Restless legs syndrome (RLS) in a case of hook worm infestation

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Abstract: Restless legs syndrome (RLS) is characterised by irresistible urge to move the leg when at rest or while trying to fall asleep. The cause of RLS mostly idiopathic. A variety of factors can cause RLS such as iron deficiency, peripheral neuropathies and uraemia and can be worsened by pregnancy, caffeine, alcohol etc. There are genetic factors contribute to RLS although as yet, the mechanism through which they cause RLS remains unknown. Iron deficiency is the most common treatable cause. Iron deficiency anemia in chronic blood loss due to hookworm infections is commonly found in rural area. Here we report a case of RLS in a patient suffering from chronic iron deficiency anaemia due to hookworm infestation. More research needed keeping the background in mind.

Keywords: Restless leg syndrome (RLS), chronic iron deficiency anaemia, Hookworm infestation.

INTRODUCTION
Restless legs syndrome (RLS) is characterised by irresistible urge to move the leg when at rest or while trying to fall asleep. The cause of RLS mostly idiopathic.

A variety of factors can cause RLS such as iron deficiency, peripheral neuropathies and uraemia and can be worsened by pregnancy, caffeine, alcohol etc. There are genetic factors contribute to RLS although as yet, the mechanism through which they cause RLS remains unknown [1].

Karl Ekbom [2,3], first described and named the disease Rest Less leg Syndrome in 1945. It is characterised by irresistible urge to move the leg when at rest or while trying to fall asleep. [4] Patient often reports crawling sensation in their legs and move the legs or stretch or walking around to alleviate the discomfort. Patient feels distress by the unpleasant sensations while lying in the bed, relaxing or before going to sleep. Sometimes patient presents with profound insomnia.

RLS is a fairly common disorder with prevalence rates of 1.6 to 12 % in Asian populations, 7.2 % of the North American and Western European population and that 2.7 % had clinically significant RLS symptoms [5]. Epidemiological studies reveal that prevalence of RLS in older adult ranges from 9-20% [6].

The most serious consequence of hookworm infection is anaemia, secondary to loss of iron and protein of gut [7]. It has been estimated that a single A. duodenale ingests about 150 µL blood per day while N. americanus sucks about 30 µL blood [8]. People who walk barefoot there is increased chance of hook worm infection. Majority of these infected individuals live in poverty-stricken areas with poor environmental sanitation [9].

Karl Ekbom first suspected iron deficiency as an underlying etiology of RLS [2,3]. Iron deficiency is the most common treatable cause and iron replacement should be considered if the ferritin level is less than 50 ng/mL. Patients susceptible for either genetic or systemic areas, deficiency of iron acts as aggravating factors. This disorder continuum may also occur in patients without iron deficiency such as peripheral neuropathies, uremia and can be worsened by pregnancy, caffeine, alcohol, antidepressants, lithium, neuroleptics, and antihistamines. Genetic factors contribute to RLS, and polymorphisms in a variety of genes (bbl9, meis1, map2k5/lbxcor, and ptprd) have been linked to RLS, although as yet, the mechanism through which they cause RLS remains unknown. Roughly one-third of patients (particularly those with an early age of onset) have multiple affected family members [1]. RLS is treated by addressing the underlying cause such as iron deficiency if present. Otherwise, treatment is symptomatic, and dopamine agonists are used most frequently.
International Study Group Diagnostic Criteria for Restless Legs Syndrome: --Essential features: (1) An urge to move the legs, usually accompanied or caused by uncontrollable or unpleasant sensations in the legs(2). The urge to move or unpleasant sensations that begins or worsens during periods of rest or inactivity such as lying down or sitting (3). The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues(4). The urge to move or unpleasant sensations are worse in evening or night than during the day or only occur in the evening or night.

A fifth criterion has just been established by the International RLS Study Group in 2012 that includes ruling out mimics of RLS (leg cramps, arthritis, neuropathies, claudication, positional discomfort, and so forth) that might confound the diagnosis. Future diagnostic manuals, such as the International Classification of Sleep Disorders (ICSD-3) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), will likely include this fifth diagnostic criterion [11].

CASE REPORT

A 52 years old, married, Muslim, male shopkeeper by profession, education up to middle school, lower socio-economic status from rural area of south 24 parganas, West Bengal, presented in our outpatient department with the chief complaints of repeated urge to move the legs, uncontrollable creepy-crawly or unpleasant sensations in the both lower limbs. The unpleasant sensations worsen during periods of rest or lying or before going to bed and partially relieved by walking or stretching. He had a difficulty in initiations of sleep as well as maintenance of sleep.

Initially these unpleasant sensations worsened at night and gradually it progressed to daytime as well while taking rest. Patient denied of any upper limb involvement. All these symptoms appear for last 5-6 months and gradually progressive.

The patient complaints of abdominal discomfort and a vague pain around the umbilicus for long time. Patient also complains of frequent diarrhoea. He had significant decreased appetite and weight loss for last 1 year. Since his childhood he used to walk mostly bare foot.

Physical examination pallor was noted. High volume pulse, Local and systemic examinations and were within normal limit, No gait abnormality.

Hematological investigations show decreased hemoglobin (8.1 gm %), and Mean Cell Volume (79fl) along with poikilocytosis which is characteristic of iron deficiency anaemia.

On biochemical investigations Urea – 25 mg/dl, Creatinine – 0.65 mg/dl. Serum iron – 18 microgram/dl (ref value – 59-148), Total iron binding Capacity (TIBC) - 669 microgram/dl (ref value- 120-470), Serum ferritine-18ng/microl.Thyroid profile within normal limit.

Routine stool examination showed: Ova of Anchylostoma Duodenalae in plenty and presence of occult blood. On Imaging Ultrasound whole abdomen was within normal limit.

Patient was treated with, Ropinarole, Gabapentine, Clonazepam (s.o.s basis for 2 weeks) and oral iron supplement. Deworming done with oral albendazole therapy. Patient got relief with therapy within 3-4 weeks.

DISCUSSION

The exact mechanism of action of primary or idiopathic RLS is not understood till date; however, a recent study indicates that low brain iron concentration caused by the dysfunction of iron transportation from serum to the central nervous system is the possible etiology behind RLS [11]. The proposed etiologies of secondary RLS are iron deficiency, renal failure, neuropathies, myopathies, pregnancy, and drugs (caffeine, serotonin reuptake inhibitors, tricyclic antidepressants, and dopamine blockers) [12].

The rationale for iron deficiency involvement of RLS is the need for iron in tyrosine hydroxylation which is the rate limiting step in the dopamine biosynthesis [13]. Magnetic resonance imaging (MRI) techniques have demonstrated decreased iron content in the nigrostriatal areas in RLS patients. Disease severity correlates the degree of nigrostriatal iron depletion [14]. Chronic blood loss is the most common cause of iron deficiency in the western world [15]. Iron deficiency anaemia in chronic blood loss due to hookworm infections is commonly found in rural area. The diagnosis of iron deficiency anaemia depends on laboratory studies. Low serum iron, ferritin and high total plasma iron binding capacity (TIBC) are diagnostic. Stool parasite and occult blood positive signifies hookworm infections as an underlying etiology of the iron deficiency anaemia[15].

The intravenous iron infusion effect can be very dramatic in approximately 60 % of patients, but patients tend to relapse after 3 to 36 months (when serum ferritin levels have typically decreased again), but these patients will respond to subsequent iron infusion therapy [10].

Iron therapy should be considered for RLS patients with low serum ferritin levels who are failing traditional therapy, especially if they also have anemia. However, the long-term effects of repeated iron infusion therapy in this population have not been...
studied, so this treatment should be instituted with caution [10].

CONCLUSION
Iron deficiency may contribute to the development of RLS but not all patients with iron deficiency develop RLS; and converse. This patient was suffering from RLS, having underlying iron deficiency anaemia due to hookworm infestations. As per our knowledge there were no such study or case reports regarding this association. Further research needed on RLS patients keeping the background in mind. So if there was iron deficiency anaemia in a case of RLS is found, the causes of iron deficiency should be thoroughly investigated and beyond iron supplement proper treatment of causes of iron deficiency is required.

REFERENCES