HYPERAMMONEMIA: AN UNUSUAL PRESENTING FEATURE OF MULTIPLE MYELOMA
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ABSTRACT
A 76 year old lady presented with altered sensorium and was found to have hyperammonemia on evaluation. She had no evidence of liver disease. For her symptomatology of backache, evaluation by bone marrow study showed evidence of multiple myeloma. She was given chemotherapy for multiple myeloma, which resulted in improvement in her sensorium, along with this there was also a rapid decline in serum ammonia levels. Hyperviscosity and hypercalcemia are common causes of altered sensorium in a patient with myeloma but in this case hyperammonemia was the likely cause.

Key Words: Hypercalcemia, hyperviscosity, sensorium

INTRODUCTION
Hyperammonemia is commonly seen in liver disease, Reye’s syndrome, inborn errors of urea synthesis, severe urinary tract infections and induced by medications like valproate. We had a patient who presented with disturbance of consciousness and flapping tremors. She was diagnosed to have hyperammonemina and multiple myeloma and there was a dramatic improvement in sensorium on treating her for myeloma with chemotherapy which paralleled the rapid decline in serum ammonia levels.

CASE REPORT
A 76 year old lady was admitted with fever and altered sensorium gradually worsening over past 3 weeks. A day prior to admission she had a fall and was unable to move right leg. She had backache since past 8 months for which she was evaluated by an orthopedic surgeon. MRI of the dorso-lumbar spine done at that time showed compression fracture of the second lumbar vertebra, degenerative changes at multiple levels and bone marrow edema. She was advised bed rest and treated with analgesics and Taylor’s brace. There was only partial relief with these measures. About 3 months back she was evaluated for generalized weakness, persistent backache, difficulty in walking, loss of appetite and intermittent irrelevant talks. Her investigations at that time were: hemoglobin 8.3 g/dL, white cell count 6800/cmm, platelet count 110,000.

REFERENCES
On examination, she was in altered sensorium, talking irrelevently, temperature 100.6 F, pulse rate of 88 per minute, blood pressure 130/90 mmHg and respiratory rate of 28/min. She was pale and had flapping tremors. There was no lymphadenopathy, icterus, petechiae or other signs of liver cell failure. There was pain on trying to move the right leg and tenderness over the right greater trochanter. Examination of her respiratory and cardiovascular system was normal. There were no dilated veins over abdomen, hepatosplenomegaly or ascites and bowel sounds were normal. Nervous system examination revealed terminal neck stiffness but there was no focal neurological deficit and both the plantars were extensors.

Her present investigations were as follows: hemoglobin 7.5 gm/dL, white cell count 21,000/cm, differential count showed 77% neutrophils, 20% lymphocytes, 2% monocytes and 1% plasma cells. The peripheral blood smear examination revealed increased rouleaux formation. Erythrocyte sedimentation rate was 153 mm at the end of 1st hour, blood urea nitrogen 40 mg/dL and creatinine 3.5 mg/dL, total bilirubin was 0.8mg/dL (direct 0.45 and indirect 3.5 mg/dL), SGOT of 16 IU/L and SGPT of 20 IU/L, Total protein of 5.8 g/dL, albumin 2.8 g/dL and globulin 3.0 g/dL. Serum ammonia was 310 lg/dL, serum calcium of 13.2 mg/dL. X-ray of the hip showed fracture of the right neck of femur. Her CT scan brain revealed no abnormality. Protein electrophoresis showed presence of monoclonal band in the µ2 globulin region with level of µ2 globulin being 31% of total proteins and suppression of beta and gammaglobulin. Bone marrow examination revealed 20% plasma cells with binucleate forms. X ray of the pelvis showed pathological fracture of the neck of right femur, however X ray of the skull did not reveal lytic lesions. There was no evidence of Bence-Jones proteinuria and ß2-microglobulin was 4 mg/L. Thus the patient was diagnosed to have multiple myeloma, stage III.[2] She was treated with melphalan 10 mg/day and prednisolone 60mg/day for 4 days.[3] In addition she also received intravenous infusion of pamidronate once a month and supportive care. There was a remarkable improvement in level of sensorium and serum ammonia levels also reduced to normal levels within 5 days.

Presently she has completed 3 cycles of melphalan and prednisolone and is doing well.

**DISCUSSION**

This patient presented with disturbance of consciousness and had clinical features suggestive of encephalopathy. She had multiple myeloma, probably since a year, which was not diagnosed till the present admission. She had hyperammonemia which could explain the disturbance of consciousness; but no evidence of liver disease or other disorders commonly associated with high ammonia levels. Hyperviscosity and hypercalcemia, commonly associated with multiple myeloma, are causes of altered sensorium in some patients. The remarkable improvement in our patient’s consciousness along with fall in ammonia level in blood with only therapy for myeloma shows that hyperammonemia was indeed due to myeloma itself. The patient also had hypercalcemia, which could be a contributing factor to disturbance of consciousness but improvement in consciousness correlated very well with decline in serum ammonia.

Reference to literature revealed mention of hyperammonemia in multiple myeloma[4] and further search revealed few case reports of hyperammonemia in myeloma.[1,2] Matsuoka et al evaluated serum levels of ammonia and amino acids in 85 patients with multiple myeloma and demonstrated hyperammonemia in six of them.[5] None of them had liver cell failure or any other known causes of hyperammonemia. All the six patients also showed serum amino acid disturbances in various degrees which were strikingly different from those seen in hyperammonemia of liver cell failure. These observations provide evidence to the existence of a peculiar amino acid metabolism in myeloma cells causing hyperammonemia.

Fuji et al have evaluated autopsy findings in four patients of myeloma and hyperammonemia and only one of them was found to have liver dysfunction with severe infiltration of liver parenchyma by myeloma cells, but all had disturbances in amino acid metabolism.[6]

Matsuoka et al have reported a patient with myeloma who developed hyperammonemia during the course of treatment of myeloma.[7] Myeloma cells were isolated and cultured and were demonstrated to secrete ammonia. Otsuki et al have also demonstrated ammonia production by myeloma cells in vitro.[7]

Our case and review of literature suggests an association between multiple myeloma and hyperammonemia and we recommend that serum ammonia should always be monitored in any patient of myeloma with disturbance of consciousness.

It is also interesting to note that majority of case of hyperammonemia with myeloma reported in literature are from Japan and not from western countries, probably suggesting regional or racial differences in amino acid metabolism which leads to ammonia production. This requires further studies to confirm.

**REFERENCES**


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LETTER TO EDITOR

SURVEY OF KNOWLEDGE, ATTITUDES AND PRACTICES OF UROGYNECOLOGICAL PROBLEMS AMONGST GYNECOLOGISTS OF DELHI

Sir,

Urogynecological problems are common problems encountered in gynecological clinics especially in elderly women, but are often neglected as most women consider them as part of normal ageing and suffer in silence. Although there is good awareness amongst gynecologists and women in western countries about these problems, as most big hospitals have developed the clinics run by gynecologists with special interest in urogynaecology, such clinics are still lacking in India.

We conducted this open-ended questionnaire survey which was pre-validated, to know the views of gynecologists (postgraduate degree or diploma in obstetrics and gynecology) of Delhi about various aspects of urogynaecological problems in their day-to-day clinical practice and the feasibility of starting urogynaecology clinics in Delhi and their views about referring their patients with urogynaecology problems to such clinics.

The mean age of the practitioners was 41.8 years. There were 86% women and 14% male gynecologists with 57% doctors from private practice and 43% were from Government hospitals. Out of average 83 patients seen by them per month, 23.6% had urogynecologic problems which were urinary tract infections (UTI) (13.2%), stress incontinence (SI) (3.8%), urge incontinence (UI) (4.1%), genital prolapse (5.1%), vesico-vaginal fistula (0.4%) and miscellaneous (2%) cases (Table 1). A total of 83% doctors thought that urogynecological problems were equally common in India and west. Eighty four percent doctors thought that women consider it part of normal ageing and suffer in silence, while 83% thought that women ignore their urogynecologic problems due to financial and other health problems. Regarding their views about various aspects of stress incontinence (SI), only 38% doctors routinely performed urodynamic studies before operating for SI. Most doctors (70%) used pelvic floor exercises as the first line of treatment for SI, while only 5% used vaginal devices. A total of 25% doctors used operation as first line of treatment for SI. About their views about choice of type of surgery for SI, 44% doctors performed Kelly's repair, 20% open Burch's colposuspension, 17% laparoscopic Burch's colposuspension, 2% Obtape, 4% sling operation while 11% used miscellaneous or combination methods. All doctors considered Burch's operation to be the best operation with high long time success of about 90%.

In their views about first line treatment for urge incontinence (UI), 68% doctors used antibiotics for suspected UTI, 7% used Flavoxate, 4% oxybutynin, 8% combination of antibiotics and Flavoxate, 9% combination of...