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Ongoing Intracerebral Bleeding despite Hemostatic Treatment Associated with a Spot Sign in a Patient on Oral Anticoagulation Therapy

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Introduction

In spontaneous intracerebral hemorrhage (ICH) hematoma size is known to be one of the most important predictors of 30-day mortality and hematoma expansion is an independent predictor of mortality and functional recovery [1]. Especially ICH patients on oral anticoagulation (OAC) are at risk of increase in hematoma size [2]. Reliable radiographic predictors of ICH growth do not exist [3]. The presence of spot signs was found to be associated with hematoma expansion and poor clinical outcome [4–7]. Spot signs are defined as very small areas of 1–2 mm diameter showing contrast enhancement on computed tomography angiography (CTA) within the hematoma, with or without clear contrast extravasation on postcontrast CT (PCCT) [4]. However, the detailed entity of spot signs is not fully understood [4–7].

Case Report

An 81-year-old woman presented to the emergency department with sudden right-sided weakness and impaired consciousness since 08:00 a.m. She was on OAC because of atrial fibrillation with an initial international normalized ratio (INR) of 3.6. Cra-

nial CT at 09:43 revealed an ICH of 17 ml volume (fig. 1a). We immediately administered 1,500 units of prothrombin complex concentrates (PCC) within 15 min. However, despite an INR of 1.5 the patient deteriorated within 1 h. CT at 10:59 revealed an expansion of the hematoma to a volume of 84 ml (fig. 1b). At this time, we also detected a spot sign within the hemorrhage on CTA source images (fig. 1c). The PCCT, which was performed 2 min after CTA, revealed massive enlargement of this hyperintense area to more than tenfold of the primary spot sign (0.15–1.67 ml) (fig. 1d). At 20:30, CT revealed further expansion of the hematoma to a volume of 99 ml (fig. 1e). The patient died 35 h after the onset of symptoms.

Discussion

The spot sign occurred in about 1/3 of patients with spontaneous ICH in a smaller prospective study [4]. Primary and secondary vessel injuries are discussed as being the reason for the occurrence of the spot sign [4–6]. Wada et al. [4] studied spot signs for the presence or absence of contrast extravasation and described them as enlarging in PCCT. Contrast extravasation on PCCT was found especially in patients on OAC [4, 5, 7], but no significant difference in final volume or change of volume of the spot signs with extravasation in contrast to spot signs without extravasation was found [4]. It thus remains unclear whether extravasation on PCCT represents only leakage of contrast medium or ongoing bleeding or both.

Our patient was on OAC, which probably amplifies the risk of hematoma enlargement [2]. We saw massive enlargement of the extravasation within 2 min and hematoma enlargement on follow-up CT, despite immediate reversal of the anticoagulatory effect to an INR of 1.5. These radiographic findings are suggestive of primary vessel injury and ongoing bleeding in this case.

Fig. 1. **a** 9:43. Cranial CT: hematoma volume of 17 ml. **b** 10:57. CT: hematoma volume enlargement to 84 ml. **c** 10:59. CTA with a spot sign within the hemorrhage (0.15 ml). **d** 11:01. PCCT with massive enlargement of the former spot sign (1.67 ml). **e** 20:30. CT: further hematoma expansion to 99 ml.

Three points may follow from these observations. Firstly, an INR of 1.5 might not be 'enough' to prevent rebleeding. Secondly, the INR does not fully reflect the pathological mechanisms of rebleeding in OAC ICH. Thirdly, further mechanisms than just the derangement of the coagulation system are responsible for ICH in patients on OAC.

To investigate the therapeutic efficacy of rFVIIa versus placebo in patients with spontaneous ICH the Spot Sign for Predicting and Treating ICH Growth Study (STOP-IT) has been started [8]. The INR normalization in patients with Coumadin-related intracranial hemorrhages trial (INCH) will compare the efficacy of PCC and fresh-frozen plasma [9]. These trials will add information on the selective power of the spot sign in spontaneous ICH and the pathophysiological mechanisms behind as well as the treatment of OAC ICH.

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Xerostomia after Acute Stroke

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Introduction

Dry mouth (xerostomia) is potentially uncomfortable, leads to increased periodontal disease [1] and may contribute to dysphagia. In acute stroke, reduced saliva may lead to abnormal oral bacterial colonisation and contribute to the risk of pneumonia [2].

Methods

We carried out a prospective study of consecutive stroke admissions to the Glasgow Royal Infirmary (June 2004 to November 2005). The study had ethics approval.

Salivary flow rates (unstimulated) were measured on a single occasion by Salivette[®] sampling [3]. The oral cavity was assessed with the Oral Assessment Guide [4], oral flora by imprint culture, and dysphagia using 3 standard assessment tools [5–7]. We recorded pre-morbid modified Rankin Scale (mRS) scores, medical history, medication, National Institutes of Health Stroke Scale (NIHSS) scores and Abbreviated Mental Test scores. Socio-economic status was derived from postcodes using Scottish Neighbourhood Statistics [8]. At a 3-month follow-up, mRS scores were determined.

Data were analysed using SPSS 15.0. Characteristics of patients with dry mouth (salivary flow <1 µl/min) were compared to those with a salivary flow of 1–120 and >120 µl/min (normal salivary flow). Statistical significance was accepted at $p < 0.05$. All probabilities are 2-tailed. To examine the independent risk factors for dry mouth after acute stroke, binary logistic-regression analysis was performed with the dependent variable dry mouth or no dry mouth (salivary flow ≥ 1 µl/min).

Results

Oral status assessment was performed in 368 of 412 eligible patients, 225 (61%) had xerostomia. In univariate analysis (table 1), pre-stroke factors associated with xerostomia included older age, female gender, number of medications and pre-stroke disability; post-stroke associates were: stroke severity, Abbreviated Mental Test score, raised C-reactive protein, urinary tract infection (UTI), other clinical infections and oral *Candida glabrata*. There was no significant association of xerostomia with socio-economic status, oral cavity health, bacterial colonisation, dysphagia, pneumonia or risk of death/disability at 3 months. The independent associates of dry mouth were pre-stroke disability, UTI and oral *Candida glabrata*.

Discussion

We found that xerostomia is very common in acute stroke patients. This study also confirmed factors associated with xerostomia in non-stroke populations (older age, female gender, number of medications, disability). In addition, we identified several as-