The "Blush" Sign on Computed Tomography Angiography is an Independent Predictor of Hematoma Progression in Primary Hypertensive Hemorrhage

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Background and purpose: Hypertension is an important etiology of intracerebral hemorrhage (ICH) in neurosurgical practice. Contrast extravasation on computed tomography angiography, known as the "spot sign", has been described as an independent predictor of hematoma progression and clinical deterioration. However, its role in hypertensive ICH alone has not been determined and is the primary aim of this study. *Materials and Methods:* A retrospective review was carried out of patients with hypertensive ICH admitted to our institution between May 2014 and December 2016. Evaluation of the neuroimaging studies of these patients revealed two distinct morphologies, "spot" and "blush" sign. These distinct signs and covariates were tested for association with hematoma expansion and mortality using multivariate logistic regression. The accuracy of the "spot" and "blush" signs as predictors of hematoma expansion and mortality was determined using receiver-operator characteristic (ROC) analysis. *Results:* A total of 54 patients were identified as hypertensive ICH during the study period. "spot" sign was observed in 11 (20.4%) of the study population. Contrast extravasation (blush-sign) was seen in 7 (14.8%) patients. The "blush" was an independent predictor of hematoma expansion (odds ratio [OR] 6.052; confidence interval [CI] 1.036-15.945 [$P = .012$]) and mortality (OR 3.305; CI 1.240-25.414 [$P = .032$]). With ROC analysis, the "blush" sign was found to have a better predictive value for significant hematoma expansion (area under the curve [AUC]: .795) than the spot sign (AUC: .432). *Conclusion:* The "blush" sign has better accuracy for predicting hematoma expansion in hypertensive ICH and could be used to risk stratify these patients for early therapeutic interventions. **Key Words:** Contrast extravasation—spot sign—intercerebral haemorrhage—hypertension.

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Introduction

Contrast extravasation on computer tomography angiography (CTA), also known as the "spot sign", is a validated predictor of hematoma expansion and worse clinical outcome in primary intracerebral hemorrhage (ICH).[1] However, previous studies validating the spot sign have largely included heterogeneous cohorts of ICH patients, with few examining its predictive value in a "pure" hypertensive ICH cohort.[2-4]

Hypertensive intracerebral bleeds typically are a result of degenerative changes in the walls of small arterioles in the brain as a result of chronic exposure to elevated

blood pressures; leading to decreased compliance, failure of autoregulation, and vessel rupture. Prolonged exposure to high blood pressures also predisposes to the development of microaneurysms in these vessels, whose rupture result in ICH.[5] These arterioles typically supply the deep subcortical structures of the brain, accounting for the higher incidence of hypertensive bleeds in the following regions: basal ganglia, thalami, cerebellum, and pons.[6]

Hypertensive ICH is a significant cause of morbidity and mortality and afflicts up to 35 of 100,000 people per year.[7] Our aim is to validate the spot sign's predictive value in this cohort in order to facilitate the introduction of protocols allowing early intervention in patients at risk of hematoma expansion.

Materials and Methods

Patient Cohort and Study Protocol

All patients admitted to our center with intracerebral hemorrhage between May 2014 and December 2016 were identified retrospectively. All of these patients underwent a CTA of the brain upon identification that they had intracerebral hemorrhage at the time of presentation to the emergency department, as part of our hospital's ICH protocol. Patients aged 21 years or older with systolic blood pressure greater than 140 mm Hg on arrival, ICH in the basal ganglia, thalami, pons, and cerebellum were admitted into our study. An interval computer tomography scan of the brain (CTB) was repeated within 24 ± 6 hours to assess for hematoma expansion. Patients with secondary causes of ICH like trauma, neoplasm, vascular malformations, aneurysmal rupture, hemorrhagic transformation of previous ischemic strokes, etc. were excluded from the study. Additionally, patients without a follow-up CTB, those who underwent early surgical intervention before follow-up CTB, were also excluded.

Patient demographic characteristics such as age and gender were collected. Premorbid medical history for diabetes mellitus, hypertension, ischemic heart disease, renal disease, and smoking status were extracted and the Charlson Comorbidity Index[8,9] was derived for each patient. Information about the premorbid use of antithrombotic agents was obtained. Blood pressure (BP) and Glasgow coma scale (GCS) were measured at presentation for all cases. Platelet count, Activated Partial Thromboplastin Time (APTT) and Prothrombin Time (PT) were measured. Process variables such as onset-to-CT time were recorded. Treatment target was to reduce systolic BP to less than 140 mm Hg within 2 hours of admission and maintain it for first 24 hours. BP was closely monitored every 15 minutes for 2 hours and then hourly for next 22 hours. Modified Rankin scale (mRS) and mortality at 3 months served as secondary outcome measures. This study was performed according to our institution's ethical guidelines.

Image Acquisition and Analysis

Upon arrival to the emergency department, noncontrast CTB and high-resolution CTA were performed as standard protocol on a 64-slice multi-detector helical scanner (Philips Inc, Santa Fe Springs, CA, USA) and images were acquired with 70 ml bolus injection of contrast. Scan parameters at our institution were: (1) slice thickness 1 mm; (2) no slice gap; (3) field of view 200 mm; (4) matrix 512×512; and (5) 230-250 mAs. Coverage was from the base of skull to the vertex and the source images were reformatted into 3 mm-thick axial, coronal, and sagittal projections. Maximum intensity projection images were routinely provided as part of the CTA.

All CTA images were anonymized and reviewed at the same workstation, independently by two experienced readers blinded to the patients' clinical information, outcome, or results of other neuroimaging modalities. The presence of the spot sign was identified according to previously published methods with high interrater reliability.[10] Spot sign was stratified into (1) the "dot" sign—identified as a 1 mm × 2 mm dot of contrast extravasation and (2) the "blush" sign—defined as contrast extravasation larger than 1 mm × 2 mm with a curvilinear jet-like appearance. The ICH locations were categorized as those based in basal ganglia, thalamic, pontine, or cerebellar regions. Clot size was calculated using the ellipsoid formula $(a \times b \times c/2)$ and units were given in ml. Additional imaging findings such as the presence of a spot sign, location of ICH and the presence of IVH were noted. CTB brain was repeated at 24 ± 6 hours. Both absolute change in hematoma size (ml) and relative percentage change were calculated to evaluate hematoma expansion. Significant hematoma expansion was the primary outcome of this study, defined as an increase in absolute hematoma size by 6 ml or relative increase of 33%.[2,11,12]

Statistical Analysis

Statistical analysis was done using SPSS Statistics 24.0 (IBM Corp, Armonk, NY). A P value of less than .05 was considered significant. Distribution of the variables are presented as percentages, and the numbers as mean ± standard deviation or median (interquartile range), as applicable. CTA "blush" sign and spot sign were entered as present or absent. Statistical significance for intergroup differences was assessed by Pearson's chi-square or the Fisher's exact test for categorical variables, and by Student's t test or the Pearson's correlation for continuous variables, as appropriate.

Using univariate logistic regression analyses, clinical and neuroimaging predictors were tested for their association with hematoma expansion (dichotomized outcome). Predictors significant at $P < .05$ from the univariate analysis were subsequently entered into a forward stepwise multivariate logistic regression model to determine factors that could be considered as independent predictors of