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CASE REPORT

Circulatory shock associated with left insular stroke and chronic steroid treatment

Mirella Russo[1,2,3] | Fedele Dono[1,2,3] | Marco Onofrj[1,2,3] | Stefano L. Sensi[1,2,3,4]

[1]Department of Neuroscience, Imaging and Clinical Sciences, "G. d'Annunzio" University of Chieti-Pescara, Chieti, Italy

[2]Center for Advanced Studies and Technology (CAST), "G. d'Annunzio" University of Chieti-Pescara, Chieti, Italy

[3]Institute of Neurology, University Hospital of Chieti, Chieti, Italy

[4]Institute for Advanced Biomedical Technologies (ITAB), "G. d'Annunzio" University of Chieti-Pescara, Chieti, Italy

Correspondence
Stefano L. Sensi, Department of Neuroscience, Imaging and Clinical Sciences, "G. d'Annunzio", University of Chieti-Pescara, Via Luigi Polacchi 11/13, Chieti, Italy.
Email: ssensi@uci.edu

Abstract

Background: Damage to the insula has been associated with various types of cardiovascular dysfunction, including arrhythmias and blood pressure imbalances. Acute neuroendocrine disturbances following insular damage have also been described.

Case Presentation: A 50-year-old right-handed man with a left insular ischemic lesion exhibited aphasia and right central VII nerve palsy. Five days after the stroke, the patient exhibited severe bradycardia and hypotension. He had been treated for ocular trauma with prednisone for the preceding 3 weeks. Cortisol and adrenocorticotropic hormone levels indicated secondary adrenal insufficiency. Despite adequate fluid intake, the patient's blood pressure dropped, requiring norepinephrine administration. Midodrine was also initiated, leading to clinical improvement. The therapy was gradually discontinued as vital signs normalized. By Day 24, electrocardiogram monitoring was unremarkable, hormonal levels normalized, and the neurological examination revealed only mild residual speech fluency impairment. Computed tomography scans confirmed a recovering ischemic lesion of the left insula.

Conclusions: This case reveals the inhibitory effect exerted by a left-sided insular stroke on the autonomic system. It also highlights the still largely unexplored neuroendocrine complications of damage to this brain region.

KEYWORDS
adrenal insufficiency, dysautonomia, insula of Reil, stroke

INTRODUCTION

The insula controls autonomic functions, emotions, and decision-making [1], thereby coordinating the intertwined activity of the central and autonomic nervous systems [1]. Damage to the right insula can elicit cardiac arrhythmia, such as transient ventricular tachycardia [2], and has been associated with a higher risk of cardio-autonomic dysfunction. Conversely, left insular lesions have been linked to repolarization abnormalities, left anterior branch block, and atrial flutter [2]. Syncope and dizziness have also been reported in left-sided insular strokes [2]. Right-sided insular damage has been previously related to increased sympathetic tone and serum levels of catecholamines [3]. However, the impact on the adrenal axis of left-side insular lesions is still largely unexplored.

CASE PRESENTATION

We report a case involving a 50-year-old right-handed man, admitted to our Neurological Unit, who exhibited sudden onset of aphasia and right central VII nerve palsy, preceded by a severe headache. The patient's medical history included a previous occurrence of a peptic

ulcer and recent eye trauma, for which he was receiving prednisone 75 mg qd, omeprazole, ciprofloxacin, diclofenac and tobramycin eye drops. The regimen was maintained during the hospitalization.

The patient's National Institutes of Health Stroke Scale (NIHSS) score was 5 (1b:2;4:1;9:2); no abnormalities in vital signs were detected. Computed tomography (CT) of the brain and neck revealed an occlusion of the left internal carotid artery. The patient underwent thrombolysis, which was interrupted due to sudden onset of emesis, right hemiparesis, and language deficits (NIHSS:16). A cardiac sonogram revealed normal systolic function with only mild tricuspid insufficiency.

The 24-h CT brain scan (Figure 1a) revealed ischemic lesions in the left insula extending into the capsular-thalamic territory. The frontal and parietal lobes also exhibited small edemic lesions. On Day 4, a small hemorrhagic infarction of the ischemic core was observed. On the fifth day, despite adequate fluid intake and normal renal function (as indicated by laboratory workup), an unexpected decline in blood pressure occurred (90/50 mmHg). Norepinephrine was administered to preserve optimal brain perfusion. Despite amine treatment, the patient developed severe bradycardia (HR: 42). Electrocardiogram (ECG) monitoring over 24 h indicated sinus bradycardia with eight isolated beats of ventricular escape rhythm. Eight days after admission, the patient's morning cortisol levels were 2.7 aeUI/dL (normal range: 3.7–19.4 aeUI/dL) and adrenocorticotropic hormone (ACTH) levels were 3.3 pg/mL (normal range: 4.7–48.8 pg/mL). These results and the clinical signs supported adrenal insufficiency. As the patient had been receiving prednisone for 3 weeks, an iatrogenic adrenal impairment was suspected. However, as the steroid regimen had remained unchanged since admission, the symptoms were unlikely to be attributable to abrupt steroid withdrawal. No other causes of hemodynamic instability were detected. Midodrine was administered, with benefit observed. After 1 week of therapy adjustment and decalage, norepinephrine infusion was discontinued. Due to a steady normalization of the patient's vital signs, steroid and midodrine tapering were initiated. On Day 24, 24-h ECG monitoring was unremarkable. Cortisol and ACTH levels were normalized. The neurological examination revealed only mild residual impairment in speech fluency. The neuroimaging follow-up (Figure 1b) showed ongoing recovery of the ischemic lesions and confirmed the left insula as the primary site of involvement.

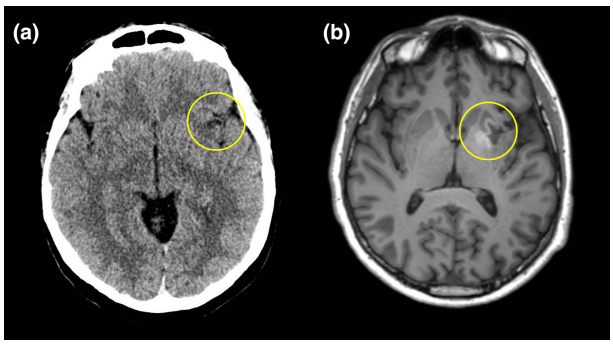

FIGURE 1 Infarction of the left anterior insula, as indicated by corresponding hypodensity on the 24-h computed tomography scan of the brain (panel a, axial view). A 1-month follow-up magnetic resonance brain scan revealed a residual lesion (panel b, axial view, T1-weighted sequence) featuring a hypointense core (malacic area) surrounded by a hyperintense signal (gliosis).

DISCUSSION

Regulation of cardiovascular function is controlled by the central autonomic network, a functional system involving the cortical, midbrain, and brainstem regions [4, 5]. The insular and medial prefrontal cortices, along with the amygdala, help process viscerosensory information and the initiation of autonomic responses [4, 5]. Studies on focal epilepsy involving the insular-opercular region and the temporal lobe have confirmed the role of these areas in the modulation of visceral-vegetative signs (as indicated by increased vagal tone in left temporal lobe epilepsy) [6, 7]. These findings are in line with clinical observations in patients with insular strokes. These patients often exhibit arrhythmogenic signs (right > left) and impaired baroreflex sensitivity (left > right) [2, 8]. Specific impairments and signs vary depending on the location and extent of the stroke, individual differences in brain anatomy, and the extent of compensation mechanisms [2]. Evidence indicates overall lateralized control of the sympathovagal tone, with the right insula associated with sympathetic and the left with parasympathetic output. However, inherited and acquired factors modulate insular functioning [9–11] and its resilience to physiological and pathological conditions [11, 12]. For instance, left insular cortical thickness positively correlates with baroreflex sensitivity [8]. Insular control of the visceral-vegetative responses is also mediated by neuroendocrine inputs. Animal models have confirmed that the insula provides sympathetic innervation to the adrenal glands [13]. Functional neuroimaging studies support a link—through the adrenal glands—between insular activation and the production of stress responses [14].

Our case shows a functional link between the occurrence of circulatory shock after a left insular stroke in a patient undergoing chronic steroid treatment. A similar situation was reported in a 14-year-old boy with Allgrove syndrome, treated for ACTH-resistant adrenal insufficiency with hydrocortisone, who, after the onset of acute left-sided insular injury, exhibited transient baroreflex dysfunction [15]. The uncommon combination of left-sided insular stroke and disruption of the adrenal axis may explain the occurrence of shock only after a "double-hit" since, taken individually, the two conditions are typically not sufficient to cause this. Our case reveals the inhibitory effect exerted by left-sided insular strokes on the autonomic system. However, the complex neuroendocrine interplay triggered by insular damage requires further investigation.

AUTHOR CONTRIBUTIONS

Mirella Russo: Conceptualization; investigation; writing – original draft; writing – review and editing. **Fedele Dono:** Investigation; writing – review and editing; writing – original draft; methodology. **Marco Onofrj:** Writing – review and editing; supervision;

validation; visualization; resources; methodology. **Stefano L. Sensi:** Conceptualization; investigation; writing – review and editing; writing – original draft; supervision; project administration; resources.

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CONFLICT OF INTEREST STATEMENT

Nothing to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

Written consent for publication was obtained. The manuscript was prepared according to CARE Guidelines.

ORCID

Mirella Russo https://orcid.org/0000-0002-9937-5923
Fedele Dono https://orcid.org/0000-0003-3575-2942

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