Case Report

Bridging therapy for achalasia in a second trimester pregnant patient

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Abstract

We present the case of a 28-year-old female who presented for primary care at 22-week gestation with type II achalasia and worsening solid/liquid dysphagia leading to pregnancy weight loss. Considering that durable therapies such as surgical myotomy and pneumatic dilatation have considerable risk, botulinum A toxin injection was selected as a temporizing bridging therapy. She had an uncomplicated post procedure course and had significant rapid improvement in dysphagia symptoms, which enabled her to progress to normal peripartum weight. This case highlights the need for early recognition of achalasia and an unique niche for use of botulinum toxin A as a temporizing therapy in this risk averse population.

Keywords: Achalasia, botulinum, dysphagia, pregnancy

Introduction

Esophageal achalasia is a rare idiopathic motility disorder characterized by an incomplete relaxation of the lower esophageal sphincter (LES).[1] Its prevalence is roughly 10 cases per 100,000, with an incidence of 0.5 cases per 100,000 population per year.[1,2] Achalasia has an insidious onset and diagnosis is usually delayed due to symptoms mimicking gastroesophageal reflux disease; a high degree of suspicion is needed for diagnosis. Patients may present to primary care with symptoms of long-standing dysphagia to both liquids/solids as well as pyrosis not responding to a trial of proton pump inhibitor. Long-term sequelae include weight loss, regurgitation of undigested food, and phagophobia. Exact pathophysiology of achalasia has not been fully discerned, although functional loss of myenteric plexus ganglion cells in the distal esophagus and LES is thought to play a role.[3] The Chicago Classification 3.0 is a well-known criteria which divides achalasia into three distinct subtypes based on high-resolution manometry. Type I (classic achalasia) has impaired relaxation without significant pressurization within the esophageal body. It is defined by 100% failed peristalsis and elevated median integrated relaxation pressure (IRP). Type II achalasia is characterized by lack of peristalsis and swallowing of liquids causing rapid pan-esophageal pressurization and an elevated IRP. Type III is associated with absent peristalsis in the context of preserved fragments of contraction or premature spastic contractions >20%. Treatment for Type I and Type II achalasia responds well to pneumatic dilation, Heller myotomy, or botulinum toxin A injections. Type III responds less to pneumatic dilation, with the treatment of choice being surgical myotomy.[1] Several treatment options exist, including diet modifications, pharmacotherapy (i.e., calcium channel blockers, nitrates, botulinum toxin A), surgical myotomy, and endoscopic pneumatic balloon dilation. Pneumatic dilation and myotomy have superior durability than botulinum toxin A injections in treating patients with achalasia, although are less appealing among pregnant patients due to increased complication risk. Botulinum toxin A is especially attractive for use in high-risk patient populations such as in pregnant or elderly patients, where surgical therapy is relatively contraindicated.

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Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_389_18

How to cite this article: Neubert ZS, Stickle ET. Bridging therapy for achalasia in a second trimester pregnant patient. J Family Med Prim Care 2019;8:289-91.

Case Presentation

We report a unique case of a 28-year-old female with Type II achalasia, G2P0 at 12-week gestational age who presented from her primary care center with pregnancy weight loss secondary to worsening solid and liquid dysphagia. She was diagnosed by high-resolution manometry 2 years ago with findings of elevated IRP, absent peristalsis, and pan-esophageal pressurization consistent with Type 2 achalasia [Figure 1]. Different treatment modalities were discussed with the patient including surgery, pneumatic balloon dilation, botulinum A toxin injections, and peroral endoscopic myotomy (POEM). Because she was in her second trimester of pregnancy, she was considered to be at high risk for esophageal perforations with pneumatic dilation, and hence, alternative treatment options were considered. Given the lower complication profile and relative ease of administering botulinum toxin A, it was felt to be the best option for bridging therapy during her pregnancy. Coordinating care via a multidisciplinary team including anesthesia and obstetrics, she was electively admitted to the hospital to undergo intravenous fluids, enteric nutritional supplementation, fetal monitoring, and endoscopic therapy with botulinum toxin A injections. Her endoscopy was notable for a puckered hypertonic gastroesophageal junction (GEJ) and dilated esophagus with retained saliva [Figure 2]. The patient was brought to the operating room with monitored anesthesia care with pre and post fetal heart monitoring. One hundred units of botulinum toxin A was mixed with 5 cc of normal saline into a syringe. A 5-mm injector needle was used to inject 4 aliquots of 1 cc (20 units) of botulinum A toxin circumferentially 1 cm proximal to the LES. The patient experienced no complications and fetal heart tones remained normal. She had immediate improvement in dysphagia symptoms over the next 3 days, and had recovery in dysphagia at 1 month follow up while delivering a healthy baby to term.

Discussion

Botulinum toxin A has had an increased role in the medical management of various diseases. Botulism toxin is a potent inhibitor of acetylcholine release from presynaptic terminals.[4] Blocking unopposed cholinergic stimulation caused by the loss of interneurons which release neurotransmitters relaxing the smooth muscle within the LES is the therapeutic objective.[4] First described in 1994 by Pasricha *et al.* for use in achalasia, it was noted that at 1 week 90% of botulism toxin groups showed significant symptom reduction and a significant decrease in mean LES pressure.[5]

Earlier recognition of dysphagia can prompt expedited referral to gastroenterology for diagnosis with endoscopy and esophageal high-resolution manometry. Treatment decisions must take into account patient's history and identify those deemed to be at higher risk for procedural complications including pregnant patients and those with multiple comorbidities such as the elderly. Botulinum toxin A injections have a relatively low complication rate, although lack longevity with a high remission rate in 65–90% of the patients after 6 months.[1,6,7] Most common side-effects include epigastric pain, chest pain, heartburn, vertigo, nausea, and vomiting.[1,7] Serious complications include mediastinitis, although reported at a low incidence of 0.04%.[1,7] Repeated botulinum toxin A injections can induce submucosal fibrosis of the GEJ and obscure surgical planes, making subsequent endoscopic myotomy or surgery more challenging.[7-9] This in turn leads to increased risk for esophageal perforation and treatment failure.[9]

Although no treatment modality is without complications, botulinum toxin A injections has proven to be a very safe, well-established treatment modality for high-risk achalasia patients. This case highlights the importance of early symptom recognition during primary care to expedite the definitive management of achalasia and reduce morbidity. Botulinum toxin injections are the mainstay bridging therapy for pregnant patients with clinically significant dysphagia caused by achalasia obviating the need for more invasive therapeutics. Ideally, a multidisciplinary approach with primary care, registered dietician, gastroenterology, and surgery is ideal for the long-term management of complicated achalasia to meet symptom and nutritional benchmarks.

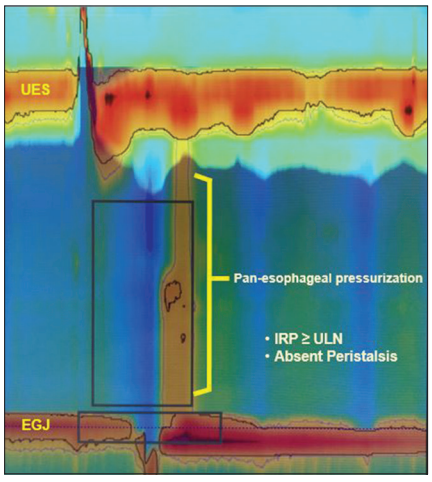

Figure 1: Characteristic findings in esophageal high-resolution manometry in Type II achalasia

Figure 2: Characteristic findings on upper endoscopy of achalasia

Informed patient consent was obtained for publication.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

An interesting case of acute disseminated encephalomyelitis following *E. coli* infection

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Abstract

Acute disseminated encephalomyelitis (ADEM) is a rare inflammatory demyelinating disease of central nervous system (CNS), characterized by multifocal white matter involvement with neurological deficits and accompanied by encephalopathy. ADEM is thought to be caused by autoimmune etiology. CNS autoantigens are produced by molecular mimicry triggered by an environmental stimulus, mostly infection (viral/bacterial) or post vaccination, in genetically susceptible individuals. ADEM is sometimes referred to as post/para-infectious or post-immunization ADEM. ADEM is characterized by multifocal neurological signs and occasionally it rapidly progresses to coma. Magnetic resonance imaging (MRI) is used to confirm the diagnosis. The treatment is based on intravenous high-dose methylprednisolone, which usually leads to a rapid improvement. Recently, the use of intravenous immunoglobulins and plasma exchange (PLEX) has also been suggested. We report a case of a 6-year-old girl who was admitted for urinary tract infection but developed neurological complications which was treated successfully.

Keywords: Acute disseminated encephalomyelitis, *Escherichia coli*, high-dose methylprednisolone, magnetic resonance imaging

Introduction

Acute disseminated encephalomyelitis (ADEM) is the disease of central nervous system (CNS) characterized by the inflammatory demyelination with multifocal white matter involvement and neurological deficits.[1] The worldwide annual incidence is 0.07–0.4 per 100,000 population per year but the true incidence of ADEM in India is unknown and this is mostly because of the underreporting of the cases. ADEM is more common among young adults and children and it does not show any predilection for sex or ethnicity.[2] The autoimmune etiology is being proposed in the majority of the cases that usually develops after the acute viral or bacterial infection, vaccination, or organ transplantation.[3,4] Though there are many bacterial and viral pathogens that leads to ADEM, the development of ADEM due to *Escherichia coli (E. coli)* has never been reported till now. Therefore, we report a case of para-infectious encephalomyelitis (ADEM) following urosepsis due to *E. coli*.

Case History

A 6-year-old female child, born to nonconsanguineous parents was brought to the hospital with 2 weeks history of dysuria, 7 days of fever, and lethargy for a day. At admission she had hypotension and was in sick-looking state but was conscious, oriented without any evidence of focal neurological deficit. Her hypotension was treated with intravenous fluids and was started on empirical cefotaxime, considering as urinary tract infection.

Her investigations revealed neutrophilic leukocytosis with plenty of pus cells in urine. She was euglycemic and her renal, hepatic parameters were within the normal range. Urine culture grew *E. coli* sensitive to cefotaxime and amikacin. Injection

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Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_402_18

How to cite this article: Balamurugesan K, Ponprabha R, Davis P. An interesting case of acute disseminated encephalomyelitis following *E. coli* infection. J Family Med Prim Care 2019;8:292-5.

amikacin was added along with cefotaxime. On the second and third day of hospitalization she remained afebrile, conscious but complaining of myalgia. On the fourth day she remained conscious but developed neurological symptoms such as difficulty in walking, diminished vision, ataxia with broad-based gait. On examination she had involvement of the pyramidal tract (hypertonia, brisk reflexes in all four limbs with positive Babinski sign, and ankle clonus), cerebellum (ataxia with broad-based gait) with intact sensory system. Ophthalmological evaluation revealed decreased visual acuity of 6/18 with normal fundus. Immunological markers of inflammation such as antinuclear antibody, C-reactive protein were negative. CT brain and lumbar puncture was done immediately and the reports are shown in Table 1.

Neurology opinion was obtained. On the basis of history, examination, cerebrospinal fluid (CSF) analysis, possibility of ADEM was considered and MRI brain was suggested. MRI brain showed nonenhancing hyperintense foci in left thalamus as in Figures 1 and 2 and left cerebellar white matter on T2-weighted fluid-attenuated inversion recovery (FLAIR) as in Figure 3, suggestive of ADEM. Possible differential diagnoses considered were the first attack of multiple sclerosis, cerebrovascular accident, meningoencephalitis, and vasculitis.

The diagnosis was made according to the guidelines given by International Pediatric Multiple Sclerosis Study Group. The patient was started on intravenous methylprednisolone 20 mg/kg for 5 days, followed by oral steroid for 4 weeks along with other supportive measures. The patient had dramatic improvement and had complete recovery without any residual sequelae.

Discussion

ADEM is a rare disease characterized by an immune-mediated inflammatory demyelination of the CNS, which predominately affects the white matter of the brain and spinal cord.[1] The ADEM is characterized by the development of acute onset encephalopathy with multifocal neurological deficits.[3,5] The ADEM usually develops following the acute viral etiology, especially exanthematous disease, bacterial as well as due to vaccination and rarely after the immune sera.[3,4] Approximately 50–75% of the ADEM is due to postinfectious cause, following measles, mumps, coronavirus, coxsackie B, dengue virus, Epstein-Barr virus, hepatitis A and C virus, Borrelia burgdorferi, Chlamydia, Legionella, Mycoplasma pneumoniae, Rickettsia rickettsi, Streptococci, Plasmodium vivax.[6,7] Nearly 5% of the ADEM occurs following the vaccination. The vaccines that are associated with the development of ADEM are hepatitis B, Japanese B encephalitis, measles, mumps,

Table 1: CT brain and CSF analysis

CT brain plain	Normal study
CSF analysis	
Total count	6-8 WBC/hpf
Cytology	Predominantly lymphocytes
Protein	48 mg/dl
Sugar	71 mg/dl
Viral serology	Negative for JE, HSV, CMV
Culture and sensitivity	No growth

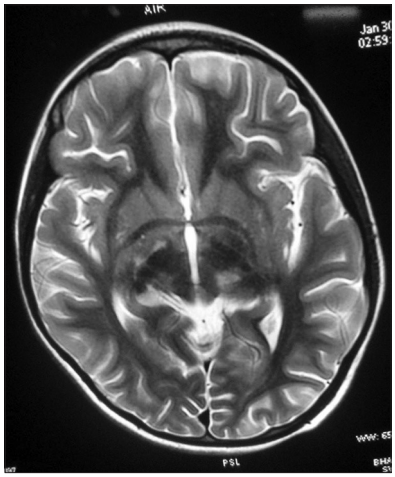

Figure 1: MRI brain T2-weighted image showing Lt thalamic hyperintensity

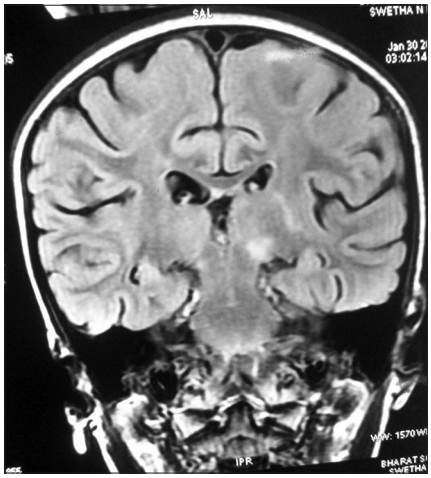

Figure 2: MRI brain sagittal section showing Lt thalamic hyperintensity

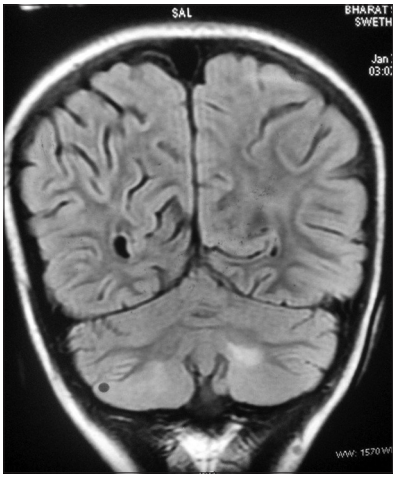

Figure 3: MRI brain showing Lt cerebellar hyperintensity

Table 2: Clinical and radiological features that may distinguish ADEM from first attack of multiple sclerosis (MS)

	ADEM	MS
Age	<10 years	>10 years
Stupor/coma	+	−
Fever/vomiting	+	−
Family history	No	20%
Sensory complaints	+	+
Optic neuritis	Bilateral	Unilateral
Manifestations	Polysymptomatic	Monosymptomatic
MRI imaging	Widespread lesions: basal ganglia, thalamus, cortical gray-white junction	Isolated lesions: peri ventricular white matter, corpus collosum
CSF	Lymphocytic pleocytosis	Oligoclonal bands
Response to steroids	+	+
Follow - up	No new lesions	New lesions

+: More likely to be present; −: Less likely to be present

Table 3: Diagnostic criteria given by International Pediatric Multiple Sclerosis Study Group

1. A first clinical attack of CNS demyelinating disease with acute or subacute onset, polysymptomatic neurologic features, and encephalopathy
2. Brain MRI showing focal or multifocal lesions, predominantly involving the white matter, without evidence of previous white matter changes
3. Encephalopathy as a presenting symptom, with the onset of encephalopathy corresponding with the occurrence of the disease state (encephalopathy is defined to include behavioral changes, such as lethargy or irritability, or severe changes in the level of consciousness such as coma)

pertussis, polio, rubella, tetanus, rabies (Semple vaccine).[8] There are two proposed concepts for the development of ADEM. The first one is the inflammatory cascade concept which is by the direct invasion of the neurotropic pathogens into the CNS. The second concept is the molecular mimicry between the pathogen and myelin proteins of the host.[9] The ADEM is characterized by the onset of fever, malaise, myalgia, headache, and vomiting but encephalopathy is the hallmark feature of the ADEM, which ranges from simple confusion to coma. Within a period of 4–13 days after the infection or vaccination, the neurological signs and symptoms will develop.[10,11] In addition to encephalopathy, other neurological signs such as hemiparesis, cranial nerve palsies, paraparesis, meningismus, ataxia, and optic neuritis may occur.[12,13] The diagnosis of the ADEM is mainly based on the clinical and radiological features. CT brain is usually normal. Cranial MRI is the imaging study of choice. T2 and FLAIR images show patchy areas of increased intensity in the white matter regions. Deep gray matter structures such as thalami, basal ganglia are often involved.[14] The CSF examination shows nonspecific changes such as increased pressure, lymphocytic pleocytosis, and raised protein. Increased amount of IgG specific for myelin protein can be noted.[14] The clinical and radiological features that distinguish ADEM from the first attack of multiple sclerosis is given in Table 2.

The International Pediatric Multiple Sclerosis Study Group gave a diagnostic criterion to diagnose ADEM in children,[15] as shown in Table 3. This criterion is very helpful to distinguish ADEM from other clinically isolated syndromes. The treatment options available for the ADEM are corticosteroids, plasma exchange, and intravenous immunoglobulins. High dose of intravenous corticosteroids is widely accepted as the first line of treatment, especially the methylprednisolone with a dose of 20–30 mg/kg per day with a maximum dose of 1 g per day should be given for 3–5 days followed by oral prednisolone for 3–6 weeks. Other modalities of treatment include intravenous immunoglobulin at a dose of 2 g/kg over 2–5 days and plasma exchange are very useful in case of steroid nonresponders.[1,11] The long-term prognosis of the ADEM is good. About 60–90% of the patients recovered without any neurological deficit in an average period of 1–6 months.[10,11]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Case Report

Nephrocalcinosis in a patient with extrapulmonary tuberculosis – A rare entity

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Abstract

Nephrocalcinosis is a rare condition in clinical practice where there is an increased renal deposition of calcium. Varied causes of this condition have been given in literature, and tuberculosis (TB) has been an important one. Hypercalcemia is a known complication of granulomatous diseases. We report a rare case explicitly showing relationship of extrapulmonary (genitourinary) TB with nephrocalcinosis.

Keywords: Extrapulmonary tuberculosis, hypercalcemia, nephrocalcinosis

Introduction

Nephrocalcinosis is a condition where there is an increased renal parenchymal deposition of calcium which has substantial overlap with hypercalcemia, nephrolithiasis, renal parenchymal damage, and reduced renal function. Nephrocalcinosis most often applies to increased renal calcium content, as opposed to the localized and focal increase in calcium seen in infarct and caseating granulomas in renal tuberculosis (TB). In patients with chronic granulomatous disease such as sarcoidosis,[1] TB,[2] and fungal diseases, excess 1,25 dihydroxy vitamin D synthesis from 25(OH) vitamin D can lead to hypercalcemia and hypercalcuria-related nephrocalcinosis.

Case Report

A 42-year-old female patient, farmer by occupation, resident of Chamba district, presented to our outpatient department with chief complaints of fever for 2 months and right-sided chest pain for the same duration. The patient was apparently well before that when she presented with fever documented up to 102° Fahrenheit with evening rise in temperature and it was associated with night sweats but not associated with any chills and rigor or any rash or skin changes. Her right-sided chest pain was localized to infra-axillary region, nonradiating, sharp, nonexertional, and got aggravated on deep inspiration and coughing. There was no history of cough and shortness of breath. Ten years ago, she took treatment for lymph node (LN) TB but defaulted after 3 months of therapy. She never took any medication for diabetes and hypertension. There was no history suggestive of any contact with TB patient, or high-risk sexual behavior. Family history, menstrual history, and recent treatment history were unremarkable. On examination, the patient had pallor and mild dependent edema. Five LNs were palpable in the right cervical region superior and middle cervical region, the largest being 2.5 cm in diameter, matted, nontender, and not associated with any overlying skin changes not fixed to the underlying structure or skin. On respiratory system examination, the right infra-scapular and infra-axillary region were dull on percussion and breath sounds were decreased with shifting dullness suggestive of right-sided pleural effusion, which was confirmed by chest X-ray. About 5 mL of straw colored fluid was tapped and sent for investigation.

Investigations revealed the following: Hb 8.9 g/dL, total leukocyte count 4970 (neutrophils 76%, lymphocytes 15%,

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Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_385_18

How to cite this article: Malakar S, Negi BD, Singh G, Sharma T. Nephrocalcinosis in a patient with extrapulmonary tuberculosis – A rare entity. J Family Med Prim Care 2019;8:296-8.

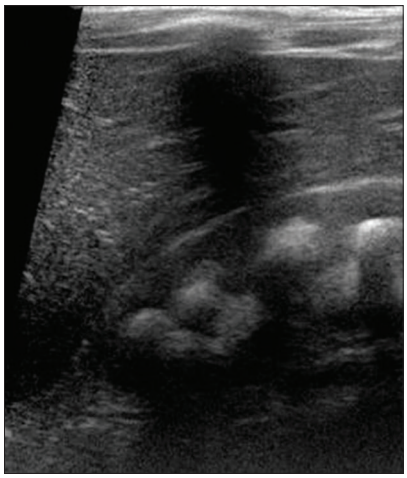

Figure 1: USG showing calcium deposition

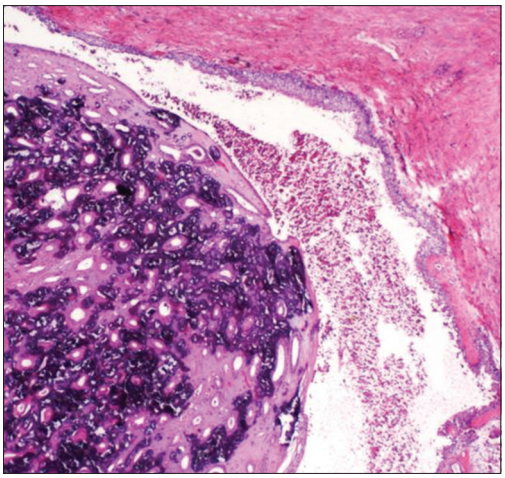

Figure 2: Renal biopsy showing Calcium deposition in medulla

eosinophils 5%, basophils 3%, monocytes 1%), platelet 320,000, serum glutamic oxaloacetic transaminase 44, serum glutamic pyruvate transaminase 34, bilirubin total 0.8, albumin 3.9, alkaline phosphatase 128, urea 96, creatinine 1.9, Na 143, K 4.5, calcium 11.3 mg/dL, phosphorous 4.9, serum and urine electrophoresis was negative, intact parathyroid hormone 20 ng/L (8–51 pg/mL), arterial blood gas showed pH of 7.38, 25(OH) vitamin D 97 ng/mL (30–100 ng/mL), angiotensin converting enzyme level 10 U/L, urine routine and microscopy were normal, and urine for acid fast bacilli was negative. Urinary calcium level was higher than normal (U Ca/Cr = 32). Chloride level was 23 mmol/L. Ultrasonography KUB and noncontrast computed tomography KUB [Figure 1] were suggestive of medullary macro-calcification without any evidences of renal TB. Renal biopsy [Figure 2] was done showing interstitial deposition of calcium without any histological evidences for renal parenchymal TB. Intravenous pyelogram was done and it did not reveal any lesion suggestive of genitourinary TB. LN biopsy revealed caseating granulomatous change with Genexpert (CB-NAAT) positive. Pleural fluid was exudative, and lymphocyte was predominant (95%) with adenosine deaminase level of 67 ng/mL. Hence, a diagnosis of extrapulmonary TB was made.

Discussion

TB is one of the most common chronic granulomatous diseases in India though nephrocalcinosis without genitourinary TB is exceedingly rare in practice. Hypercalcemia is known to occur in granulomatous diseases among which sarcoidosis[1] is the most common and the others are TB, fungal infections, berylliosis, and lymphoma. Though infrequent, hypercalcemia is a recognized complication of active TB.[2] The results of various studies from different countries reporting hypercalcemia incidence in TB did not match, probably because of ethnic and racial disturbances, the amount of sun exposure, and difference in vitamin D and calcium intake. In the United States, hypercalcemia is reported in 16%–28% of pulmonary TB, whereas low percentage of hypercalcemia (5.2%) was found in another study from Pakistan.[3] Hematogenous dissemination of *Mycobacterium tuberculosis* can result in infection of any organ. The commonly affected are the brain, the kidneys, the bones, and the cervical LNs that drain the pulmonary vessel. The most common extrapulmonary cases reported were pleural (16%), LN (40%), bone or joint (10%), genitourinary tract (5%), meningeal (6%), and peritoneal (6%).[4] Renal TB typically presents late with advanced disease because the early stages cause few symptoms and signs.[5] But extrapulmonary TB can lead to hypercalcemia secondary to increased 1,25 dihydroxy vitamin D[6] in a patient with normal vitamin D level, especially people who have adequate sunlight exposure complicating into hypercalcuria and hypercalcemic medullary nephrocalcinosis without any genitourinary TB. This case report is rare as it explains uncommon relationship of TB with nephrocalcinosis. In view of rampant urogenital TB, medullary nephrocalcinosis complicating TB should always be kept as differential diagnosis in a patient presenting to primary care physicians with renal failure and the patient should be evaluated as described above. Since with the treatment of granulomatous conditions such as TB hypercalcemia will be treated and nephrocalcinosis will also recover.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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