Successful outcome after evacuation of intracranial hematoma following thrombolysis in acute myocardial infarction

Tarig S. Al-Khuwaitir, MRCP (UK), ABIM, *Bashir A.Wani,* MD, DM,
Helmi A. Dawood, MBBS, MD, *Mohammed A. Khan,* MBBS, FRCS.

ABSTRACT

Thrombolytic therapy is the modality of choice for the treatment of life threatening thrombosis in various vascular territories and nowadays, is used extensively in setting of acute myocardial infarction. There is, however, the omnipresent danger of serious bleeding inherently associated with the use of all thrombolytics which if it occurs in the brain, can lead to potentially serious neurological impairment and even death. In our report, we describe the successful surgical management of a streptokinase-induced intracranial hemorrhage. Timely neurosurgical intervention is advocated as the optimal approach for this particular side effect of thrombolytic agents.

Saudi Med J 2005; Vol. 26 (1): 130-132

Intracranial hemorrhage (ICH) is a well known complication of thrombolytic therapy for acute myocardial infarction (AMI) occurring in 0.9 – 1% of cases.[1,2] The risk factors for ICH include among others, age more than 65 years, weight less than 70 kg, uncontrolled hypertension and use of tissue plasminogen activator.[2] If 3 risk factors are present, the prevalence of ICH goes to 2.17%.[3] We present an Indian male with ICH following streptokinase administration for AMI, which was successfully evacuated and patient was discharged home ambulatory without any neurological deficit. Immediate surgical removal of intracranial hematoma following fibrinolysis offers the best hope for such patients.

Case Report. A 40-year-old Indian male was admitted to our coronary care unit (CCU) in February 2004 with 3 hours history of chest pain associated with sweating. He was in sinus rhythm with heart rate of 90/minute, blood pressure (BP) 240/140 mm Hg in emergency department, and BP 190/110 mm Hg in CCU, afebrile, with a respiratory rate of 18 per minute. His systemic examination was unremarkable apart from a fourth heart sound at the apex. All peripheral pulses were normal and synchronous with each other.

His electrocardiogram revealed a hyperacute inferior, posterior and lateral wall AMI with normal sinus rhythm. His BP was controlled with intravenous nitroglycerin (NTG), atenolol and captopril to a level of BP 150/102 mm Hg. At this stage, the patient was given streptokinase (SK) as per standard protocol, as well as aspirin (ASA), as he continued to have pain despite NTG, atenolol and repeated incremental doses of morphium. He had a

From the Department of Internal Medicine (Al-Khuwaitir), Department of Cardiology (Wani), Department of Neurology (Dawood) and the Department of Neurosurgery (Khan), Riyadh Medical Complex, Ministry of Health, Riyadh, *Kingdom of Saudi Arabia.*

Received 19th July 2004. Accepted for publication in final form 27th September 2004.

Address correspondence and reprint request to: Dr. Tarig S. Al Khuwaitir, Riyadh Medical Complex, PO Box 3847, Riyadh 11481. *Kingdom of Saudi Arabia.* Tel./Fax. +966 (1) 4783446. E-mail: tarig_alkhuwaitir@hotmail.com

successful clinical reperfusion following SK. He did not receive heparin, as we waited for his coagulation profile post-SK to normalize.

The investigations had revealed a white blood cell count of 16 x 10^9/L, hemoglobin of 12.6 g/dl, platelet (PLT) count of 212. Blood glucose of 9 mmol/l, with normal uric acid level, and electrolytes. The total cholesterol level was 5.4 mmol/l and triglycerides of 0.8 mmol/l. Creatinine kinase (CK) and lactate dehydrogenase (LDH) showed serial elevation of AMI pattern, with CK peak of approximately 5669 u/l, with creatine kinase-MB fraction (CK-MB) of 467 u/l, and LDH peak of approximately 1521 u/l later. Liver function tests revealed an aspartate aminotransferase level of 612 u/l, and alanine aminotransferase level of 141 u/l. His basal coagulation profile showed a prothrombin time (PT) 14.30 second, a activated partial thromboplastin time (APTT) of 24.40 second and an international normalized ratio (INR) of 0.96. Chest radiograph was normal with normal sized aorta. Transthoracic echocardiography revealed normal-sized left ventricle with good systolic function with inferior and lateral wall hypokinesia, and no evidence of dissection or pericardial effusion. During the night of admission 8 hours post-SK, our patient complained of drowsiness, severe headache, effortless vomiting and mild left sided weakness of grade 3-4/5. Blood pressure recorded was 150/107 mm Hg. Coagulation profile this time revealed fibrinogen degradation products of more than 4, fibrinogen level of less than 50 mgs/dl, PT of more than 100 seconds, APTT of 60 seconds, and an INR of more than 10. The PLT count decreased to 148. Computed tomography scan (CT) of brain revealed an intracranial hematoma in the right temporo-parietal area (**Figure 1**). Aspirin was discontinued. Mannitol 20% was administered 250 ml intravenously every 12 hours for 2 days. Immediate neurosurgical consultation was sought after and the patient was given 3 units of fresh frozen plasma. The coagulation profile thereafter almost normalized within 7.5 hours, to a PT 19.90 seconds and a PTT 28.10 seconds, with an INR 1.42, as the fibrinolytic state due to SK is short lived, and normalized the next day to PT 14.90 seconds, PTT 26.50 seconds and an INR 1. Neurosurgical advice was to treat the patient conservatively in view of high risk involved in general anesthesia. The next day our patient became drowsier, almost stuporose and weakness on left side of his body increased. Computed tomography scan was repeated, which showed new bleeding on top of the first one, with midline shift in the same area (**Figure 2**).

The neurosurgeon reviewed the case in consultation with our neurophysician and decided to intervene in spite of high risk involved due to the

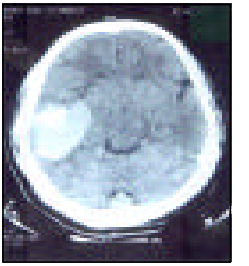

Figure 1 - Computed tomography scan of the brain without contrast showing an intracranial hematoma in the right temporo-parietal region.

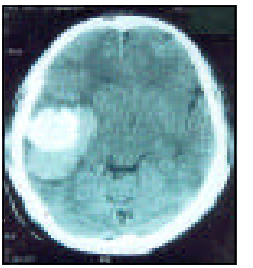

Figure 2 - Computed tomography scan of the brain without contrast showing re-bleeding in the right temporo-parietal region associated with midline shift.

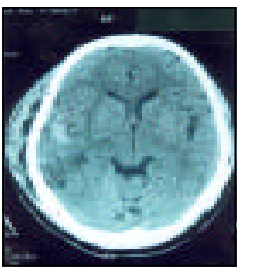

Figure 3 - Computed tomography scan of the brain without contrast on second post-operative day revealing complete removal of the blood clot.

presence of the concomitant AMI, and a large organized clot could be removed successfully in one piece via craniotomy. The following day, the patient improved dramatically as regards to headache, weakness and the level of consciousness. The patient was normal as regards to his neurological status within a week. The CT scan carried out on the second day post-operative is shown in **Figure 3**. Our patient was discharged home with uneventful recovery 4 weeks later on follow up.

Discussion. The major complications of SK include hypotension, allergic reactions and ICH.[3] In our CCU, we receive on an average 3 - 4 patients of myocardial infarction per day, being the major referral center of the Ministry of Health, Riyadh, Kingdom of Saudi Arabia. During the last 10 years, we have seen 3 ICH post-SK therapy. One of these has had a previous hypertensive hematoma, which was unknown to the admitting physician and the patient died from severe hemorrhage; the second one had history of hypertension with fundal changes; he sustained an ICH that left him with mild hemiparesis only. The third patient is the one presented in this report. Our patient followed the symptomatology described in the current literature for ICH after thrombolytics, in that the first clinical sign was a decreased level of consciousness with an initial maximal neurological deficit within 6 hours of onset.[4] The majority of post thrombolytic ICHs are large solitary and supratentorial.[5] Neurosurgical evacuation is controversial, as problems to secure hemostasis include clots formed after thrombolytic therapy that remain liquid and lead to continued local bleeding even after drainage, and cerebral amyloid angiopathy in senescent patients in addition to the finding that the outcome does not improve, especially after alteplase induced ICH.[3,6] From the global utilization of streptokinase and tissue plasminogen in acute myocardial infarction (GUSTO) database 30 days mortality for hemorrhagic stroke in myocardial infarction is 60%.[7] Immediate surgical evacuation is the best option for patients who fail to respond to fresh frozen plasma, fresh blood, platelet transfusions, or cryoprecipitate as otherwise it has been shown that 87% of patients die or have a disabling stroke.[8] In a study of patients with post AMI hemorrhagic stroke, in GUSTO-1 trial 30 days survival was significantly higher with evacuation (65% versus 35% without evacuation) and there was a trend towards improved functional status due to higher incidence of non disability stroke (20% versus 21%).[8] Predictors of mortality in hemorrhagic stroke in the setting of myocardial infarction, as per GUSTO data base, were as follows: low Glasgow coma scale, age, interval between thrombolysis and stroke, hydrocephalus, herniation, mass effect, intraventricular extension and volume of hemorrhage.[7] Our patient did not fit into the risk factor categories described above except for male gender, as he was young, weight approximately 65 kg, with no past history of hypertension, and as he re-bleed in less than 24 hours in spite of a normal coagulation profile, we opted for neurosurgical intervention, which was successful. This therapeutic intervention in our opinion and after review of the pertinent literature is a possible choice to prevent lifelong disability in this worst case scenario particularly in younger patients.

References

1. Gore JM, Granger CB, Simoons ML, Sloan MA, Weaver WD, White HD, et al. Stroke after thrombolysis. Mortality and functional outcomes in the GUSTO-I trial. Global Use of Strategies to Open Occluded Coronary Arteries. ***Circulation*** 1995; 92: 2811-2818.
2. Patel SC, Mody A. Cerebral hemorrhagic complications of thrombolytic therapy. ***Prog Cardiovasc Dis*** 1999; 42: 217-233
3. Simoons ML, Maggioni AP, Knatterud G, Leimberger JD, de Jaegere P, van Domburg R, et al. Individual risk Assessment for intracranial hemorrhage during thrombolytic therapy. ***Lancet*** 1993; 342: 1523-1528.
4. Sloan MA, Price TR, Petito CK, Randall AM, Solomon RE, Terrin ML, et al. Clinical features and pathogenesis of intracerebral hemorrhage after rt –plasminogen and heparin therapy for acute myocardial infarction: the Thrombolysis in Myocardial Infarction (TIMI) II Pilot and Randomized Clinical Trial combined experience. ***Neurology*** 1995; 45: 649-658.
5. Gebel JM, Sila CA, Sloan MA, Granger CB, Mahaffey KW, Weisenberger J, et al. Thrombolysis-related intracranial hemorrhage: a radiographic analysis of 244 cases from the GUSTO-I trial with clinical correlation. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. ***Stroke*** 1998; 29: 563-569.
6. LeBlanc R, Haddad G, Robataille Y. Cerebral hemorrhage from amyloid angiopathy and coronary thrombolysis. ***Neurosurgery*** 1992; 31: 586-590
7. Sloan MA, Sila CA, Mahaffey KW, Granger CB, Longstreth WT, Koudstaal P, et al. Prediction of 30–day mortality among patients with thrombolysis-related intracranial hemorrhage. ***Circulation*** 1998; 98: 1376-1382.
8. Mahaffey KW, Granger CB, Sloan MA, Green CL, Gore JM, Weaver WD, et al. Neurosurgical Evacuation of intracranial hemorrhage after thrombolytic therapy for acute myocardial infarction: Experience from the GUSTO-I trial. Global Utilization of Streptokinase and tissue-plasminogen acute myocardial infarction: Experience from the GUSTO-1 Trial. ***Am Heart J*** 1999; 138: 493.