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Case Report

Postpartum Heart Failure Complicated With Thyroiditis: A Concealed Aggravator of Peripartum Cardiomyopathy?

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See editorial by Tremblay-Gravel and Pacheco, pages 710–711 of this issue.

ABSTRACT

The etiology of peripartum cardiomyopathy (PPCM) remains unestablished, but the involvement of abnormal autoimmunity has been suggested. We report a case of PPCM that was triggered by postpartum thyroiditis. Despite the presence of myocardial damage indicated by cardiac magnetic resonance imaging, the patient's cardiac function completely recovered with the addition of bromocriptine to standard therapies. We discuss the role of thyroid hormones in the development of PPCM through aggravation of a prolactin-dependent antiangiogenic effect, and we argue that more attention should be paid to postpartum thyroiditis as a novel risk factor for PPCM.

RÉSUMÉ

L'étiologie de la cardiomyopathie du péripartum (CMPP) n'a pas encore été caractérisée, mais l'hypothèse d'une anomalie de l'autoimmunité a été avancée. Nous présentons un cas où la CMPP a été déclenchée par la thyroïdite du post-partum. Malgré la présence d'une atteinte myocardique révélée par imagerie par résonance magnétique cardiaque, la fonction cardiaque de la patiente s'est complètement rétablie après ajout de bromocriptine aux traitements standard. Nous analysons le rôle des hormones thyroïdiennes dans l'apparition de la CMPP par l'intermédiaire de l'aggravation d'un effet anti-angiogénique prolactine-dépendant et nous préconisons qu'une plus grande attention soit accordée à la thyroïdite du post-partum à titre de nouveau facteur de risque de la CMPP.

Peripartum cardiomyopathy (PPCM) is a potentially life-threatening heart failure that mostly occurs in the first month postpartum.[1] The mechanisms of PPCM onset remain unestablished, but the involvement of abnormal autoimmune action in the development of PPCM has been proposed.[1]

Case

A 33-year-old Japanese woman (gravida 4, para 1, abortus 0), 31 days postpartum, following 40 weeks of gestation, was referred to our hospital for the management of heart failure. She began to experience palpitation and dyspnea 1 week after delivery and was found to have left ventricular systolic dysfunction by echocardiography at 22 days postpartum. Except for age, she had no risk factors for PPCM including high-risk ethnicity, tocolytic therapy, hypertensive disorder, and multiple gestations. At admission, she showed tachycardia (120 beats per minute) and low-grade fever (37.1°C [98.78°F]) with normal blood pressure (114/73 mm Hg) and oxygen saturation (98% on room air), and there were no remarkable findings on physical examination except for perspiration.

Electrocardiography showed sinus tachycardia with left axis deviation and poor R-wave progression in precordial leads (Fig. 1A), and a chest x-ray film (Fig. 1B) revealed cardiomegaly (CTR: 54.3%). NT-proBNP was prominently elevated (4907 pg/mL). Left ventricular ejection fraction (LVEF) assessed by cardiac magnetic resonance imaging (CMR) was 38%, and there was mid-wall late gadolinium enhancement (LGE) in the lateral region (Fig. 1C). Laboratory tests revealed prominent hyperthyroidisim (free triiodothyronine (T3), 11.44 pg/mL; free thyroxine, 3.79 ng/dL; thyroid-stimulating hormone (TSH), <0.01 μIU/mL). An antibody for the TSH receptor was negative, and uptake of $^{99m}TcO_4^-$ into the thyroid (Fig. 1D) was low (0.56%), leading to a diagnosis of postpartum destructive thyroiditis. Results of an antibody against thyroid peroxidase (TPO) test was positive (6.4 IU/mL). After initial treatment with diuretics for 1 week, we decided to use

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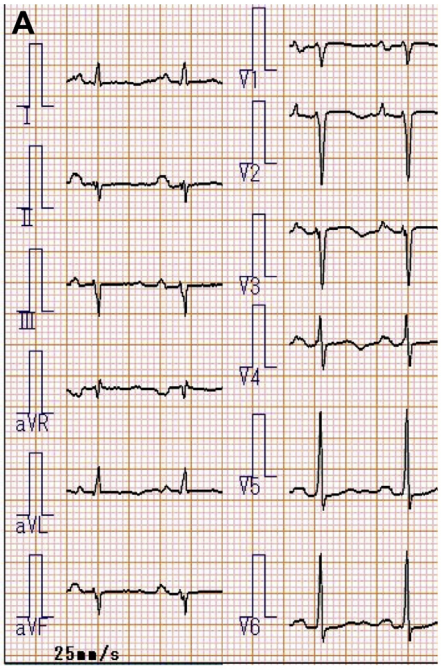

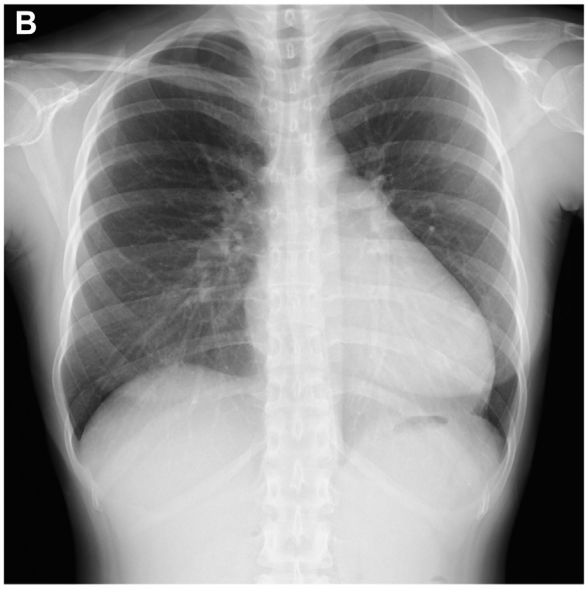

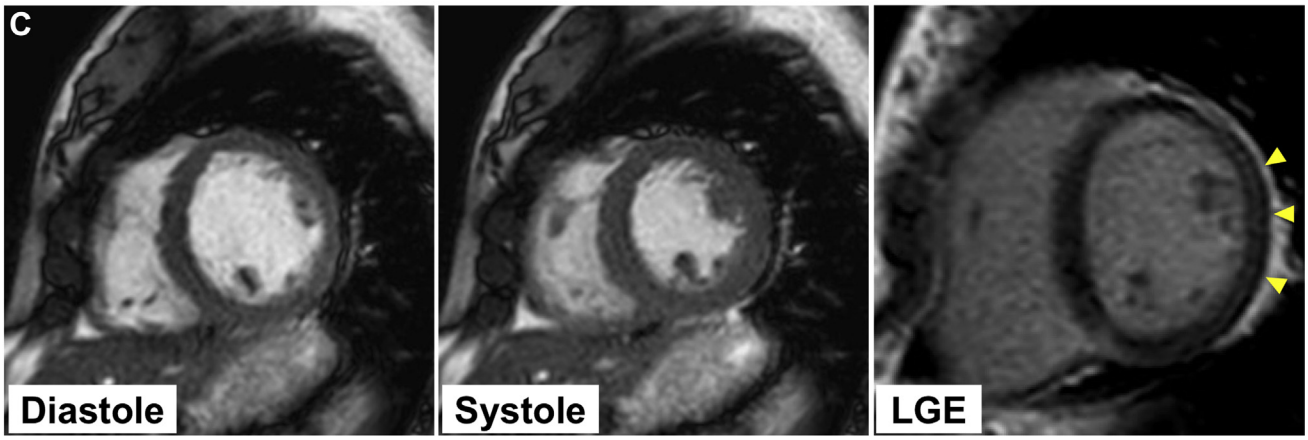

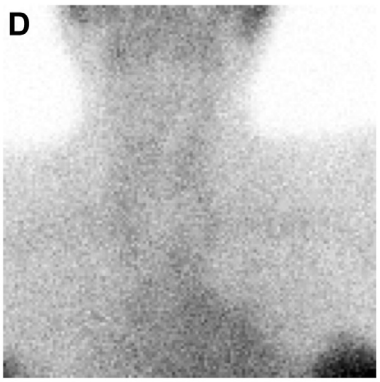

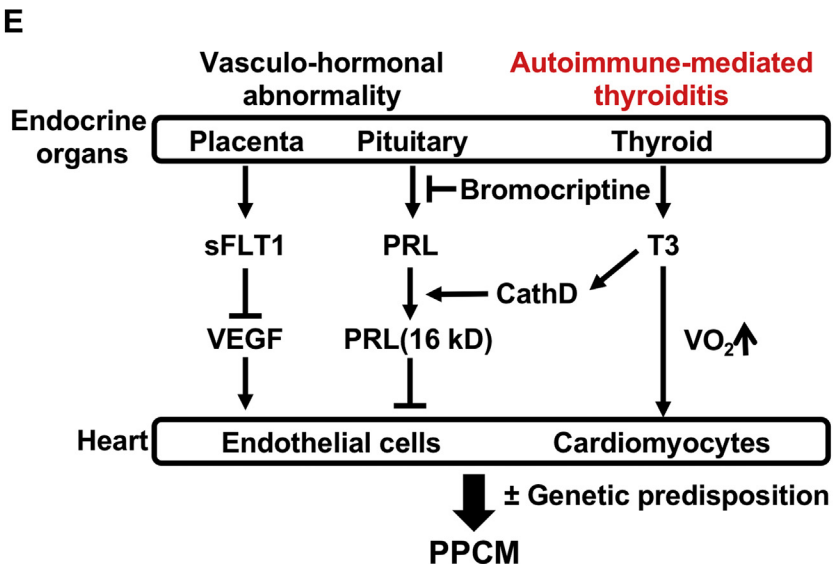

Figure 1. (**A**) Twelve-lead electrocardiography. (**B**) Chest x-ray. (**C**) Cardiac magnetic resonance imaging at diastole (**left**), systole (**middle**), and late gadolinium enhancement (**right**). **Yellow arrowheads** indicate positive for LGE. (**D**) $^{99m}TcO_4^-$ thyroid scintigraphy. (**F**) A schematic of the hypothesis of involvement of postpartum thyroiditis as a "concealed aggravator" for development of peripartum cardiomyopathy.

bromocriptine (2.5 mg twice daily) because cardiac function remained unchanged, with slight pericardial effusion, and because prolactin level remained high (336 ng/mL) despite cessation of lactation. D-dimer was monitored for potential thrombotic risk with bromocriptine treatment, and it remained within the normal range during the 2-week treatment period. The patient was also treated with a β-blocker and angiotensin-converting enzyme inhibitor after stabilization. Thyroid hormones were normalized 4 weeks later, and her LVEF showed partial improvement (48%). A follow-up CMR after 6 months revealed full recovery of LVEF (60%), although mid-wall LGE was persistently observed.

Discussion

The pathogenesis of PPCM is thought to be multifactorial, but recent basic research has suggested that the formation of cleaved prolactin by activated cathepsin D plays a crucial role through its antiangiogenic action, leading to the therapeutic application of bromocriptine, a prolactin inhibitor, in clinical settings.[1]

Autoimmune diseases remit during pregnancy but flare or even unmask in the early postpartum period. Asymptomatic pregnant women with autoimmune thyroiditis are known to experience destructive thyroiditis after delivery caused by rebound activation of the immune system, which is called "postpartum thyroiditis." Its incidence in the general population is not low (8%), and significantly higher incidences (40% to 60%) have been reported in patients who have an anti-TPO antibody. Postpartum thyroiditis usually begins 1 to 4 months after delivery, being consistent with the period when PPCM frequently develops.

Thyrotoxicosis adversely increases myocardial oxygen demand through its effect on chronotropy and contractility, possibly contributing to the manifestation of heart failure. Importantly, treatment with T3 was shown to increase cathepsin D activity *in vitro* and *in vivo*.[2,3] Thus, destructive thyroiditis-induced enhancement of T3 level in the early postpartum period may promote cathepsin D activation, leading to the production of antiangiogenic prolactin fragments (Fig. 1E), which serves as a concealed aggravator of PPCM. This hypothesis is supported by the results of a recent study showing that thyroid disorders, including toxic nodular goiter and thyrotoxicosis, were independent risk factors for the development of PPCM in a large cohort of patients.[4] Taken together, hyperthyroidism in this case may have contributed to the development of PPCM, although whether bromocriptine treatment is particularly effective in this subset of PPCM patients warrants further investigation.

There is an obvious difference between the prevalence of postpartum thyroiditis and that of PPCM. Advances in genetics have revealed that a subset of PPCM shares genetic predispositions with dilated cardiomyopathy (DCM), which predicts worse functional recovery.[5] We did not perform genetic analysis in our patient, but mid-wall LGE, which is detectable in 30% of patients with DCM, was persistently observed even after complete recovery of LVEF. These findings lead us to speculate that our patient had a potential predisposition to DCM, which was unmasked by hyperthyroidism just after delivery. Further comprehensive analysis including genetic and thyroid function tests is needed to determine whether this "2-hit hypothesis" is true of a subset of PPCM cases.

Disclosures

The authors have no conflicts of interest to disclose.

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