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ISOLATED CORTICAL VEIN THROMBOSIS IN AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE 2

Cerebral venous sinus thrombosis (CVST) is not commonly associated with endocrine disorders. However, it has been reported in the setting of ketoacidosis and severe dehydration in children with type 1 diabetes as well as in hyperthyroidism.^{1,2}

Autoimmune polyglandular syndrome type 2 (APS-2, or Schmidt syndrome) is characterized by the presence of autoimmune adrenal disease (Addison disease) and at least one other endocrine disorder: either autoimmune thyroid disease or type 1 diabetes. The coexistence of an autoimmune thyroid disorder and type 1 diabetes has been defined as APS type 3 (APS-3). Ischemic strokes have been reported in 2 young patients with APS-2 and in a middle-aged man with APS-3.^{3–5}

We report a patient with APS-2 who developed an isolated cortical vein thrombosis (ICVT) in the setting of newly diagnosed diabetic hyperglycemia. This report underscores the potential association between APS-2 and strokes. This may be the first patient in the literature with APS and a nonarterial stroke.

Case report. A 68-year-old woman with a history of primary adrenal insufficiency, autoimmune

hypothyroidism, pernicious anemia, and vitiligo was referred for a left homonymous hemianopia. She had a 6-day history of persistent positive visual symptoms (worm-like photopsias) and distorted images in her left visual field. She also had worsening headaches and a sandy feeling in both eyes in the prior 2–3 weeks. In the previous 3 months, she had had polyuria, polydipsia, and nocturia, and a nonintentional 16-pound weight loss within the prior year. She denied history of trauma, infections, or clots. Family history was negative for autoimmune conditions. Neurologic examination revealed an intermittent left homonymous hemianopia. The remainder of her examination was normal. A brain MRI revealed a thrombosed right parietal cortical vein with mild leptomeningeal enhancement (figure) without evidence of parenchymal hemorrhage, restricted diffusion, vasogenic edema, or venous sinus thrombosis. EEG was normal. Complete blood count, erythrocyte sedimentation rate, and C-reactive protein were normal. Activated partial thromboplastin time was 28 seconds (ref: 22–31 seconds), prothrombin time was 11 seconds (ref: 9–12 seconds), and international normalized ratio was 1.1. Hemoglobin A1C was 13.8% (ref: 4.8–6.0%), glucose level was 533 mg/dL (ref: 65–99 mg/dL), and C peptide was 8.9 ng/mL (ref: 1.1–4.4 ng/mL). Islet cell, insulin, and antiglutamic acid decarboxylase antibodies were negative. Angiotensin-1 converting

Figure (A) Axial fluid-attenuated inversion recovery, (B) axial gradient echo (GRE), (C) axial susceptibility-weighted imaging (SWI), (D–F) axial postgadolinium T1-weighted images

Right parietal cortical vein thrombosis (arrows) with signal blooming on GRE and SWI. Right parietal leptomeningeal enhancement seen in F.

enzyme was normal. Anti-SSA/Ro and anti-SSB/La, antinuclear, double-stranded DNA, Smith, cardiolipin, lupus anticoagulant, and B2-glycoprotein antibodies were negative. Homocysteine, protein C and S, and anti-thrombin III levels were normal. Factor V Leiden and prothrombin mutations were not detected. Colonoscopy and mammogram screening were negative for malignancy. The patient was treated with warfarin, levetiracetam, and insulin. The positive visual symptoms and hemianopia disappeared within the first week, her headaches significantly improved, and symptoms of polyuria, nocturia, and polydipsia subsided following strict control of her blood glucose level.

Discussion. We present a case of ICVT in a woman with APS-2. Poorly controlled new onset type 2 diabetes mellitus was diagnosed on admission following a 3-month history of polyuria, nocturia, and polydipsia. None of the classical risk factors for ICVT (or CVST) were identified. We then suspected that both her preexisting APS-2 condition and the newly diagnosed severe hyperglycemia contributed to the development of her ICVT.

APS-2 is the most common polyglandular syndrome. The prevalence of APS-2 is 1:20,000, it has a marked female predilection (male-to-female ratio is 1:3), and it usually debuts in the third or fourth decade of life. Other autoimmune diseases such as pernicious anemia and vitiligo (both present in our patient) may also be part of the clinical spectrum of APS-2. Neurologic complications in APS are considered to be a consequence of the metabolic, hormonal, and autoimmune derangements that occur in these syndromes.⁶ The pathogenic mechanism for strokes remains speculative but the presence of an autoimmune background has been postulated as a potential cause for these ischemic events.^{3–5} We present the first patient in the literature with APS and ICVT. The fact that both arterial and nonarterial strokes are associated with APS reinforces the theory of an underlying autoimmune process as the cause of a hypercoagulable state in these patients. Also, a prothrombotic state has been demonstrated in a patient with transverse sinus thrombosis and uncontrolled diabetes mellitus in the absence of any other risk factor.⁷

In up to 15% of cases of CVST (and possibly ICVT) a classical prothrombotic risk factor cannot be identified. Endocrine disorders, either autoimmune or nonimmune, might be playing an underestimated role in this group of patients. We postulate that diabetic hyperglycemia (rather than diabetes per se) should be considered a hypercoagulable risk factor for CVST or ICVT.

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Author contributions: Dr. Gonzalez-Perez: collection of clinical data and drafting of the manuscript. Dr. Correia: collection of clinical data and drafting of the manuscript. Dr. Capizzano: interpretation of brain images, drafting and revision of the manuscript. Dr. Adams: collection of clinical data, drafting and revision of the manuscript.

Study funding: No targeted funding reported.

Disclosure: The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

Received September 25, 2015. Accepted in final form November 20, 2015.

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1. Sasiadek MJ, Sosnowska-Pacuszko D, Zielinska M, Turek T. Cerebral venous thrombosis as a first presentation of diabetes. *Pediatr Neurol* 2006;35:135–138.
2. Bensalah M, Squizzato A, Ould Kablia S, Menia H, Kemali Z. Cerebral vein and sinus thrombosis and hyperthyroidism: a case report and a systematic review of the literature. *Thromb Res* 2011;128:98–100.
3. Watson S, Raj S, Eugster E, Sanchez J. Acute mental status change as the presenting feature of adrenal insufficiency in a patient with autoimmune polyglandular syndrome type II and stroke. *J Pediatr Endocrinol Metab* 2014;27:545–548.
4. Hopkins SE, Somoza A, Gilbert DL. Rare autosomal dominant POLGI mutation in a family with metabolic strokes, posterior column spinal degeneration, and multi-endocrine disease. *J Child Neurol* 2010;25:752–756.
5. Kanazawa Y, Matsuo R, Fukushima Y, Fukuda K, Kamouchi M, Kitazono T. Progression of right internal carotid artery stenosis in ischemic stroke patient with autoimmune polyglandular syndrome: a case report. *Rinsho Shinkeigaku* 2013;53:531–535.
6. Berger JR, Weaver A, Greenlee J. Neurologic consequences of autoimmune polyglandular syndrome type 1. *Neurology* 2008;70:2248–2251.
7. Nagai T, Tomizawa T, Tonooka N, Mita Y, Misumi S, Mori M. Diabetes mellitus with left transverse sinus thrombosis and right transverse sinus aplasia. *Diabetes Res Clin Pract* 2001;51:39–43.