

Mesoamerican nephropathy: A kidney illness that is not entirely unknown

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ABSTRACT

Since 2000, the risk of chronic renal disease with no recognised cause has increased significantly throughout the Mesoamerican region. Various theories have attempted to explain the aetiology of the novel disease known as Mesoamerican Nephropathy (MEN), including de-hydration, heat stress, environmental or chemical exposure, or even infections. Young men and agricultural labourers who operate in hot environments are affected by MEN. MEN courses have a wide range of symptoms, including as low-grade fever, dysuria, and progressive kidney disease with disturbed

hydroelectrolyte balance. A kidney bi-opsy must be performed to confirm the diagnosis of tubule interstitial nephritis (usually at chronic stage). Even though MEN diseases have a high morbidity rate in endemic areas, there is no specific treatment for them, and only prophylactic measures have shown any effect on prognosis (avoid heat stress, constant hydration).

Key Words: Mesoamerican nephropathy; Heat stress; Tubule-interstitial nephritis

INTRODUCTION

Since 2000, an epidemic of instances of Chronic Kidney Disease (CKD) with unclear causes has been reported in the Mesoamerican region, which includes Southeast Mexico, Guatemala, El Salvador, western Nicaragua, and northwestern Costa Rica. This condition is known as endemic Mesoamerican Nephropathy (MEN). After there was evidence of a large increase in patients with advanced CKD in El Salvador, Authors released a research with an epidemiological description of this new disease. In this study, 205 incident dialysis patients were examined, and it was found that although they had a significant exposure to pesticides and insecticides, at least 67% of them had no established risk factors for the development of kidney disease [1]. Since then, Central America has seen a significant increase in the frequency of CKD with an unexplained aetiology. In the endemic locations, the MEN is also currently the main factor contributing to young adults dying prematurely. El Salvador's Bajo Lempa region has a 7-fold higher incidence of advanced CKD on Renal Replacement Therapy (RRT) than its neighbouring nations, and CKD mortality is 30 times higher [2]. There is limited information regarding the mechanisms involved in its development, the diagnostic standards, and potential treatments, despite the frightening results generated by MEN. The

goal of this publication is to provide a review of MEN using a representative clinical case as a unifying theme. Exposure to high temperatures, environmental pollutants, and pesticides have been postulated as key initiators in the pathogenesis of this nephropathy, which typically affects young men from agricultural communities in the aforementioned geographic areas. These regions are known for their warm climate. The evidence we now have regarding the origins of this illness is, however, relatively scant. Environmental, occupational, and familial variables are among the risk factors for the development of MEN. Regarding environmental conditions, many experts believe that dehydration from any source is the primary pathogenetic process. The high temperatures to which workers are subjected, intense physical activity, and heat stress cause frequent episodes of dehydration (and, as a result, frequent episodes of acute renal failure), in which the loss of water is greater than the loss of sodium, increasing the osmolarity of the plasma [3]. The posterior pituitary's secretion of vasopressin and the enzyme aldose reductase are the two main processes that this hyperosmolarity stimulates. A substrate for fructokinase in the proximal tubule, fructose is produced when the latter transforms glucose to sorbitol, it might cause fructose, a substrate for fructokinase in the proximal tubule, to develop. This process, which raises the uric acid levels inside the

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proximal tubule cells, has the potential to activate the inflammatory mediators that cause tubulointerstitial damage and the subsequent decline in glomerular filtration. The muscle injury brought on by the aforementioned circumstances results in the re-lease of nucleotides, which results in hyperuricemia and uricosuria in addition to the loss of salt and water. Urate crystals may form if the concentration of uric acid in urine is greater than its solubility. These are the mechanisms that aid in MEN's tubular damage. The pathophysiology of MEN, which is almost exclusively seen in endemic regions and has an increased prevalence despite the use of automated farming equipment, cannot be fully explained by these processes, nor can the disease's extrarenal involvement. Heavy metals found in the environment, such as lead, arsenic, cadmium, and silica, as well as agricultural chemicals like paraquat and glyphosphate have been discussed as contributing to the pathophysiology of MEN, although there is little data to draw firm conclusions regarding this [4,5]. In fact, data from several published meta-analyses concur that there isn't enough evidence to conclusively link chemicals and pesticides to the emergence of MEN. However, some research has indicated a connection between the development of CKD and several metals, including silica. A common occupational activity for people with MEN is burning sugar cane, and one of the elements found in the ashes produced by this burning is silica. Other theories that need to be verified include the concurrent emergence of MEN and particular illnesses, most specifically zoonoses. Yang et al. suggested in a recent review that there is an epidemiological link between leptospira infections and CKD of unknown origin, and that MEN geographically overlap with the regions where MEN had been reported. In fact, researchers have been looking for a possible environmental or occupational component that could link Sri Lankan nephropathy to the Membranous Nephropathy (MEN) of sugarcane workers. accessible population. The sample in this review was a total of 20 articles with concepts on cardiac rehabilitation programme which were retrieved. Out of the total only 8 articles meet the criteria. Finally, several families with CKD of uncertain origin have demonstrated genetic risk. In children and adolescents with MEN who had never worked on a farm, some studies discovered an increase in urine biomarkers of kidney injury like lipocalin associated with Neutrophil Gelatinase (NGAL) and N-Acetyl-d-Glucosaminidase (NAG). This confirms the link between urine biomarker values and the onset of MEN. All of these may indicate a genetic predisposition or possibly a link between early exposure to high quantities of certain chemicals and subclinical kidney injury. MEN's cause has not yet been determined, however it is likely the result of a combination of risk factors, including dehydration, exposure to particular metals, or genetic predispositions. MEN's often affects middle-aged men without a significant medical history, such as high blood pressure or diabetes mellitus, who have worked in agriculture in hot, humid conditions. MEN starts out with general symptoms such as asthenia, arthralgia, low-grade fever, vertigo, muscle cramps, and/or preclinical rhabdomyolysis. Self-limited acute renal injury that continues over time and results in CKD characterises the disease's early stages [6]. As CKD progresses, symptoms including lumbar discomfort, nocturia, and dysuria that point to renal involvement appear. Medical therapy based on symptoms and occasionally the indiscriminate administration of antibiotics or anti-inflammatory medicines results from the failure to recognise a kidney illness and the lack of access to

diagnostic tests, which ups the chance that CKD may advance. The primary ionic abnormalities associated with MEN illness include hyponatremia, hypokalemia, hypomagnesemia, and hyperuricemia. It also causes tubulointerstitial damage. Typically, non-nephrotic range proteinuria, leukocyturia, isosthenuria, and urate crystals are seen in the urine. A physical exam will typically reveal indicators of volume depletion, including hypotension and orthostatism, as well as all these changes. The ultrasound initially shows normal kidneys, but as the disease advances, there are changes in the cortical echogenicity. Unfortunately, people typically contact with doctors when they have advanced CKD, uremic symptoms, and an urgent need for RRT because most MEN endemic communities lack access to healthcare. The histopathological findings that have been reported as of late are based on a limited number of clinical cases. According to the study, tubulointerstitial involvement is widespread and predominate, with varied levels of chronicity and inflammation. Fischer et al. were able to create a histological description of the earliest stage of renal lesions despite the fact that the early diagnosis of MEN has been a diagnostic problem. Microscopy data in a prospective investigation of 11 native Nicaraguan patients identified tubulointerstitial nephritis as the kidney histological abnormalities. Additionally, they explain for the first time how interstitial edoema and acute inflammation coexisted with the already well-known chronic diseases in the early stages, including T cells and monocytes at the corticomedullary junction and neutrophil infiltration in the tubular lumen [7]. The authors also note that the architecture of the glomeruli is entirely intact, indicating that interstitial involvement is the major lesion at the renal level. The clinical trial conducted in Nicaragua, in which 326 sugar workers without a history of disease were prospectively assessed, adds to the clinical translation of these histological findings. In this patient group, 34 individuals experienced an immediate decline in kidney function due to occupational exposure; up to 50% of these workers went on to develop Chronic Kidney Disease (CKD) within a year. Late glomerular involvement is characterised by different degrees of global sclerosis, Bowman's capsule thickening and/or periglomerular fibrosis, folding of the glomerular basement membrane, slight thickening of the mesangial matrix without cellular proliferation, as well as symptoms of chronic glomerular ischemia. Immunofluorescence is often negative. MEN exhibits modest and non-specific vascular modifications along with podocyte alterations (including segmental loss of pedicels and inclusions of vacuoles, lipid droplets, and entities comparable to lipofuscin in the cytoplasm). Recent fascinating research suggests a same pathogenic mechanism for lysosomal lesions in the proximal tubule and those identified in patients with nephrotoxicity from anticalcineurics [8]. Therefore, involvement at the tubulointerstitial level is where the histological findings of MEN begin, while glomerular and vascular abnormalities develop secondarily oxygen molecules on the haemoglobin, thereby lowering oxygen tension in the blood. As a result, the patient is at risk of hypoxia. This risk could intensify for a cardiac patient, whose cardiac output and delivery of oxygen to the tissues is at stake. Therefore, the literature recommends smoking cessation for patients after cardiac surgery as the cornerstone for health. The European Association for Cardiovascular Prevention and Rehabilitation recommends that all smokers should be encouraged to stop smoking, and patients referred for special programmes. Once kidney injury has been identified, the primary goal of treatment is to lessen its adverse

effects, particularly changes in water and electrolytes. This covers the use of dietary and/or oral potassium, magnesium, and, of course, sodium and water supplements. Some writers even suggest the use of low-dose potassium-sparing diuretics in cases of intractable hypokalemia brought on by severe interstitial damage. The majority of treatments with a more experimental bent have only been studied on animals. Based on the notion that heat stress increases the synthesis of uric acid, a study in a mouse model shown that therapies intended to lower hyperuricemia also aid to lower oxidative stress and the activation of the inflammasome. In a study, a scientist examined how the xanthine oxidase inhibitor allopurinol affected mice that had repeatedly been exposed to heat. The findings showed that allopurinol had a protective effect on mice's kidney function, and that this effect was connected with the intra renal quantity of uric acid. Despite the fact that patients frequently exhibit metabolic alkalosis as a result of volume constriction, bicarbonate usage has been demonstrated to be beneficial in MEN [9,10]. It should be kept in mind that the fundamental causes of MEN might lead to bouts of rhabdomyolysis, in which case urine alkalinization performs a critical protective role and bicarbonate encourages the solubility of urate crystals. Additionally, it has been demonstrated that treating metabolic acidosis in advanced CKD stages can halt future CKD progression. Since these individuals are at a high risk of AKI related to dehydration, the use of angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers is debatable and there are no particular studies to support it. However, it might be taken into consideration with a very careful titration in a stable condition and extrapolating the antiproteinuric action of these medications. The use of anti-inflammatory medicines, particularly in the early stages, may help to lessen acute inflammatory infiltrates, despite the fact that no cases of MEN have been explicitly treated to date, perhaps as a result of the disease's late detection. Leukocytosis has actually been proven to be a reliable indicator of a positive prognosis for kidney function in several specific studies. With high rates of progression to severe CKD and considerable mortality, the prognosis for MEN is bleak. Although it is true that small series of cases have shown that other determinants (some modifiable) such as anaemia, paresthesia, or lack of breaks during the work may negatively contribute to the development of this disease, the factors affecting poor evolution probably are related with the late diagnosis of the disease and in the lack of access to specialised health resources. In conclusion, MEN is a chronic tubulointerstitial illness with an unknown aetiology that is based on volume depletion and dehydration in employees who have been exposed to chemicals in the environment. The foundation of its management is the management of water and electrolyte changes and the prevention of episodes of extreme heat, despite the lack of particular therapeutic approaches [11].

CONCLUSION

The main ionic abnormalities linked to MEN disease are hyperuricemia, hyponatremia, hypokalemia, and hypomagnesemia. Tubulointerstitial injury is another effect. Urine typically contains urate crystals, leukocyturia, isosthenuria, and proteinuria in the non-nephrotic range. Indicators of volume depletion, such as hypotension and orthostatism, as well as all these alterations, are

often discovered during a physical examination. The kidneys appear normal on ultrasonography at first, but as the condition worsens, the cortical echogenicity changes. Because most MEN-endemic villages lack access to healthcare, persons usually only seek medical attention when they have advanced CKD, uremic symptoms, and an urgent need for RRT. As a result of volume loss and dehydration in workers who have been exposed to environmental toxins, MEN is a chronic tubulointerstitial sickness with an unclear origin. Despite the lack of specific therapeutic methods, the management of hydration and electrolyte changes and the prevention of periods of excessive heat form the basis of its therapy.

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