Iraq).

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Consent

An informed consent was obtained from all patients through their families, guardians, or next of kin.

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