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Rapidly Progressive Renal Failure: A Rare Clinical Presentation of Renal Sarcoidosis

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Abstract: ***A 54 -year-old woman presented with history of easy fatiguability for last 3 months, breathlessness for last 2 months and feverish feelings for last 2 weeks. Initial laboratory findings of a raisedserum creatinine & BUN which was increased by 1mg/dl in more than 2 weeks indicative of RPRF (Rapidly progressive renal faliure). Alongwith other investigations including raised serum calcium, raised serum protein (9.5 g/l) and normal serum albumin (4.3 g/l), lead to an initial working diagnosis of multiple myeloma as a cause of RPRF. However, later serum protein electrophoresis found a polyclonal gammopathy and further investigations lead us to think about granulomatous disorders, and ultimately we reach the diagnosis of systemic sarcoidosis. The patient responded well to steroids. Sarcoidosis is a rare cause of RPRF & polyclonal gammopathy is a less well recognised manifestation of sarcoidosis, its presence should make clinicians to think about the diagnosis of sarcoidosis.***

Keywords: RPRF, GIN, polyclonal gammopathy, etc

1. Introduction

In clinical setting we sometimes encounter patients who present with progressive renal impairment of seemingly unknown etiology. The duration of disease is brief or may even be undefined. These patients are neither acute kidney injury norchronic kidney disease. The initial clinical diagnosis of these cases may be called rapidly progressive renal failure (RPRF), which may be defined as progressive renal impairment over a period of few weeks (2 weeks to 3 months). On ultrasonography of the kidneys, patients with RPRF have normal sized kidneys, while the presence of small contracted echogenic kidneys establishes the diagnosis of CKD.[1]

The renal histopathology shows lesions affecting any or a combination of the three traditional renal compartments: glomerular, tubulointerstitial or vascular.

Acute Interstitial Nephritis The clinical presentation of acute interstitial nephritis (AIN) may be like RPRF or sometimes even AKI. About half of all cases of AIN are caused by drugs. The other causes include various infections, malignancies and sarcoidosis.[2]

Renal involvement in sarcoidosis is clinically a rare and protean feature and significant renal failure appears in less than 2% of cases. Renal failure is mainly related to various associations of hypercalcemia and hypercalciuria with interstitial granulomatous nephritis (IGN).[3,4]

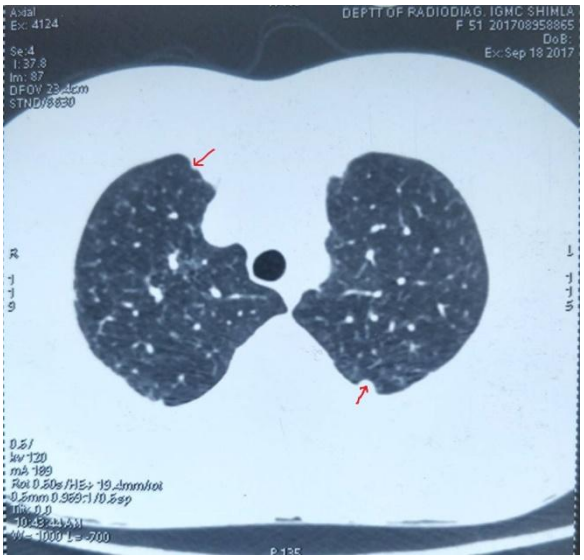
2. Case Report

A 54 -year-old woman presented with history of easy fatiguability for last 3 months, breathlessness for last 2 months and feverish feelings for last 2 weeks. Initial laboratory findings of a raised serum creatinine & raised BUN which was increased by 1mg/dl in more than 2 weeks indicative of RPRF (Rapidly progressive renal failure). Urine examination suggestive of proteinuria (1250mg/24hrs) & hypercalciuria. Ultrasonography showing normal kidneys. Along with other investigations including raised serum calcium (12.4 mg/dl), raised ESR (100 mm in 1 hr), raised serum protein (9.5 g/l) and normal serum albumin (4.3 g/l), lead to an initial working diagnosis of multiple myeloma as a cause of RPRF.

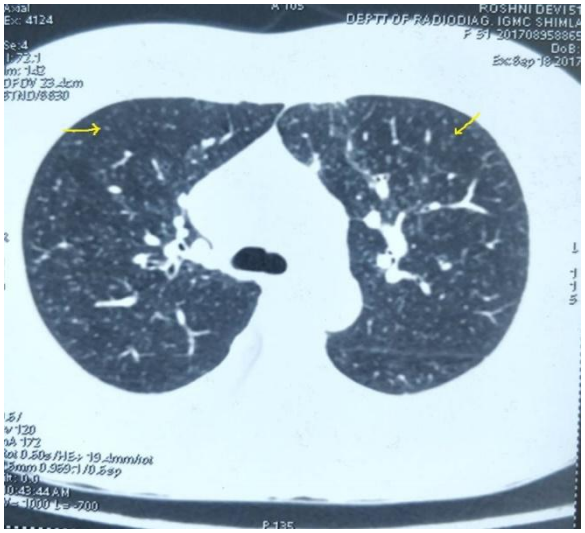
Serum vitamin D and iPTH levels were low.

However, later serum protein electrophoresis found a polyclonal gammopathy and further investigations lead us to think about granulomatous disorders andinfective etiology. Routine fever work up was normal. Chest X- ray was grossly normal. Mantoux test showed anergy.

HRCT chest showing:



(A)



(B)

Figure 1(A & B): Multiple pleural based nodules (A) & parenchymal based nodules (B) with possibility of granulomatous disorder.

Bronchoscopy was done. Bronchoalveolarlavage reveal no AFB, negative CBNAAT and negative fungal culture. Bronchoscopic biopsy report was inconclusive.
ACE levels were elevated.

Renal biopsy showing:

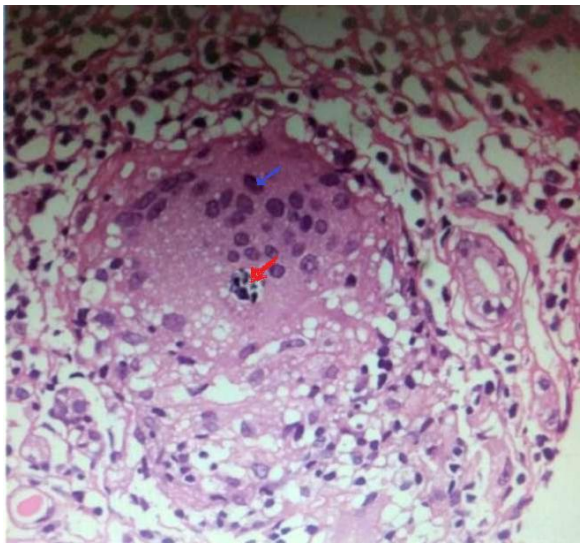


Figure 2: Multiple epitheloid cell granulomas composed of foamy histiocytes with giant cells (blue arrow) suggestive of granulomatous interstitial nephritis (GIN) with nocaseous necrosis, and few giant cells shows calcification with in their cytoplasm (red arrow). These findings were suggestive of renal sarcoidosis (GIN).

Ultimately collaboration of all findings we reach the diagnosis of systemic sarcoidosis [Pulmonary stage III + Renal (GIN)]. The patient was put on steroids. Initially methyl-prednisolone pulse for three days followed by oral prednisolone 60 mg per day (1mg/kg/day) for 4 weeks then tapered by 5 mg per week after looking response to treatment. Patient responded well to steroids clinically as well as laboratory parameters.

Response to treatment: significant improvement in serum creatinine, BUN& normalization of serum calcium.

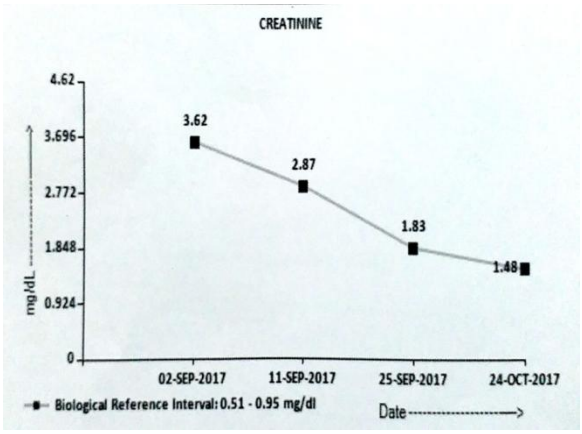


Image 3: Response of steroids on renal function in renal sarcoidosis

3. Discussion

Although sarcoidosis is mentioned as an uncommon cause of RPRF, but exact incidence of RPRF in renal sarcoidosis is not known. [2]

Sarcoidosis is a multisystem disease of unknown etiology represented with noncaseating epithelioid-cell granulomas that is a common finding developed in the affected tissues. In most cases the mediastinal lymph nodes and the lungs are involved (in >95% of patients).[5] Extra pulmonary sarcoidosis (liver, spleen, skin, parotid gland, peripheral lymph nodes, central nervous system and so on) is reported with a variable frequency (16.6 to 80%).[6]

Renal biopsy is the gold standard in diagnosing renal sarcoidosis and is warranted when the suspicion of kidney involvement is there.[7]

Granulomatous interstitial nephritis (GIN) is one of the renal pathological manifestations of sarcoidosis. It is usually clinically silent, but may present occasionally as acute kidney injury.[8]

In sarcoidosis and other granulomatous disorders, 1-alpha hydroxylase is synthetized by granulomas and activated macrophages. This enzyme activity is responsible for the increase in 1, 25-dihydroxy vitamin D and is resistant to normal negative feedback mechanisms.[9]

As a result, 1, 25-dihydroxy vitamin D levels in sarcoidosis are directly related to the availability of its substrate, 25-hydroxy vitamin D. 1, 25-dihydroxy vitamin D augments the gastro-intestinal calcium absorption, stimulates the osteoclast activity and bony reabsorption and increases renal tubular calcium reabsorption. The net result is an increase in plasma calcium and thus hypercalcaemia. Additionally, the rise in 1,25-dihydroxy vitamin D causes a suppression of parathyroid hormone (PTH) by a direct as well as an indirect mechanism by producing hypercalcaemia. This decreased PTH synthesis along with an increased renal calcium load results in the development of hypercalciuria leading to nephrocalcinosis and renal dysfunction.[9, 10]

Granulomatous interstitial nephritis is the most common renal lesion seen on biopsy. It can present either as acute or chronic renal failure.[9] The true incidence is unknown, but in autopsy studies of patients with sarcoidosis, a granulomatous infiltrate is found in the kidneys in 7–23%, although many remained clinically silent.[10,11]

GIN is a rare histological diagnosis present in 0.5–0.9 % of native renal biopsies.[12] GIN has been associated with pharmacotherapy, infection, sarcoidosis, crystal deposits, paraproteinemia, and granulomatosis with polyangiitis (GPA), and is also seen in an idiopathic form.[13]

Most authors recommend treatment of GIN starting with a dose of 0.5–1 mg per kg oral prednisone once daily for 1 month (or iv pulse methylprednisolone for initial 3 days) depending on the severity of the disease.[9,10,11]

4. Conclusion

The constellation of raised serum protein, ESR and calcium with normal albumin initially pointed towards theinitial diagnosis of multiple myeloma.

Sarcoidosis is a rare cause of RPRF & polyclonal gammopathy is a less well recognized manifestation of sarcoidosis, its presence should make clinicians to think about the diagnosis of sarcoidosis by correlating with clinical features & other laboratory investigations.

Renal involvement is rare insarcoidosis, but when it occurs, treatment is always required given the substantial risk of the development of renal failure. A disordered calcium metabolism is the most important cause of renal failure. Granulomatous interstitial nephritis is the most typical histological finding. A guideline for treatment is currently lacking. However glucocorticoids are the mainstay of treatment as per literature & should be started as soon.

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