A 67-Year-Old Man With an Acute Neurological Event: Management

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As was described in the previous installment of "What's the 'Take Home'?" ("A 67-Year-Old Man With an Acute Neurological Event: Presentation, Diagnosis, and Prognosis"),[1] a 67-year-old man was brought to the emergency department (ED) for evaluation of an evolving neurological event. He had been watching evening TV with his wife as is usual for them when he reported having an acute headache and nausea. He got up to go into the bathroom in case of emesis and to obtain some analgesics, but shortly thereafter, his wife heard him fall. She called emergency medical services, and her reported immediate findings combined with those of the ambulance personnel revealed that he was significantly aphasic within minutes and had paralysis of his right arm and leg. Facial asymmetry was also noted. There were no seizures.

His medical history was positive for mild type 2 diabetes, which had been well-controlled (recent hemoglobin A_{1c} level of 6.0%) with diet and metformin. He had had hypertension for many years, which was currently being treated with losartan, 100 mg/d, and a diuretic. There was no history of antecedent transient ischemic attack or other neurological event.

On physical examination, vital signs were as follows: blood pressure (BP), 170/105 mm Hg; pulse rate, 66 beats/min; respiratory rate, 12 breaths/min; and temperature, 37 °C. Doll's eye movement was present, and pupils were equal, round, and reactive to light and accommodation, without nystagmus. There were no carotid bruits. The lungs were clear, and the heart had regular rhythm without murmurs. There was bilateral 2+ ankle and pedal edema. Neurological examination showed a retained gag reflex. He was arousable but significantly obtunded with depressed mentation. There was flaccid paralysis of his right side.

Stat laboratory tests revealed a normal complete blood cell count. Results of a basic metabolic panel showed a glucose level of 136 mg/dL, normal electrolyte levels, and a creatinine clearance of 59 mL/min/1.73 m^2. The partial thromboplastin time (PTT) was normal, the prothrombin time (PT) was 14 seconds (reference value, 12 seconds), and the international normalized ratio was 1.2. Troponin levels were within normal limits, and electrocardiography showed regular rhythm and no injury currents. Voltage criteria for left ventricular hypertrophy were present.

The patient was stabilized in the ED and was found to have a Glasgow Coma Scale (GCS) score of 11. Urgent CT scans revealed the presence of a supratentorial intraparenchymal hemorrhage (IPH) in the region of the thalamus measuring approximately 25 to 30 mL. There was no associated intraventricular hemorrhage and no findings typical of cerebral amyloid angiopathy (CAA). The patient was promptly placed into the neurological intensive care unit (ICU), with urgent consultation with neurology and neurosurgery specialists.

Which one of the following approaches is the most appropriate in this patient's early management?

A. Reverse any hemostatic defects encountered using fresh frozen plasma or recombinant factor VIIa.

B. Initiate BP control using calcium-channel blockers with the aim of reducing systolic BP (SBP) to less than 140 mm Hg.

C. Initiate prompt antiseizure prophylaxis.

D. If no clinical improvement seen within 12 hours, open craniotomy surgical drainage should be performed.

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TAKE-HOME MESSAGE

Solid data exist for the optimal early management of IPH. Stroke unit or ICU care is needed, since mortality and morbidity rates are far better there than in general ward care. There exist essentially acute indications for early neurosurgical intervention—the presence of hydrocephalus, cerebellar hematomas of more than 3 cm, and significant worsening coma and diminished levels of consciousness. In the remainder of cases, an important medical maneuver is acute lowering of SBP into the range of 110 to 140 mm Hg using calcium-channel blocker titrated infusion. Antiseizure medications are indicated only when seizures are encountered, and routine seizure prophylaxis otherwise is counterproductive. Patients should be monitored clinically (eg, level of consciousness, GCS score) and radiologically (eg, hematoma growth, hydrocephalus) to guide further therapeutic strategies.

Answer: B, initiate BP control using calcium-channel blockers with the aim of reducing SBP to less than 140 mm Hg.

The American Heart Association/American Stroke Association have established guidelines for treating patients with IPH.[2,3] These guidelines review and address the medical and surgical issues surrounding cerebral IPH management. An area that was much discussed and controversial decades ago and, sure enough, that is pertinent in the presented patient's case is early BP management.

One of the dominant and independent markers associated with prognosis and outcome in IPH is growth (or not) of the intracerebral hematoma, and the extent of that growth. Hematoma growth, monitored radiologically, occurs in roughly one-third of IPH cases and is an independent marker for poor prognosis. SBP is a key factor in and determinant of such growth—generally, the higher the BP, the more growth. So the Holy Grail of BP that is not too high such that hematoma growth is favored, yet not too low so as to risk diminished brain perfusion and ischemic damage, has been sought for decades.

In patients who present with numbers typical of hypertensive crisis (eg, SBP above 220 mm Hg), immediate lowering to less than 140 mm Hg using calcium-channel blockers is the standard of care.[2,4] For less severe hypertension—an SBP of 150 to 220 mm Hg—there are data showing that hematoma size expansion will be less when SBP is reduced to a target of 110 to 139 mm Hg compared with a target of 140 to 179 mm Hg.[4,5] (In this author's opinion, although these data are indeed "statistically significant," they are still clinically quite subtle, requiring large numbers of patients to demonstrate quite small absolute difference numbers of poor outcomes.) All of this BP titration absolutely should take place in an ICU setting, since there is no doubt that there are outstanding data for diminished mortality and improved functional capacity when ICU care vs standard ward care are compared. Thus, **Answer B** is accurate and is the most appropriate choice offered for the early medical and/or surgical management of IPH.

Two other early medical management issues presented above as options involve hemostasis and seizures. The presented patient has an INR that is ever so minimally elevated at 1.2, with a PT of 14 seconds compared with the normal reference value of 12 seconds. There are no obvious etiologies for these findings in the patient's history and physical examination. And, he has lived his 67 years without any prior bleeding diathesis or history of bleeding with surgical procedures or trauma. Such minimal abnormalities would not be expected to cause abnormal bleeding in any event. But even if we assume these are bona fide findings, the supportive measures offered in **Answer A** would not be the preferred therapies. Factor VIIa is an excessively used and even more excessively discussed general hemostatic "glue" that is given in (too) many circumstances whenever there is even a hint of coagulopathy. Quality trials for IPH have yielded data suggestive of a trend in lower hematoma size at 24 hours but *no* difference in mortality or severe disability from the IPH, and an actual statistical *increase* in arterial adverse events when factor VIIa is used.[6] Thus, it is currently not recommended. If one were going to chase that mini-elevation of INR, 4-component prothrombin plasma concentrates are preferred over fresh frozen plasma, since available evidence indicates better efficacy regarding hematoma growth, with fewer volume overload issues and thromboembolic morbidity risks. Thus, **Answer A** is not correct here.

Answer C refers to seizure prophylaxis. Of course, when seizures are present, antiseizure medication is indicated. But in the absence of seizures, routine prophylaxis is not indicated and may actually be associated with worse outcomes.[2,7] and is not the correct approach.

Finally, the role of surgery needs be addressed. Indeed, essentially immediate neurosurgery consultation is mandatory in cases of IPH. But these invaluable consultations are to determine whether or not such surgery is indicated, what procedure(s) to

perform, and when to perform them. The blanket statement offered in **Answer D** is far too general and is not accurate. The literature supports early surgical intervention in cases of large (>3 cm) cerebellar hemorrhages in IPH, with obvious radiologic evidence of hydrocephalus, regardless of site, and perhaps supratentorial IPH with decreasing level of consciousness with time.[2] The outcomes data for the latter—good recovery with moderate disability—were not different between early craniotomy vs conservative therapy, and this is a complex neurosurgical decision above the complexity of this vignette. Vanguard studies are evaluating whether minimally invasive surgical techniques of hematoma evacuation are able to improve efficacy and outcome in IPH,[2] again in the very specialized provinces of neurosurgery. The answer presented in **Answer D** is too general for the facts of our case.

PATIENT FOLLOW-UP

The patient was started on intravenous infusion calcium-channel blockers, and by hour 6, the SBP had stabilized in the 130 to 135 mm Hg range. A repeated coagulation panel showed totally normal PT and PTT, and no therapy was applied in that regard. At 24 hours, the patient—although still somewhat obtunded—was more arousable and had an improved GCS score, from 11 to 7. Repeated imaging studies demonstrated essentially unchanged hematoma size, still less than 30 mL, with no evidence of hydrocephalus or blood in the ventricles. A consulting neurosurgeon favored a conservative therapy approach. ■

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