Hypercalcemic Encephalopathy as the Presenting Manifestation of Sarcoidosis

Sir,

Sarcoidosis is an autoimmune inflammatory granulomatous disorder with multiorgan involvement. Typical manifestations include bilateral hilar adenopathy, pulmonary reticulo-nodular opacities, skin, joint or eye lesions. Although hypercalcemia is a known metabolic complication in sarcoidosis,[1] it is rarely a presenting complication manifesting as encephalopathy.

We report a 58-year-old female patient who was brought to the emergency department with history of confusion, lethargy, reduced food intake, irrelevant speech of one week duration. She progressively worsened and lapsed into altered sensorium. There was no history of fever, cough, weight loss, shortness of breath, chest pain or joint pains. No history of headache visual symptoms or seizures.

She was not a known hypertensive or diabetic. She reached menopause 10 years ago and was not on any medication or vitamin supplementation. There was no history of any significant chronic illness. She was afebrile, had dry tongue with pulse rate of 120/min regular and blood pressure of 110/70 mm of Hg. On neurological examination, she was drowsy, disoriented and arousable to painful stimulus with Glassgow Coma Scale of 11/15. Fundus examination was normal, bilateral pupils were equal and reacting to light. No asymmetry of limb movements and plantars were withdrawals. Neck movements were painful and restricted. Respiratory examination revealed bilateral infrascapular fine crepitations. Cardiovascular and abdominal examination was unremarkable.

Laboratory evaluation revealed Serum creatinine - 1.8 mg/dl, Blood Urea -69 mg/dl, HBA1C - 5.6%, random blood sugar 96 mg/dl, erythrocyte sedimentation rate 48 mm/1 hr. Hemogram, serumelectrolytes, liver function tests, thyroid profile, serum ammonia, arterial blood gas analysis were within normal limits. Serology for HIV 1 and 2, RA factor, ANA were negative. Chest X-ray revealed prominent right hilum with mild prominence of bronchovascular markings. ECG, 2D echo and Ultrasound abdomen and pelvis did not reveal any abnormality.

Computed tomography of chest revealed symmetric multiple enlarged bilateral hilar adenopathy with reticulo-nodular interstitial thickening with fissural nodules in bilateral lung fields [Figure 1]. Magnetic Resonance Imaging (MRI) of brain, electroencephalogram and cerebrospinal fluid analysis were unremarkable. In view of persistent encephalopathy, further evaluation included serum calcium, which was found to be 14.2 mg/dl and ionised calcium 8.36 mg/dl both were significantly high and serum phosphorus was within normal limits. Etiological workup for hypercalcemia revealed iPTH - 7.33 pg/ml -suppressed, 25 hydroxycholecalciferol- 55.4 ng/ml -normal, 1,25 dihydroxycholecalciferol >200 pg/ml-significantly elevated. Serum angiotensin converting enzyme also significantly elevated with a value of 164 units/L. Based on the laboratory and chest imaging findings a provisional diagnosis of sarcoidosis was considered. Fiber optic bronchoscopy revealed widened carina, granular mucosa in bilateral tracheobronchial tree (cobblestone appearance) [Figure 2a]. Broncho alveolar lavage was negative for Acid Fast Bacilli, GeneXpert for mycobacteria was negative and culture was sterile. Endobronchial biopsy showed multiple non caseating granulomas [Figure 2b]. Final diagnosis of sarcoidosis with hypercalcemia and encephalopathy was made.

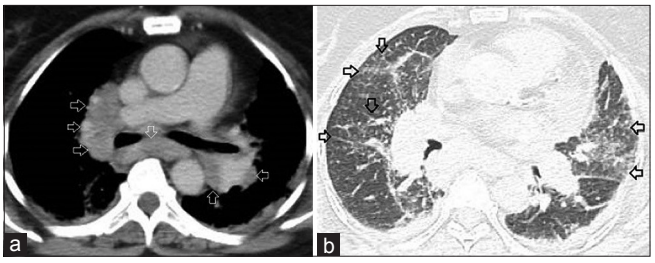

Figure 1: (a) Axial contrast enhanced CT chest image showing multiple bilateral enlarged subcarinal and hilar nodes with homogeneous enhancement and no necrosis (arrows) and (b) Axial HRCT chest images showing reticulonodular interstitial thickening with fissural nodules (arrows)

In intensive care unit under close monitoring of hemodynamic parameters, she was managed with forced diuresis with normal saline and frusemide. Inj zoledronic acid 5 mg in 100 ml normal saline over 30 minutes single dose, intravenous hydrocortisone 100 mg 8th hourly were also given. Her clinical and biochemical parameters improved significantly over next three days with total serum calcium of 11.2 mg/dl, ionised calcium of 6.12 mg/dl and serum creatinine of 1.1 mg/dl. By day 7 of admission, she was conscious, oriented and ambulant without support and was discharged with total serum calcium of 9.6 mg/dl and oral prednisolone prescription of 60 mg per day. At one month follow-up, she maintained both clinical and biochemical improvement.

Rapidly increasing serum calcium levels may result in encephalopathy ranging from mild drowsiness to coma. Common etiologies of hypercalcemia include primary hyperparathyroidism, malignancy, milk alkali syndrome etc.[2]

Hypercalcemia in sarcoidosis is a result of increased activity of 1 alpha hydroxylase enzyme in alveolar macrophages which converts 25 hydroxycholecalciferol into active form of 1,25 dihydroxycholecalciferol. Disease severity may correlate with the degree of expression of 1 alpha

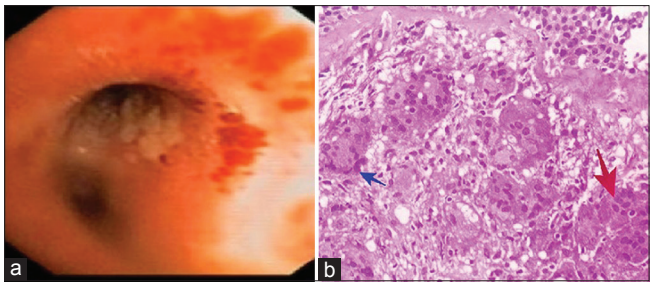

Figure 2: (a) Fiber Optic Bronchoscopy picture showing Cobble stone appearance of endobronchial mucosa at left upper lobe bronchus and (b) Endobronchial Biopsy from the Cobble stone lesions showing Non-caseating epitheloid granuloma (Red arrow) and Langerhans Giant cells (Blue arrow)

hydroxylase enzyme.[3] Another mechanism of hypercalcemia in sarcoidosis is via increased production of parathyroid hormone related protein, which causes upregulation of 1 alpha hydroxylase.[4] Unlike PTH, PTHrP is not regulated by calcium but by interleukin 2 and TNF alpha both of which are increased in sarcoidosis.

Previous reports on sarcoidosis described acute renal failure and pancreatitis with hypercalcemia as the presenting complications.[5,6] However, encephalopathic presentation as described in the present report is an extremely rare phenomenon in sarcoidosis. In view of significant clinical improvement with normalization of serum calcium and negative work up for alternative causes, hypercalcemia is the likely sole etiology for encephalopathy in our patient.

This case highlights a rare clinical presentation of sarcoidosis as reversible encephalopathy with hypercalcemia. Etiological workup for hypercalcemia should be included in otherwise unexplained encephalopathies, especially when brain imaging is normal.

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.

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Conflicts of interest

There are no conflicts of interest.

B. Saroj Kumar Prusty, Kiran Kumar Ramineni[1], G. Krishna Mohan Reddy[2], Ravi Kanth Jakkani[3], Ugandhar Bhattu Chakrahari[4]

Consultants of Intensivist, [1]Neurologist, [2]Physcian, [3]Radiologist, [4]Pulmonologist, Yashoda Superspeciality Hospital, Malakpet, Hyderabad, Telangana, India

Address for correspondence:
Dr. Kiran Kumar Ramineni, Consultant Neurologist, Yashoda Superspeciality Hospital, Near Nalgonda Cross Roads, Malakpet, Hyderabad - 500 036, Telangana, India.
E-mail: ram.kirankumar.dm@gmail.com

References

1. Harrel G, Fisher S. Blood chemical changes in Boeck's sarcoid with particular reference to protein, calcium and phosphatase values. J Clin Invest 1939;18:687-93.
2. Kharb S, Gundgurthi A, Pandit A, Brar KS, Garg MK. Hypercalcemic encephalopathy due to milk alkali syndrome and injection teriparatide. Indian J Endocr Metab 2012;16:1026-8.
3. Inui N, Murayama A, Sasaki S, Suda T, Chida K, Kato S, *et al*. Correlation between 25-hydroxyvitamin D3 1 alpha-hydroxylase gene expression in alveolar macrophages and activity of sarcoidosis. Am J Med 2001;110:687-93.
4. Zeimer HJ, Greenaway TM, Slavin J, Hards DK, Zhou H, Doery JC, *et al*. Parathyroid-hormone-related protein in sarcoidosis. Am J Pathol 1998;152:17-21.
5. Ponce C, Gujral JS. Renal failure and hypercalcemia as initial manifestations of extrapulmonary sarcoidosis. South Med J 2004;97:590-2.
6. Sharma V, Rana SS, Chaudhary V, Sharma RK, Nahar U, Gupta D, *et al*. Sarcoidosis presenting as acute pancreatitis. J Dig Endosc 2015;6:29-31.

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