Primary bilateral macronodular adrenal hyperplasia is a rare cause of Cushing's syndrome and is more often diagnosed as bilateral adrenal incidentalomas with subclinical cortisol production. We summarize the recent insights concerning its epidemiology, diagnosis, genetics, pathophysiology, and therapeutic options.

Recent publications have modified our notions on the genetics and pathophysiology of bilateral macronodular adrenal hyperplasia. Combined germline and somatic mutations of armadillo repeat containing 5 gene were identified in familial cases, in approximately 50% of apparently sporadic cases and in the relatives of index cases; genetic testing should allow early diagnosis in the near future. The recent finding of ectopic adrenocortical production of adrenocorticotropic hormone in clusters of bilateral macronodular adrenal hyperplasia tissues and its regulation by aberrant hormone receptors opens new horizons for eventual medical therapy using melanocortin-2 receptor and G-protein-coupled receptor antagonists. Finally, some medical and surgical treatments have been updated.

Recent findings indicate that bilateral macronodular adrenal hyperplasia is more frequently genetically determined than previously believed. Considering the role of paracrine adrenocorticotropic hormone production on cortisol secretion, the previous nomenclature of adrenocorticotropic hormone-independent macronodular adrenal hyperplasia appears inappropriate, and this disease should now be named primary bilateral macronodular adrenal hyperplasia [1)].

1)
De Venanzi A, Alencar GA, Bourdeau I, Fragoso MC, Lacroix A. Primary bilateral macronodular adrenal hyperplasia. Curr Opin Endocrinol Diabetes Obes. 2014 Jun;21(3):177-84. doi: 10.1097/MED.0000000000000061. Review. PubMed PMID: 24739311.