



## Restless Legs Syndrome Associated with Clove Pica: A Case Report

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### ABSTRACT

The coexistence of restless leg syndrome and iron deficiency anemia is very common. Pica is the irresistible eating of non-food items for more than 1 month. The etiology of pica is unclear but the association with iron deficiency is very clear. Many different types of pica have been described in the literature. Clove pica is very rare. In this article, we present a case with clove pica and iron deficiency anemia who presented with restless leg syndrome because of its rarity.

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### INTRODUCTION

Restless legs syndrome (RLS) and iron deficiency anemia (IDA) are often associated. Pica is the irresistible eating of non-food items for more than 1 month. Pica may develop due to IDA, may also increase IDA and cause neurologic findings. Low iron level closely affects the dopaminergic system. In the pathophysiology of RLS, local decrease in dopamine which causes hyperadrenergic state and abnormal iron metabolism, dopaminergic dysfunction and some abnormalities in the central opiate system are responsible. If iron deficiency is corrected, pica and neurologic findings resolve within weeks. To date, ice pica has been reported most frequently and clove pica is very rare in the literature (1-4). This case is presented to emphasize the importance of detecting pica in patients with neurologic findings associated with IDA and to draw attention to the fact that pica and neurologic symptoms completely resolve in a short period of time with iron treatment.

### CASE REPORT

In December 2023, a 45-year-old woman was admitted to the neurology clinic with a 2-month history of restlessness in her arms and legs that kept her awake at night. These complaints were relieved by movement, cold application and massage. Restless Legs Syndrome (RLS) was considered and routine blood tests and EMG were ordered for etiology. EMG was normal and anemia was detected in blood tests. The patient was questioned about the etiology in the anamnesis and it was learned that the patient had eaten more than 150 clove flowers per day for the last three months. It was thought that the patient had a clove eating pica. Neurologic examination of the patient who had no significant features in her family history was normal. On physical examination, the skin and mucous membranes were pale. Vital signs were stable. Blood tests revealed hemoglobin 8.8 g/dL (normal:11.9-14.6), hematocrit 29.9% (normal:36.6-44), white blood cells 9.38 x10<sup>9</sup>/L (normal:4.49-12.68), platelets 573 x10<sup>9</sup>/L (normal:173-390), MCV 65.7 fL (normal:82.9-98), MCH 19.3 pg (normal:27-

32.9), MCHC 29.4 g/dL (normal:31.8-34.7), RDW 18.9% (normal:12.1-14.3), RBC 4.55  $\times 10^{12}$ /L (normal:3.92-5.08), Iron level 14  $\mu$ g/dL (normal:30-160), serum iron binding capacity 405  $\mu$ g/dL (normal:135-392), serum ferritin level 5.39 ng/ml (normal:13-50). Peripheral smear revealed hypochromia and microcytosis. Serum B12, folic acid, serum electrolytes, renal and liver function tests were normal. As a result of these investigations, the patient was diagnosed with RLS and an unusual variant of pica syndrome, Iron Deficiency Anemia (IDA) caused by excessive clove consumption. Iron treatment was started. At the follow-up visit 3 weeks after receiving treatment, it was learned that the clove eating pica and RLS symptoms improved.

## DISCUSSION

RLS is a neurological disorder characterized by increased desire to move and uncomfortable sensations in the legs at rest, which is seen in 5-8% of the general population. Women are more likely to be affected than men. Over 40 years of age, prevalence of RLS is increasing. These uncomfortable sensations may be due to primary or secondary causes. Iron deficiency (ID), pregnancy and kidney disease are the most common comorbid conditions with RLS. Although the pathophysiology of the disease has not been fully elucidated. Currently, the prevailing theory is that brain iron deficiency is a key biological driver in RLS, likely resulting from various factors including low peripheral iron and/or genetics (1).

Iron deficiency anemia (IDA) is defined by the WHO as a hemoglobin level of less than 12.0 g/dL in non-pregnant women and less than 13 g/dL in men. Anemia can develop with inadequate iron intake or loss. It is rarely symptomatic until IDA develops (2). Our patient presented with severe RLS symptoms and had a rare clove-eating pica, which was found to be the etiology of IDA.

Karl Ekbom, who first reported the relationship between iron and RLS. Many studies point to a possible relationship with peripheral iron levels, showing that RLS severity increases with decreasing peripheral iron levels. In a population-based study, it was determined that RLS was not associated with plasma ferritin levels (1). In RLS patients with normal ferritin level, CSF iron level may indicate local ID. In one study, CSF ferritin level in patients with RLS decreased by 65% compared to normal people and CSF transferrin increased 3-fold compared to normal (3). Several imaging studies have revealed a strong association between iron metabolism and RLS, particularly in the brain. Iron plays a role in dopamine synthesis at multiple levels (1). Iron is required as a cofactor for the hydroxylation of tyrosine hydroxylase, the rate-limiting enzyme in dopamine production. The level of this enzyme is increased in ID and RLS. Iron is also a part of the dopamine type 2 receptor (3). In addition, iron is associated with vesicular release of dopamine. Consequently, ID indirectly leads to decreased dopamine production (1).

According to the DSM-5, the definition of pica is the repeated ingestion of developmentally inappropriate, non-nutritive substances for at least one month. Many different non-nutritive foods such as soil, ice, rice or starch are often consumed. Also,

there are many unusual types of pica reported, such as mothballs, eggshells, paper, cardboard and others. Clove pica is very rare and has only been reported in one pediatric case to date (4). Clove (*Syzygium aromaticum*) is a traditional spice used in food preservation and has various pharmacological activities. Studies have documented its analgesic, antioxidant, anticancer, antiseptic, antidepressant, antispasmodic, anti-inflammatory, antiviral, antifungal and antibacterial activity against various pathogenic bacteria. WHO has proven that the acceptable daily amount of cloves in humans is 2.5 mg/kg body weight. One clove flower is approximately 2 g and our patient was consuming much more than the acceptable daily amount of cloves. Janes et al. documented acute side effects of clove (e.g. disseminated intravascular coagulopathy, generalized seizures and hepatotoxicity). Allergic contact dermatitis in guinea pigs has also been reported in another in vivo study (5).

To date, 6 case reports with neurologic findings associated with pica have been reported. In one case, CNS toxicity and ID developed with repeated naphthalene ingestion. In another case, trichotillomania accompanied by ID presented with lead poisoning. In a case study by Aık, different patients with desiderosmia (the desire to smell certain odors) developing due to ID were presented. Another neurologic finding, as in our case, included a patient with RLS and an excessive desire to eat tofu in a patient with IDA. Another different patient presented with coprophagia due to moderate dementia and concomitant IDA. The last patient was a patient presenting with pica-related hypomagnesemia and seizures. In all patients presenting with neurologic symptoms, all symptoms of pica resolved with ID treatment. Other complications associated with pica include intestinal problems, dental damage, electrolyte disturbances (2).

This is the second case in the literature who presented with RLS symptoms after the development of IDA associated with clove eating, a rare pica. This case supports other studies showing the relationship between RLS and iron. It is also concluded that pica causes ID and ID facilitates the dysfunction that causes pica. Complete resolution of RLS and pica with iron treatment will prevent unnecessary drug use and complications that may develop due to pica.

## Author contributions

The author contributed to the concept or design of the study, acquisition of the data, analysis or interpretation of the data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. The author had full access to the data, contributed to the study, approved the final version for publication, and takes responsibility for its accuracy and integrity.

## Conflicts of interest

The author declares no conflicts of interest.

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## **Ethics**

The patient was treated in accordance with the Declaration of Helsinki and has provided informed consent for the publication of the report.

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