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COMMENT

Primary aldosteronism and obstructive sleep apnea: the strong ties between them

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Primary aldosteronism (PA) is a common cause of secondary hypertension, and is reported to be present in 5–10% of patients with hypertension [1]. PA is mainly categorized into aldosterone-producing adenoma (APA) and bilateral idiopathic hyperaldosteronism (IHA) [1]. Although the majority of APA is known to have somatic mutations of *KCNJ5* [2], aldosterone-producing cell clusters (APCCs) in IHA mainly contained somatic mutations of *CACNA1D* [2]. Additionally, patients with IHA had significantly higher levels of BMI, obesity prevalence, triglyceride, and HbA1c than patients with APA [3]. Therefore, APA and IHA may possibly have different etiologies. Moreover, some PA (APAs) are known to secrete cortisol autonomously [4, 5], and PA patients with mild autonomous cortisol secretion (MACS) were demonstrated to have higher incidence of renal dysfunction, diabetes mellites, and dyslipidemia than PA patients without MACS [5]. Therefore, PA demonstrates heterogeneous clinical findings depending on its type.

Recently, the relationship between PA/aldosterone and obstructive sleep apnea (OSA) has been intensely examined [6, 7]. As indicated in Fig. 1, aldosterone overproduction induces sodium-water reabsorption and elevates the nocturnal fluid shifting to the neck, which results in pharyngeal edema and the upper airway obstruction to worsen OSA [6, 7]. In contrast, intermittent hypoxia-induced by OSA activates renin-angiotensin system [8], which also results in aldosterone overproduction. Moreover, in relation to obesity-related hypertension, it has recently been proposed that undetermined adipocyte-derived factor(s) secreted from adipocytes may also induce aldosterone secretion [9]. Interestingly, both ACTH and cortisol levels have been reported to be increased in OSA patients [10], suggesting that OSA also activates hypothalamic–pituitary–adrenal axis. Although the expression level of 11β-hydroxysteroid dehydrogenase type 2, which converts cortisol to cortisone in the distal nephron, in OSA has not been reported, it is possible that the increased cortisol may also induce the sodium-water reabsorption since both cortisol and aldosterone bind to mineralocorticoid receptors with similar affinities [11]. However, the prevalence of PA among OSA remains uncertain, and it is still controversial whether hypertensive patients with OSA should be screened for PA.

Heizhati et al. [12] recently explored the cross-sectionally prevalence and associated factors of PA in co-existent hypertension and OSA, and demonstrated that PA prevalence was significantly higher in hypertensives with OSA (13.2%) than in those without OSA (10.0%). In gender specific-analysis, PA prevalence was significantly higher in hypertensive men with OSA (13.8%) than in those without OSA (7.7%), but not in hypertensive women. Moreover, PA prevalence was significantly higher in hypertensive men with OSA aged <45 years (12.7% vs 7.0%), 45–59 years (16.6% vs 8.5%), and with overweight and obesity (14.1% vs 7.1%) than in those without OSA. Taken together, hypertensive men complicated with OSA, especially in the young/middle-aged and with overweight/obesity, have higher prevalence of PA. Therefore, it is necessary to screen those patients for the correct diagnosis and treatment of PA. In the present study, although they have defined PA positive as plasma renin activity (PRA) < 1 ng/mL/hour and plasma aldosterone concentration (PAC) measured by radioimmunoassay (RIA) ≥ 12 ng/dl or aldosterone to renin ratio (ARR) ≥ 20, they cannot distinguish APA and IHA since they have not shown any data regarding the adrenal venous sampling [13]. Additionally, the existence of MACS [5] in APA patients is not

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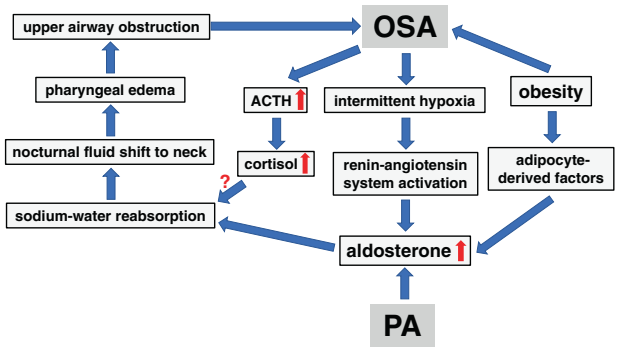

Fig. 1 The relationship between PA and OSA

clear due to the lack of serum cortisol data in this study. Since IHA is reported to have higher prevalence of obesity, higher levels of triglyceride and HbA1c than APA [3], and APA with MACS had higher incidence of renal dysfunction, diabetes mellites, and dyslipidemia than APA without [5], it will be extremely important to define the PA characteristics among PA patients complicated with OSA in the future. Additionally, since the diagnostic criteria of PA have recently been changed drastically according to the change of the measuring method of PAC from RIA to chemiluminescent enzyme immunoassay (CLEIA) in 2021 [14], future reassessments of the data may be also necessary for the correct diagnosis.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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