

# Nontraumatic Acute Intraparenchymal Hemorrhage: Algorithm for Workup and Differential Diagnosis

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Nontraumatic spontaneous intracerebral hemorrhage (ICH) accounts for 8%-15% of all strokes<sup>1</sup> and has a poor prognosis, with a mortality rate of almost 50% within the first month and 80% rate of dependency at 6 months from onset.<sup>2</sup>

The high rate of early neurologic deterioration after ICH is thought to be related to active bleeding that may occur for hours after symptom onset. Prompt neuroimaging is therefore critical, and it has been shown that patients with symptomatic ICH that undergo earlier neuroimaging are more likely to demonstrate hematoma expansion on subsequent imaging.<sup>3,4</sup> Identification of patients who are more likely to have hematoma expansion is an active area of research, and there are many ongoing therapeutic trials targeting this specific patient population at risk, including Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH-II), The Spot Sign for Predicting and Treating ICH Growth Study (STOP-IT), and "Spot Sign" Selection of Intracerebral Hemorrhage to Guide Hemostatic Therapy (SPOTLIGHT).

In this article, we review the different imaging modalities and provide an algorithm (Fig. 1) for the workup of patients presenting with nontraumatic intraparenchymal hemorrhage (IPH). A differential diagnosis of etiologies and imaging manifestations of primary vs secondary IPH has also been presented.

## Imaging of IPH

Neuroimaging is not only critical in identifying IPH in patients who often have decreased level of consciousness and unreliable findings on physical examination but also in determining the underlying etiology and thus assisting in making important therapeutic decisions. There are several imaging modalities available in the workup of patients who present with IPH, including computed tomography (CT), magnetic resonance imaging (MRI), and digital subtraction angiography (DSA).

## Computed Tomography

Noncontrast CT has traditionally been the workhorse for imaging patients with acute IPH because of its widespread availability, relatively fast acquisition, and accuracy in detecting acute hemorrhage.

Multidetector CT angiography (MDCTA) can accurately identify patients with ICH who have an underlying vascular etiology (secondary ICH). Several recent studies comparing MDCTA with conventional angiography and autopsy findings demonstrated sensitivities ranging from 89%-96% and overall accuracy rates of 91%-99% for MDCTA.<sup>5-8</sup> CT angiography (CTA) is also a useful tool for identifying the CTA spot sign in both primary and secondary IPH. The spot sign is an indicator of active bleeding that has been shown to be a predictor of hematoma expansion and poor outcome in multiple studies.<sup>9-11</sup> Examples of the spot sign are shown in Figures 2 and 5.

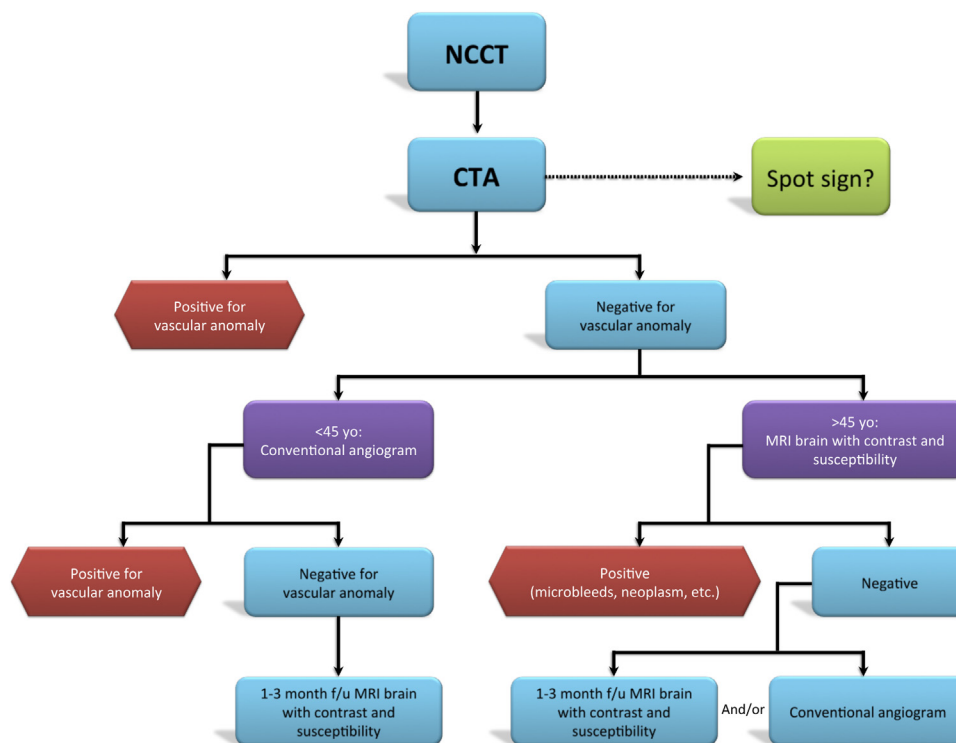
A concern with CTA is the risk of contrast-induced nephropathy in patients with poor renal function. In patients with IPH who present in an emergent condition with decreased level of consciousness, it is often impractical to wait for laboratory results that would delay timely therapeutic interventions. Studies of patients with acute hemorrhagic and ischemic stroke evaluated with CTA found that the incidence of acute contrast-induced nephropathy in this patient population is low and that this risk is no higher in patients whose baseline creatinine value is unknown at the time of scanning.<sup>12,13</sup>

Radiation dose from CT is also a concern; however, the risks and benefits of the procedure, and the drawbacks of not making a timely diagnosis need to be considered. It is important that CT protocols be optimized to deliver the lowest radiation dose possible while still obtaining quality diagnostic images.

## Magnetic Resonance Imaging

MRI is as accurate as CT in identifying acute ICH and is more accurate than CT in identifying chronic hemorrhage, particularly microbleeds associated with cerebral amyloid angiopathy (CAA) or hypertension.<sup>14</sup> The MRI signal characteristics

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**Figure 1** Algorithm for the workup of patients presenting with suspected nontraumatic acute intraparenchymal hemorrhage. NCCT, noncontrast computed tomography. (Color version of figure is available online.)

of various stages of intracranial hemorrhage are reviewed in Table 1. The magnetic susceptibility effect of paramagnetic blood products (deoxyhemoglobin, intracellular methemoglobin, and hemosiderin) is exploited on gradient recalled echo (GRE) pulse sequences in which these blood products appear as areas of signal loss.<sup>15-17</sup> Susceptibility-weighted imaging (SWI), a type of GRE sequence that uses both magnitude and phase images, has been shown to be more sensitive than conventional T2\*-weighted GRE sequences in detecting intracranial hemorrhage, as is demonstrated in Figure 4.<sup>18,19</sup>

Other MRI sequences are also valuable in determining the etiology of IPH. Time-of-flight MR angiography as well as SWI sequences have high sensitivity for identification of vascular lesions and assessment of flow dynamics without intravenous contrast agents and are accurate in demonstrating arteriovenous shunting.<sup>20,21</sup> Contrast-enhanced sequences are useful for the identification of some underlying pathologies such as neoplasms.

Despite its accuracy, there are limitations to the use of MRI, particularly in the emergent setting, these include MRI availability, time, cost, proximity to the emergency department (ED), patient tolerance and clinical status, and contraindicated medical implants including pacemakers.<sup>22</sup>

### Digital Subtraction Angiography

DSA, or conventional angiography, is reserved for those cases where a cause for hemorrhage is not identified with less invasive imaging modalities and for therapeutic purposes. It should be considered in all patients who have subarachnoid blood associated with IPH and in patients with recurrent

hemorrhage. In normotensive patients younger than 45 years, the likelihood of an underlying secondary cause of ICH is high, and these patients should also undergo DSA if noninvasive imaging modalities fail to reveal a cause for ICH.<sup>23</sup> A study on 206 patients with spontaneous ICH found that in patients younger than 45 years without preexisting hypertension or coagulopathy, the angiographic yield was 48% in those with putaminal, thalamic, or posterior fossa ICH and 65% in those with lobar ICH, as compared with 0% and 10%, respectively, in patients older than 65 years with preexisting hypertension.<sup>24</sup>

## Etiologies of IPH

ICH is classified as either primary or secondary, depending on the underlying cause of bleeding. Primary ICH is due to spontaneous rupture of small vessels damaged as a result of chronic hypertension or amyloid angiopathy and is far more common, making up 78%-88% of all cases of ICH.<sup>25</sup> Secondary ICH most frequently occurs in patients with impaired coagulation, underlying neoplasms, vascular anomalies or vasculopathies, venous sinus thrombosis, hemorrhagic transformation (HT) of an arterial infarct, and certain infectious conditions.

### Primary ICH

#### Hypertension

Hypertension is the most important risk factor for spontaneous intracranial hemorrhage.<sup>26</sup> Chronic hypertension leads to hypertensive cerebral angiopathy characterized by intimal

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