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RESEARCH ARTICLE

ATRAUMATIC DISTAL TIBIAL FRACTURE AS THE FIRST PRESENTATION OF SJÖGREN SYNDROME WITH DISTAL RENAL TUBULAR ACIDOSIS, HYPOKALEMIC PARESIS, AND NEPHROCALCINOSIS

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Abstract

Distal renal tubular acidosis (dRTA) is an uncommon disorder characterized by impaired distal urinary acidification resulting in persistent metabolic acidosis. In adults, acquired dRTA is frequently associated with autoimmune diseases, particularly Sjögren syndrome. Chronic metabolic acidosis contributes to nephrocalcinosis and metabolic bone disease whereas severe hypokalemia can lead to acute neuromuscular weakness. In the past, osteomalacia and fractures have been reported in patients with Sjögren syndrome-associated dRTA, but atraumatic fracture as the first event preceding recognition of an underlying autoimmune disease remains an uncommon presentation. We report a case of a 45-year-old woman with primary hypothyroidism on treatment who presented with acute progressive weakness of all four limbs following two days of vomiting and diarrhea. On further history, she reported a right leg fracture two months earlier that had occurred while briskly walking. On examination she had generalized hypotonia, 4/5 power in all four limbs, and diminished deep tendon reflexes. Laboratory investigations reported severe hypokalemia (2.64 mmol/L), hyperchloremia (113.4 mmol/L), and normal-anion-gap metabolic acidosis (pH 7.30, bicarbonate 9.2 mmol/L). Urine pH was alkaline at 7.5 with spot urine electrolytes suggestive of a positive urine anion gap. Ultrasonography demonstrated bilateral nephrocalcinosis. Additional evaluation revealed xerostomia and xerophthalmia of three years' duration, with markedly abnormal Schirmer testing and minor labial salivary gland biopsy showed histopathological findings suggestive of Sjögren syndrome. Autoimmune evaluation demonstrated positive ANA with strong Ro52 positivity, and the patient was diagnosed clinically with primary Sjögren syndrome-associated dRTA. We treated her with intravenous and oral potassium supplementation, potassium citrate, sodium bicarbonate, calcium supplementation, corticosteroids, and symptomatic treatment for sicca symptoms.

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Her neurological symptoms and electrolyte abnormalities improved, and she remained asymptomatic with stable renal function at one-month follow-up. This case underscores an unusual skeletal presentation of Sjögren syndrome-associated dRTA. An atraumatic fracture may be an important clinical clue to chronic metabolic bone disease in patients with unrecognized dRTA. In such patients presenting with hypokalemic weakness, nephrocalcinosis, or unexplained fractures along with normal-anion-gap metabolic acidosis, clinicians should consider presence of dRTA and actively evaluate for underlying autoimmune disease, particularly Sjögren syndrome.

Introduction:-

Sjögren syndrome is a systemic autoimmune disorder characterized primarily by lymphocytic infiltration and dysfunction of the lacrimal and salivary glands. It is characterized by sicca manifestations and can also involve multiple extraglandular organs. Renal involvement most commonly occurs in the form of tubulointerstitial nephritis, which may result in tubular dysfunction, particularly distal renal tubular acidosis[1]. Distal RTA results from impaired hydrogen ion secretion by the distal nephron and is characterized by hyperchloremic metabolic acidosis with an inappropriately high urinary pH during systemic acidemia. In patients with Sjögren syndrome, dRTA may be clinically silent or may present with hypokalemia, muscle weakness, paralysis, nephrolithiasis, or nephrocalcinosis. Several reports have described hypokalemic paralysis as an initial manifestation of Sjögren syndrome[2,3].

Chronic metabolic acidosis also has important skeletal consequences. Bone participates in buffering chronic acid loads, and sustained acidosis promotes bone mineral dissolution and resorption, potentially contributing to reduced bone mass and osteomalacia. Studies have described osteomalacia, pseudofractures, and fractures in patients with dRTA, including those with Sjögren syndrome[4,5]. We present a case of a 45-year-old woman in whom an atraumatic distal tibial fracture preceded recognition of Sjögren syndrome, followed by presentation with hypokalemic paresis, severe metabolic acidosis, and bilateral nephrocalcinosis. The case highlights the necessity to recognize skeletal manifestations of chronic dRTA and to investigate autoimmune causes in adults with otherwise unexplained distal RTA. This article was presented as a paper at the Indian Society of Nephrology West Zone Mid Term 2024 meeting on July 28, 2024.

Case Presentation:-

A 45-year-old woman with a history of primary hypothyroidism on treatment presented to the emergency department with vomiting and loose stools for two days, followed by sudden-onset, gradually progressive weakness involving all four limbs. There was no history of fever, abdominal pain, respiratory difficulty, seizures, altered sensorium, loss of consciousness, sensory symptoms, or bowel or bladder dysfunction. However, she had sustained a right leg fracture two months before the current admission while briskly walking, without significant trauma. The fracture was managed conservatively with cast immobilization for four weeks. There was no documented history of previous fractures. She had no history of diabetes mellitus, hypertension, tuberculosis, cerebrovascular disease, or other significant chronic systemic illness. She had undergone two previous cesarean sections and had three living children. She had been menopausal for two years.

On examination, she was conscious and oriented. Her blood pressure was 100/70 mmHg, pulse rate 90/min, respiratory rate 16/min, and oxygen saturation 98%. Cardiovascular, respiratory, and abdominal examinations were unremarkable. Neurological examination revealed decreased tone, power of 4/5 in all four limbs, and diminished deep tendon reflexes, with preserved higher mental functions and sensation. Initial laboratory investigations showed hemoglobin 10.4 g/dL, serum creatinine 1.1 mg/dL, urea 55 mg/dL, sodium 134 mmol/L, potassium 2.64 mmol/L, chloride 113.4 mmol/L, calcium 8.8 mg/dL, and phosphate 3.5 mg/dL. Arterial blood gas analysis showed pH 7.30, pCO₂ 26 mmHg, and bicarbonate 9.2 mmol/L, with an anion gap of 11.8 mmol/L. Urinalysis was abnormal, showing a urine pH of 7.5, 1+ proteinuria, and no glycosuria, ketonuria, hematuria, or significant pyuria. Urine spot electrolytes were sodium 17 mmol/L, potassium 14 mmol/L, and chloride 21 mmol/L. The reported urine anion gap on presentation was +10 mmol/L. Urine albumin-to-creatinine ratio was 348 mg/g. The combination of severe normal-anion-gap metabolic acidosis, hypokalemia, and an inappropriately alkaline urine pH along with a positive urine anion gap was consistent with distal renal tubular acidosis. She was worked up for bone-mineral abnormalities which showed elevated serum alkaline phosphatase (184 U/L), elevated parathyroid hormone (110 pg/mL), and decreased 25-hydroxyvitamin D level (18 ng/mL) indicating bone-mineral disease with vitamin D insufficiency. Ultrasonography of the abdomen showed kidneys of normal size with increased cortical echogenicity and maintained corticomedullary differentiation. Multiple hyperechoic calculi were seen scattered throughout the renal parenchyma bilaterally, consistent with nephrocalcinosis. Plain radiograph of the right ankle demonstrated a distal

tibial fracture with malalignment. The fracture had occurred approximately two months before the current presentation without significant trauma.

Evaluation for Sjögren syndrome:-

On further questioning, the patient gave history of dryness of the eyes and mouth and difficulty swallowing for approximately three years. She denied recurrent joint pain, oral ulcers, alopecia, and photosensitivity. On ophthalmic evaluation, Schirmer testing showed markedly reduced tear production, measuring 2 mm in the right eye and 4 mm in the left eye over five minutes. Autoimmune evaluation showed an ANA titer of 1:100 with nucleolar, cytoplasmic, and speckled patterns. The Ro52 antibody was strongly positive, while the reported SSA/SSB, dsDNA, Sm, Scl-70, Jo-1, nucleosome, histone, and ribosomal P antibodies were negative. Minor labial salivary gland biopsy was reported to show histopathological findings suggestive of Sjögren syndrome. These findings along with a longstanding history of sicca symptoms, abnormal Schirmer test, autoimmune serological profile and renal manifestations are crucial in establishing the diagnosis of primary Sjögren syndrome with associated distal RTA.

Treatment and follow-up:-

The patient received intravenous potassium chloride 40 mEq daily for three days, oral potassium citrate 1080 mg three times daily, sodium bicarbonate 1000 mg three times daily, and calcium carbonate 500 mg twice daily. Symptomatic therapy with lubricant eye drops was initiated, and oral prednisolone 40 mg daily was started. Her weakness and electrolyte abnormalities improved during hospitalization, and she was discharged on potassium citrate, sodium bicarbonate, oral prednisolone and calcium-vitamin D supplements. At one-month follow-up, she remained asymptomatic with normal renal function and serum electrolytes.



Figure 1. Radiographic images of the ankles and feet. (A) Lateral radiograph of the right ankle showing right distal tibial fracture with malalignment. (B) Lateral radiograph of the left ankle for comparison. (C) Anteroposterior radiograph of both ankles and feet.

Table 1. Laboratory investigations at presentation

Investigation	Parameter	Result
Complete blood count	Hemoglobin	10.4 g/dL
	Total leukocyte count	8,200/mm ³
	Platelet count	2.5 lakh/mm ³
Renal function	Serum creatinine	1.1 mg/dL
	Urea	55 mg/dL
Serum electrolytes	Sodium	134 mmol/L
	Potassium	2.64 mmol/L
	Chloride	113.4 mmol/L

	Calcium	8.8 mg/dL
	Phosphate	3.5 mg/dL
Glycemic profile	HbA1c	5.6%
Thyroid profile	TSH	6.27 IU/mL
	Free T3	3.41 pmol/L
	Free T4	1.16 ng/dL
Arterial blood gas	pH	7.30
	PaO ₂	85 mmHg
	PaCO ₂	26 mmHg
	Bicarbonate (HCO ₃ ⁻)	9.2 mmol/L
	Anion gap	11.8 mmol/L (as reported)
Urinalysis	Urine pH	7.5
	Protein	1+
	Glucose / ketones	Negative / negative
	Red blood cells	0
	Pus cells	2–3
	Casts / crystals	Absent / absent
Spot urine electrolytes	Sodium	17 mmol/L
	Potassium	14 mmol/L
	Chloride	21 mmol/L
	Urinary anion gap	+10 mmol/L
Urine albumin-to-creatinine ratio	Urine ACR	348 mg/g
Bone-mineral profile	Alkaline phosphatase (ALP)	184 U/L
	Parathyroid hormone (PTH)	110 pg/mL
	25-hydroxyvitamin D	18 ng/mL

Abbreviations: ACR, albumin-to-creatinine ratio; ALP, alkaline phosphatase; HbA1c, glycated hemoglobin; PTH, parathyroid hormone; TSH, thyroid-stimulating hormone.

Table 2. Autoimmune serological workup

Investigation	Result
Antinuclear antibody (ANA), indirect immunofluorescence	Positive at 1:100; nucleolar, cytoplasmic, and speckled patterns
ANA immunoblot	Anti-Ro52 (52 kDa): strongly positive
Anti-SSA/Ro and anti-SSB/La	Negative
Anti-dsDNA and anti-Sm	Negative
Anti-Scl-70	Negative
Anti-Jo-1	Negative
Anti-nucleosome, anti-histone, and anti-ribosomal P antibodies	Negative

Abbreviations: ANA, antinuclear antibody; dsDNA, double-stranded DNA; SSA, Sjögren syndrome-related antigen A; SSB, Sjögren syndrome-related antigen B.

Discussion:-

Primary Sjögren syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands and a wide spectrum of extraglandular manifestations. Renal involvement most commonly occurs as tubulointerstitial nephritis and may result in distal renal tubular acidosis (dRTA). Although hypokalemia, nephrocalcinosis, and nephrolithiasis are recognized manifestations of dRTA, metabolic bone disease severe enough to present with fractures is an uncommon initial manifestation of pSS [5,6].

The present case illustrates an unusual sequence in which an atraumatic right distal tibial fracture occurred approximately two months before the patient presented with hypokalemic paresis. Initial evaluation revealed severe normal-anion-gap metabolic acidosis, hypokalemia, an inappropriately alkaline urine, and bilateral nephrocalcinosis. Further evaluation prompted by longstanding sicca symptoms and abnormal Schirmer testing, along with minor labial salivary gland biopsy findings led to the diagnosis of pSS-associated dRTA. This sequence highlights the

importance of considering an underlying renal tubular disorder in patients presenting with atraumatic fractures, particularly when accompanied by electrolyte abnormalities or muscle weakness.

Pathophysiology of metabolic bone disease in distal RTA:-

Chronic metabolic acidosis adversely affects skeletal metabolism. Bone acts as a buffer for sustained acid loads, and prolonged acidosis promotes mineral dissolution, increases osteoclastic bone resorption, and may suppress bone formation. These processes can reduce bone mineral content and impair skeletal mineralization, potentially contributing to osteomalacia, reduced bone density, and fractures. Vitamin D deficiency, secondary hyperparathyroidism, hypophosphatemia, and proximal tubular dysfunction may further compromise skeletal health in individual patients [5,6]. In the present patient, the serum bicarbonate concentration was 9.2 mmol/L, indicating severe metabolic acidosis. The alkaline phosphatase was 184 U/L, parathyroid hormone was 110 pg/mL, and 25-hydroxyvitamin D was 18 ng/mL. These findings suggest abnormalities in bone-mineral metabolism that may have contributed to skeletal fragility. However, in the absence of bone mineral density measurements, detailed fracture imaging, or confirmatory evidence of osteomalacia, the precise skeletal pathology cannot be established. The fracture should therefore be interpreted in the context of possible metabolic bone disease associated with chronic dRTA, with vitamin D insufficiency and secondary hyperparathyroidism as potential additional contributors.

Comparison with previously reported cases:-

Several reports have described metabolic bone disease as the presenting feature of pSS-associated renal tubular dysfunction. Khandelwal et al. reported three patients in whom metabolic bone disease led to the identification of renal tubular acidosis secondary to pSS, emphasizing that skeletal manifestations may precede recognition of the underlying autoimmune disease [6]. Cherif et al. subsequently described a 31-year-old woman who presented with muscle weakness, bone pain, and Looser's zones in the femoral neck. Further evaluation established osteomalacia associated with pSS and dRTA [5]. A particularly relevant comparator is the report by Abdulla et al., which described a 57-year-old woman presenting with a pathological femoral-neck fracture. Despite negative conventional antinuclear antibody, anti-SSA/Ro, and anti-SSB/La testing, minor salivary gland biopsy supported the diagnosis of Sjögren syndrome. The authors attributed the fracture to dRTA-associated metabolic bone disease and secondary hyperparathyroidism [7]. This case is particularly pertinent because it demonstrates that a fracture may lead to the recognition of previously unrecognized Sjögren syndrome, even in the absence of conventional serological markers.

Nagae et al. described a woman with generalized bone pain, a pubic bone pseudofracture, and osteomalacia associated with dRTA and proximal tubular dysfunction. Notably, overt sicca symptoms were absent, and the autoimmune diagnosis emerged during the evaluation of the renal tubular disorder [8]. Shen et al. reported adult-onset hypophosphatemic osteomalacia associated with Sjögren syndrome, illustrating that phosphate disturbances may represent an additional mechanism of skeletal disease in selected patients [9]. Jain et al. described a child with pSS-associated dRTA and severe metabolic bone disease, including multiple fractures and Looser's zones, further demonstrating the potential consequences of prolonged unrecognized tubular dysfunction [10].

More recently, Mukherjee et al. reported bilateral femoral-neck pseudofractures initially mistaken for stress fractures in a patient subsequently diagnosed with Sjögren syndrome-associated dRTA [11]. Islam et al. described a patient presenting with recurrent hypokalemic quadriplegia and proximal myopathy associated with osteomalacia complicating dRTA due to pSS [12]. These reports demonstrate the heterogeneous skeletal and neuromuscular manifestations of Sjögren-associated tubular disease. Collectively, the literature establishes that osteomalacia, pseudofractures, and pathological fractures can precede recognition of pSS-associated renal tubular dysfunction. The clinical value of this case lies in the sequence of an atraumatic distal tibial fracture followed by hypokalemic paresis, identification of severe dRTA and nephrocalcinosis, and subsequent recognition of previously unrecognized Sjögren syndrome. It also highlights involvement of multiorgan systems in pSS without conventional SS-A/SS-B positivity.

Hypokalemic paresis and nephrocalcinosis as diagnostic clues:-

The acute presentation was characterized by generalized weakness, decreased muscle tone, diminished deep tendon reflexes, and a low serum potassium concentration of 2.64 mmol/L. Arterial blood gas analysis demonstrated acidemia with a pH of 7.30 and bicarbonate concentration of 9.2 mmol/L, accompanied by hyperchloremia and a normal serum anion gap. The urine pH of 7.5 despite systemic acidemia supported impaired distal urinary acidification. The urinary anion gap was positive at +10 mEq/L, calculated from the reported urine sodium, potassium, and chloride concentrations. Although the urinary anion gap is an indirect surrogate for ammonium excretion and has recognized limitations, the finding was compatible with reduced urinary ammonium excretion in this clinical context. Bilateral nephrocalcinosis provided additional evidence of chronic distal tubular dysfunction.

Persistently alkaline urine and altered calcium handling in dRTA promote calcium phosphate precipitation within the renal parenchyma. The coexistence of nephrocalcinosis, hypokalemia, and normal-anion-gap metabolic acidosis should prompt investigation for dRTA and its acquired causes, including pSS.

Diagnostic implications and clinical lessons:-

The present case also illustrates the importance of evaluating sicca symptoms in adults with otherwise unexplained dRTA. The patient reported three years of ocular and oral dryness, with Schirmer test measurements of 2 mm and 4 mm over five minutes. Conventional SSA/SSB testing was reported as negative, whereas anti-Ro52 was strongly positive. Minor labial salivary gland biopsy was reported to show findings suggestive of Sjögren syndrome. Together with the clinical presentation and objective ocular findings, these results supported the clinical diagnosis.

Conclusion:-

In conclusion, an atraumatic fracture is an uncommon presentation of distal RTA which may precede the recognition of underlying autoimmune disease such as Sjögren syndrome. The combination of bone-mineral disease, hypokalemic paresis, normal-anion-gap metabolic acidosis, inappropriately alkaline urine, and nephrocalcinosis should prompt evaluation for an underlying renal tubular disorder and autoimmune disease. Early recognition and correction of the acid-base disturbance with vigorous alkali therapy, together with assessment and treatment of associated bone-mineral abnormalities, may help prevent further renal and skeletal complications and improve quality of life.

References:-

1. Jung SW, Park EJ, Kim JS, et al.: Renal tubular acidosis in patients with primary Sjögren's syndrome. *Electrolyte Blood Press.* 2017, 15:17-22. 10.5049/EBP.2017.15.1.17
2. Soy M, Pamuk ON, Gerenli M, Celik Y: A primary Sjögren's syndrome patient with distal renal tubular acidosis, who presented with symptoms of hypokalemic periodic paralysis: report of a case study and review of the literature. *Rheumatol Int.* 2005, 26:86-9. 10.1007/s00296-005-0587-9
3. Sedhain A, Acharya K, Sharma A, Khan A, Adhikari S: Renal tubular acidosis and hypokalemic paralysis as a first presentation of primary Sjögren's syndrome. *Case Rep Nephrol.* 2018, 2018:9847826. 10.1155/2018/9847826
4. Fulop M, Mackay M: Renal tubular acidosis, Sjögren syndrome, and bone disease. *Arch Intern Med.* 2004, 164:905-9. 10.1001/archinte.164.8.905
5. Cherif E, Ben Hassine L, Kaouache Z, Khalfallah N: Osteomalacia as inaugural manifestation of Sjögren syndrome. *BMJ Case Rep.* 2013, 2013:bcr2013201052. 10.1136/bcr-2013-201052
6. Khandelwal D, Bhattacharya S, Gadodia A, Khadgawat R, Tandon N, Ammini AC: Metabolic bone disease as a presenting manifestation of primary Sjögren's syndrome: three cases and review of literature. *Indian J Endocrinol Metab.* 2011, 15:341-345. 10.4103/2230-8210.85599
7. Abdulla MC, Zuhara S, Kara Parambil AA, Ram N: Pathological fracture in Sjögren's syndrome due to distal renal tubular acidosis. *Int J Rheum Dis.* 2017, 20:2162-2164. 10.1111/1756-185X.13193
8. Nagae H, Noguchi Y, Ogata S, Ogata C, Matsui R, Shimomura Y, Katafuchi R: Osteomalacia secondary to renal tubular acidosis due to Sjögren's syndrome: a case report and review of the literature. *CEN Case Rep.* 2012, 1:123-127. 10.1007/s13730-012-0027-0
9. Shen G, Zhang Y, Hu S, Liu B, Kuang A: Adult-onset hypophosphatemic osteomalacia associated with Sjögren syndrome: clinical case report. *Medicine (Baltimore).* 2017, 96:e6493. 10.1097/MD.0000000000006493
10. Jain G, Kalra S, Vasnik G, Bhandari S: Primary Sjögren's syndrome manifesting with distal renal tubular acidosis and severe metabolic bone disease. *BMJ Case Rep.* 2020, 13:e234929. 10.1136/bcr-2020-234929
11. Mukherjee S, Arjunan D, Bhadada S, Shaharyar A: Unusual presentation of Sjögren's syndrome. *BMJ Case Rep.* 2024, 17:e256661. 10.1136/bcr-2023-256661
12. Islam MS, Ahmed QMU, Ahmed F, Uddin MA, Naher N: Sjögren's syndrome presenting with proximal myopathy due to osteomalacia complicating renal tubular acidosis: a case report. *Cureus.* 2025, 17:e82206. 10.7759/cureus.82206