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HYPERCALCEMIA CAUSING DIAGNOSTIC DILEMMA IN AN ELDERLY FEMALE : A CASE REPORT

General Medicine

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ABSTRACT

Hypercalcemia is incidentally detected on routine laboratory evaluation in a number of patients .Very often it gives a diagnostic clue to the underlying disorder .A combination of hypercalcemia with a raised immunoreactive parathormone(IPTH) gives a diagnostic clue to the underlying disorder and helps to differentiate benign from malignant disorder. Here , an interesting case of hypercalcemia with raised IPTH and anaemia is presented in an elderly female, which was diagnostic of primary hyperparathyroidism with an incidentally detected single parathyroid adenoma . It was differentiated from tertiary hyperparathyroidism by absence of chronic kidney disease and lack of secondary hyperparathyroidism which leads to tertiary hyperparathyroidism.

KEYWORDS

Hypercalcemia ,IPTH ,primary hyperparathyroidism

INTRODUCTION

Hypercalcemia is an important diagnostic clue to many disorders.It presents with variable clinical features .But, sometimes it gives a clue to the associated disorder. A combination of hypercalcemia with reduced IPTH raises the possibility of multiple myeloma and other malignant disorders, whereas , hypercalcemia with raised IPTH is diagnostic of hyperparathyroidism which may be primary, secondary or tertiary.

Case Report

A 66 years old non diabetic, non hypertensive, non addict Hindu female,house wife by occupation presented with generalised weakness for the last 3 months with pain abdomen for similar duration.She had history of intermittent loose motions following an episode of constipation which was due to laxative use as per history.

The patient had no history of fever, vomiting,joint pain, skin rash,bone pain or any history of bleeding from any site.There was no history of heaviness of the abdomen or any history of early satiety.There was generalised bodyache,which had caused some movement restriction for the last 1 month.

Pain abdomen was in the epigastric region without any definite localisation, radiation,aggravating or relieving factors.It was dull aching without any definite relation to food.There was no family history of any malignancy.The dietary history revealed that the patient was on a mixed diet.There was no significant treatment or vaccination history.There was no history suggestive of weight loss.

On examination, the patient was alert,conscious,co operative.General survey revealed severe pallor without any icterus, lymphadenopathy, edema. Patient was hemodynamically stable with normal body temperature.

On systemic examination,there was no organomegaly ,ascites on GIT examination.On hematology system examination, there was no sternal tenderness, lymphadenopathy. Examination of other systems were unremarkable.

A provisional diagnosis of iron deficiency anemia was made and investigations were sent for Complete blood count, urea, creatinine, sodium, potassium, calcium, magnesium, phosphate,vitamin D3, LFT. Chest X ray, ECG,2d echo and CD with ivc collapsibility were done along with USGWA.

Hemoglobin was 8.1 gm/dl with normal WBC and platelet counts.PBS revealed microcytic hypochromic anemia.MCV was reduced with rise of RDW.Urea,creatinine were normal with mild hyponatremia,but calcium was elevated with values of 12.6 mg/dl revealing mild hypercalcemia (>10.5 mg/dl).Vitamin D3 was low normal.LFT revealed mild rise of ALP with normal levels of albumin and globulin, bilirubin,AST,ALT.CXR was normal with Echo revealing mild concentric LVH with normal LVEF.

A diagnosis of hypercalcemia was made.USG WA revealed bilateral nephrolithiasis.

Patient was put on iv fluids with one unit PRBC transfusion.Injection PPI was given with sos injection drotaverine.Injection frusemide was added iv sos.

Calcium levels decreased to 12.1 mg/dl, the next day with volume correction.Serum protein electrophoresis,immunofixation with FLCA was normal with high rise of immunoreactive PTH with levels of 612 pg/ml(15-65).HRCT thorax revealed increased density with small lytic lesions in the visualised bones of the thorax,expansile bony lesion in the posterior aspect of the 9th rib and a well defined hypodense lesion abutting inferior pole of the left lobe of the thyroid gland suggesting parathyroid origin(Fig 1a,b,).CT neck confirmed the parathyroid SOL A provisional diagnosis of primary hyperparathyroidism was made.CT abdomen revealed bl nephrolithiasis with mixed density lytic-sclerotic lesions in lumbo sacral vertebrae and pelvic bones corroborating the diagnosis.CT brain revealed mixed lytic sclerotic lesions in skull.24 hours urinary calcium was elevated ruling out familial hypocaliuric hypercalcemia(FHH). Cautious vitamin D3 supplementation was given at 40,000 units once weekly for one month with follow up vitamin D3 and IPTH were adviced after one month of therapy.

The patient was discharged with referral to Endocrine surgery for parathyroidectomy and is expected to follow up after the procedure.The rise of ALP with rise of IPTH and mixed sclerotic lesions ruled out multiple myeloma and normal protein electrophoresis excluded monoclonal gammopathy.Absence of CKD,without any secondary hyperparathyroidism which presents with hypocalcemia ruled out tertiary hyperparathyroidism which follows prolonged periods of secondary hyperparathyroidism.

DISCUSSION

Primary hyperparathyroidism is a disorder of the endocrine system presenting with increased secretion of parathyroid hormone causing hypercalcemia with renal as well as skeletal manifestations.It is diagnosed by excluding secondary causes and treatment is done by parathyroid surgery in symptomatic cases with medical therapy by calcimimetics or bone resorptive medicines for some cases.

Fuller Albright termed"stones,bones and groans and moans" to describe the clinical features,most patients are asymptomatic.[1]Stones depict nephrolithiasis induced by hypercalcemia,groans denote hypercalcemia induced constipation.Bone pain occurs due to bone remodelling defects,osteoporosis, fractures.23% of cases present with depression,anxiety, cognitive abnormalities as neuro psychiatric manifestations.

Radio imaging features are brown tumours,osteitis fibrosa cystica,salt and pepper skull appearance, subperiosteal resorption of bones etc.

Though,radiological presentations are now uncommon,,bone densitometry helps in pre clinical detection.[2]The condition involves excess PTH production by 1 out of 4 parathyroid glands close to the

posterior aspect of thyroid gland,just like the case presented here.

Parathyroids are made up of chief cells and oxyphil cells.Chief cells are the commonest PTH producers,whereas the oxyphil cells support the chief cells[3].

PTH is inversely related to ECF ionised calcium as detected by PTH CaSR(Calcium sensing receptor).As ECF calcium increases,receptor activates and chief cells reduce production and PTH secretion.[4,5]

PTH also increases renal formation of 1,25 dihydroxy vitamin D.[6] Primary hyperparathyroidism is the 3rd commonest hormonal disorder.Single adenoma is the presentation in 85% of cases with others presenting as hyperplasia of all 4 glands.Multiple adenomas and parathyroid carcinoma are present in 2-4% and 1 % cases respectively.[7,8]In10% cases adenomas may be extra parathyroidal in ectopic locations like thyroid,thymus etc.[9,10]

Parathyroid carcinomas usually presents in younger patients with more aggressive hypercalcemia and are rare.[11]

Commonest cause of malignancy induced hypercalcemia is squamous cell lung malignancy and renal cancers due to PTH related protein.[12,13]

PTH related proteins are high,but IPTH is low differentiating it from primary hyperparathyroidism.[12,13,14] Genetic conditions associated with primary hyperparathyroidism are MEN(Nultiple eendocrine neoplasia),FHH ,Tumour jaw syndrome etc.

Primary hyperparathyroidism presents mostly in women after menopause,with females being affected 3-4 times commoner than men,with peak age being 50-60 years.[15]Risk factors are mutations,chronic low calcium intake,prolonged furosemide ue,neck radiation treatment,lithium, hypertension etc.[16-21]Thiazides unmask parathyroid disorder.[22]

The patient presented here had non specific symptoms without any risk factors,but had incidental detection of hypercalcemia with raised IPTH with elevated alkaline phosphatase and normal serum protein electrophoresis ruling out multiple myeloma.Absence of secondary hyperparathyroidism, chronic renal disorder ruled out tertiary hyperparathyroidism which occurs after prolonged secondary hyperparathyroidism and presents with diffuse hyperplasia in 44 % cases,adenoma in 5% of cases and rest with nodular hyperplasia.[23]

CONCLUSION

Hypercalcemia with raised IPTH helps in the diagnosis of primary hyperparathyroidism after excluding other causes.It is important to differentiate it from hypercalcemia of malignancy which presents with low IPTH.Treatment of primary hyperparathyroidism is by Surgery by an expert team with definitive investigation and post operative treatment facility.

The patient presented here was diagnosed and referred to Endocrine surgery for further treatment.

The importance of the case lies in the fact that primary hyperparathyroidism should not be missed by clinicians as it is a treatable condition often being diagnosed by asymptomatic hypercalcemia and other investigations.

Conflicts Of Interest- None
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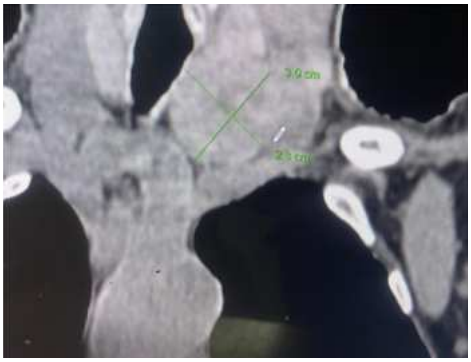

Fig 1a. Coronal section of parathyroid adenoma

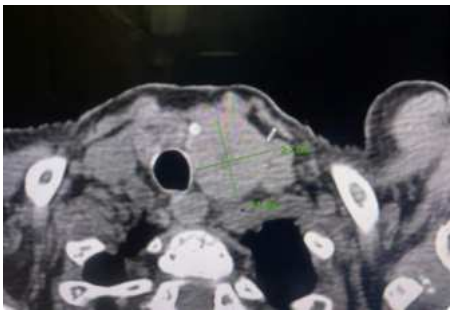

Fig 1b: Axial section of parathyroid adenoma

REFERENCES

1. ALBRIGHT F. A page out of the history of hyperparathyroidism. J Clin Endocrinol Metab. 1948 Aug;8(8):637-57. [PubMed]
2. Joborn C, Hetta J, Johansson H, Rastad J, Agren H, Akerström G, Ljunghall S. Psychiatric morbidity in primary hyperparathyroidism. World J Surg. 1988 Aug;12(4):476-81. [PubMed]
3. Misiorowski W, Czajka-Oraniec I, Kochman M, Zgliczyński W, Bilezikian JP. Osteitis fibrosa cystica-a forgotten radiological feature of primary hyperparathyroidism. Endocrine. 2017 Nov;58(2):380-385. [PMC free article] [PubMed]
4. Chen RA, Goodman WG. Role of the calcium-sensing receptor in parathyroid gland physiology. Am J Physiol Renal Physiol. 2004 Jun;286(6):F1005-11. [PubMed]
5. Minisola S, Arnold A, Belaya Z, Brandi ML, Clarke BL, Hannan FM, Hofbauer LC, Insogna KL, Lacroix A, Liberman U, Palermo A, Pepe J, Rizzoli R, Wermers R, Thakker RV. Epidemiology, Pathophysiology, and Genetics of Primary Hyperparathyroidism. J Bone Miner Res. 2022 Nov;37(11):2315-2329. [PMC free article] [PubMed]
6. Sell J, Ramirez S, Partin M. Parathyroid Disorders. Am Fam Physician. 2022 Mar 01;105(3):289-298. [PubMed]
7. Bilezikian JP, Bandeira L, Khan A, Cusano NE. Hyperparathyroidism. Lancet. 2018 Jan 13;391(10116):168-178. [PubMed]
8. Barczyński M, Bränström R, Dionigi G, Mihai R. Sporadic multiple parathyroid gland disease--a consensus report of the European Society of Endocrine Surgeons (ESES). Langenbecks Arch Surg. 2015 Dec;400(8):887-905. [PMC free article] [PubMed]
9. Agirre L, de la Quintana A, Martínez G, Arana A, Servide MJ, Larrea J. Surgical results and the location of pathological glands in the treatment of primary sporadic hyperparathyroidism with negative preoperative ^{99m}Tc-sestamibi scintigraphy. Cir Esp (Engl Ed). 2020 Dec 18; [PubMed]
10. Nudelman IL, Deutsch AA, Reiss R. Primary hyperparathyroidism due to mediastinal parathyroid adenoma. Int Surg. 1987 Apr-Jun;72(2):104-8. [PubMed]
11. Fingeret AL. Contemporary Evaluation and Management of Parathyroid Carcinoma. JCO Oncol Pract. 2021 Jan;17(1):17-21. [PubMed]
12. Vakiti A, Anastasopoulou C, Mewawalla P. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Apr 16, 2023. Malignancy-Related Hypercalcemia. [PubMed]
13. Mirrakhimov AE. Hypercalcemia of Malignancy: An Update on Pathogenesis and Management. N Am J Med Sci. 2015 Nov;7(11):483-93. [PMC free article] [PubMed]
14. Guise TA, Wysolmerski JJ. Cancer-Associated Hypercalcemia. N Engl J Med. 2022 Apr 14;386(15):1443-1451. [PubMed]
15. Bilezikian JP. Primary Hyperparathyroidism. J Clin Endocrinol Metab. 2018 Nov 01;103(11):3993-4004. [PMC free article] [PubMed]
16. Vaidya A, Curhan GC, Paik JM, Kronenberg H, Taylor EN. Hypertension, Antihypertensive Medications, and Risk of Incident Primary Hyperparathyroidism. J Clin Endocrinol Metab. 2015 Jun;100(6):2396-404. [PMC free article] [PubMed]
17. Boehm BO, Rosinger S, Belyi D, Dietrich JW. The parathyroid as a target for radiation damage. N Engl J Med. 2011 Aug 18;365(7):676-8. [PubMed]
18. Szalat A, Mazeh H, Freund HR. Lithium-associated hyperparathyroidism: report of four cases and review of the literature. Eur J Endocrinol. 2009 Feb;160(2):317-23. [PubMed]
19. Vaidya A, Curhan GC, Paik JM, Wang M, Taylor EN. Physical Activity and the Risk of Primary Hyperparathyroidism. J Clin Endocrinol Metab. 2016 Apr;101(4):1590-7. [PMC free article] [PubMed]
20. Vaidya A, Curhan GC, Paik JM, Wang M, Taylor EN. Body Size and the Risk of Primary Hyperparathyroidism in Women: A Cohort Study. J Bone Miner Res. 2017 Sep;32(9):1900-1906. [PMC free article] [PubMed]
21. Paik JM, Curhan GC, Taylor EN. Calcium intake and risk of primary hyperparathyroidism in women: prospective cohort study. BMJ. 2012 Oct 17;345:e6390. [PMC free article] [PubMed]
22. Griebeler ML, Kearns AE, Ryu E, Thapa P, Hathcock MA, Melton LJ, Wermers RA. Thiazide-Associated Hypercalcemia: Incidence and Association With Primary Hyperparathyroidism Over Two Decades. J Clin Endocrinol Metab. 2016 Mar;101(3):1166-73. [PMC free article] [PubMed]
23. Rebecca Charnock,Michelle D Williams7-Thyroid and Parathyroid Glands:Gnepp,s Diagnostic Surgical Pathology of the Head and Neck(Third Edition) 2021,pg 606-688.