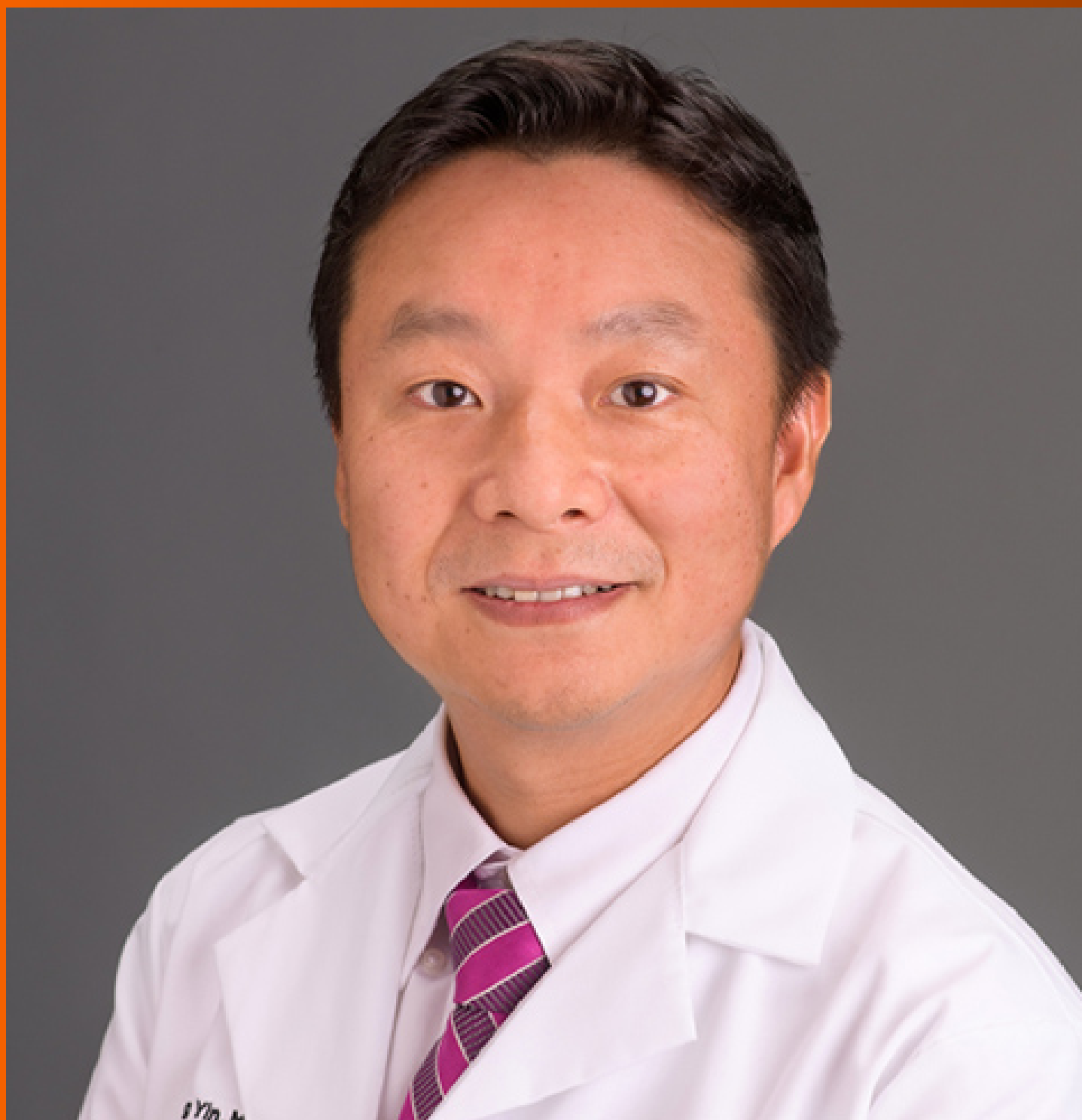


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World J Clin Cases 2022 March 6; 10(7): 2053-2362



Contents

Thrice Monthly Volume 10 Number 7 March 6, 2022

FIELD OF VISION

- 2053 Personalized treatment - which interaction ingredients should be focused to capture the unconscious
Steinmair D, Löffler-Stastka H

MINIREVIEWS

- 2063 Patterns of liver profile disturbance in patients with COVID-19
Shousha HI, Ramadan A, Lithy R, El-Kassas M

ORIGINAL ARTICLE

Clinical and Translational Research

- 2072 Prognostic and biological role of the N-Myc downstream-regulated gene family in hepatocellular carcinoma
Yin X, Yu H, He XK, Yan SX

Case Control Study

- 2087 Usefulness of the acromioclavicular joint cross-sectional area as a diagnostic image parameter of acromioclavicular osteoarthritis
Joo Y, Moon JY, Han JY, Bang YS, Kang KN, Lim YS, Choi YS, Kim YU

- 2095 Correlation between betatrophin/angiogenin-likeprotein3/lipoprotein lipase pathway and severity of coronary artery disease in Kazakh patients with coronary heart disease
Qin L, Rehemuding R, Ainiwaer A, Ma X

Retrospective Study

- 2106 Postoperative adverse cardiac events in acute myocardial infarction with high thrombus load and best time for stent implantation
Zhuo MF, Zhang KL, Shen XB, Lin WC, Hu B, Cai HP, Huang G

- 2115 Develop a nomogram to predict overall survival of patients with borderline ovarian tumors
Gong XQ, Zhang Y

Clinical Trials Study

- 2127 Diagnostic performance of Neutrophil CD64 index, procalcitonin, and C-reactive protein for early sepsis in hematological patients
Shang YX, Zheng Z, Wang M, Guo HX, Chen YJ, Wu Y, Li X, Li Q, Cui JY, Ren XX, Wang LR

- 2138 Previously unexplored etiology for femoral head necrosis: Metagenomics detects no pathogens in necrotic femoral head tissue
Liu C, Li W, Zhang C, Pang F, Wang DW

Observational Study

- 2147** Association of types of diabetes and insulin dependency on birth outcomes
Xaverius PK, Howard SW, Kiel D, Thurman JE, Wankum E, Carter C, Fang C, Carriere R
- 2159** Pathological pattern of endometrial abnormalities in postmenopausal women with bleeding or thickened endometrium
Xue H, Shen WJ, Zhang Y
- 2166** *In vitro* maturation of human oocytes maintaining good development potential for rescue intracytoplasmic sperm injection with fresh sperm
Dong YQ, Chen CQ, Huang YQ, Liu D, Zhang XQ, Liu FH
- 2174** Ultrasound-guided paravertebral nerve block anesthesia on the stress response and hemodynamics among lung cancer patients
Zhen SQ, Jin M, Chen YX, Li JH, Wang H, Chen HX

META-ANALYSIS

- 2184** Prognostic value of YKL-40 in colorectal carcinoma patients: A meta-analysis
Wang J, Qi S, Zhu YB, Ding L
- 2194** Prognostic value of neutrophil/lymphocyte, platelet/lymphocyte, lymphocyte/monocyte ratios and Glasgow prognostic score in osteosarcoma: A meta-analysis
Peng LP, Li J, Li XF

CASE REPORT

- 2206** Endovascular stent-graft treatment for aortoesophageal fistula induced by an esophageal fishbone: Two cases report
Gong H, Wei W, Huang Z, Hu Y, Liu XL, Hu Z
- 2216** Quetiapine-related acute lung injury: A case report
Huang YX, He GX, Zhang WJ, Li BW, Weng HX, Luo WC
- 2222** Primary hepatic neuroendocrine neoplasm diagnosed by somatostatin receptor scintigraphy: A case report
Akabane M, Kobayashi Y, Kinowaki K, Okubo S, Shindoh J, Hashimoto M
- 2229** Multidisciplinary non-surgical treatment of advanced periodontitis: A case report
Li LJ, Yan X, Yu Q, Yan FH, Tan BC
- 2247** Flip-over of blood vessel intima caused by vascular closure device: A case report
Sun LX, Yang XS, Zhang DW, Zhao B, Li LL, Zhang Q, Hao QZ
- 2253** Huge gastric plexiform fibromyxoma presenting as pyemia by rupture of tumor: A case report
Zhang R, Xia LG, Huang KB, Chen ND
- 2261** Intestinal intussusception caused by intestinal duplication and ectopic pancreas: A case report and review of literature
Wang TL, Gong XS, Wang J, Long CY

- 2268** Mixed neuroendocrine-nonneuroendocrine neoplasm of the ampulla: Four case reports
Wang Y, Zhang Z, Wang C, Xi SH, Wang XM
- 2275** Y-shaped shunt for the treatment of Dandy-Walker malformation combined with giant arachnoid cysts: A case report
Dong ZQ, Jia YF, Gao ZS, Li Q, Niu L, Yang Q, Pan YW, Li Q
- 2281** Posterior reversible encephalopathy syndrome in a patient with metastatic breast cancer: A case report
Song CH, Lee SJ, Jeon HR
- 2286** Multiple skin abscesses associated with bacteremia caused by *Burkholderia gladioli*: A case report
Wang YT, Li XW, Xu PY, Yang C, Xu JC
- 2294** Giant infected hepatic cyst causing exclusion pancreatitis: A case report
Kenzaka T, Sato Y, Nishisaki H
- 2301** Cutaneous leishmaniasis presenting with painless ulcer on the right forearm: A case report
Zhuang L, Su J, Tu P
- 2307** Gastrointestinal amyloidosis in a patient with smoldering multiple myeloma: A case report
Liu AL, Ding XL, Liu H, Zhao WJ, Jing X, Zhou X, Mao T, Tian ZB, Wu J
- 2315** Breast and dorsal spine relapse of granulocytic sarcoma after allogeneic stem cell transplantation for acute myelomonocytic leukemia: A case report
Li Y, Xie YD, He SJ, Hu JM, Li ZS, Qu SH
- 2322** Synchronous but separate neuroendocrine tumor and high-grade dysplasia/adenoma of the gall bladder: A case report
Hsiao TH, Wu CC, Tseng HH, Chen JH
- 2330** Novel mutations of the Alström syndrome 1 gene in an infant with dilated cardiomyopathy: A case report
Jiang P, Xiao L, Guo Y, Hu R, Zhang BY, He Y
- 2336** Acute esophageal obstruction after ingestion of psyllium seed husk powder: A case report
Shin S, Kim JH, Mun YH, Chung HS
- 2341** Spontaneous dissection of proximal left main coronary artery in a healthy adolescent presenting with syncope: A case report
Liu SF, Zhao YN, Jia CW, Ma TY, Cai SD, Gao F
- 2351** Relationship between treatment types and blood-brain barrier disruption in patients with acute ischemic stroke: Two case reports
Seo Y, Kim J, Chang MC, Huh H, Lee EH
- 2357** Ultrasound-guided rectus sheath block for anterior cutaneous nerve entrapment syndrome after laparoscopic surgery: A case report
Sawada R, Watanabe K, Tokumine J, Lefor AK, Ando T, Yorozu T

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The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Posterior reversible encephalopathy syndrome in a patient with metastatic breast cancer: A case report

Chae Hyun Song, Seung Jun Lee, Ha Ra Jeon

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Abstract

BACKGROUND

Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic encephalopathic state with clinical symptoms such as headache, altered consciousness, visual disturbances, and seizures. Vasogenic edema occurs predominantly in the posterior occipital and parietal lobes of the brain. PRES is caused by various diseases, and its mechanism remains unclear. However, it can be easily diagnosed based on characteristic lesions on magnetic resonance imaging.

CASE SUMMARY

A 51-year-old woman with unremarkable past medical history presented with progressively worsening back pain since 2 mo. Physical examinations revealed paraspinal muscle tenderness, a large lesion on the right breast and several mass-like lesions on both breasts. The blood pressure (BP) was elevated (150/90 mmHg), and did not respond to antihypertensive medication. On the seventh day of hospitalization, she exhibited a confused mental status and generalized tonic-clonic seizures. On magnetic resonance imaging, bilateral cortical and subcortical edema of the occipital lobes, suggestive of PRES, was observed. The serum calcium was 15.8 mg/dL. After two days of treatment with nifedipine, elcatonin, and zoledronic acid, her BP was 130/91 mmHg and serum calcium was 10.1 mg/dL. The patient regained consciousness and her mental status improved. Fluorodeoxyglucose-positron emission tomography revealed right breast cancer with extensive metastases.

CONCLUSION

Although rare, hypercalcemia can lead to PRES by causing uncontrolled hypertension. Prompt diagnosis can help prevent severe mental disturbances and even death.

Key Words: Posterior reversible encephalopathy syndrome; Breast cancer; Hypercalcemia; Hypertension; Case report

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Core Tip: Posterior reversible encephalopathy syndrome (PRES) is a treatable but potentially fatal encephalopathic state that can accompany various conditions. Although hypercalcemia-related PRES is rare, it may occur in certain diseases. In this case report, metastatic breast cancer led to hypercalcemia, which led to uncontrolled hypertension and finally, PRES.

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INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic encephalopathic state with clinical features such as headache, vomiting, altered consciousness, visual disturbances, and seizures. The radiologic findings demonstrate vasogenic edema in the posterior occipital and parietal lobes of the brain[1]. The pathogenesis of PRES remains unclear, but it is likely related to cerebral autoregulatory failure and endothelial dysfunction.

Hypertension is the most common cause of PRES. Post-transplantation, immune suppression, infection, or autoimmune disease are also risk factors for PRES. In cancer patients, wide use of chemotherapy and targeted agents can be associated with PRES. Hypercalcemia rarely causes PRES, but there have been few reports on hypercalcemia-induced PRES[2].

Hypercalcemia is a common finding in patients with advanced stage cancer. Hypercalcemia develops in cancer patients *via* parathyroid hormone-related peptide (PTHrP) production, osteolytic metastasis, excessive calcium release from the bone, ectopic 1-alpha-hydroxylase activity, and 1,25-dihydroxycholecalciferol formation[3].

We present a case of PRES caused by hypercalcemia and hypertension in a patient with advanced breast cancer with multiple bone metastasis who had never received chemotherapy.

CASE PRESENTATION

Chief complaints

A 51-year-old woman with unremarkable medical history was admitted to the hospital *via* the emergency room for lower back pain.

History of present illness

She complained of worsening back pain after lifting a heavy object two months ago. The numeric rating scale (NRS) score for back pain was seven points.

History of past illness

The patient had an unremarkable medical history.

Personal and family history

The patient had an unremarkable personal and family history.

Physical examination

Physical examination revealed paralumbar muscle tenderness, a 5 cm × 8 cm skin ulcer on her right breast, and several mass-like lesions on both breasts. We planned to evaluate the multiple breast masses under the impression of breast cancer while treating her lumbar pain.

Her blood pressure on admission was 150/90 mmHg despite no history of hypertension. When the patient complained of severe pain, the blood pressure elevated to 170-180 mmHg, and when the pain was relieved, it decreased to 150 mmHg. Therefore, we concluded that the increased blood pressure was likely due to the uncontrolled pain, since the patient did not have a history of hypertension. Attempts to

alleviate the pain included physical therapy, trigger point injection, and medication (intravenous nefopam and methocarbamol, as well as oral acetaminophen and tramadol). However, the pain and elevated blood pressure persisted (systolic BP, 160–180 mmHg). On the 4th day of admission, the patient continued to complain of severe pain (NRS score 8–9), and the patient's blood pressure was measured up to 186/106 mmHg. Therefore, we added oral and intravenous antihypertensive drugs to control her BP, but no improvement was observed.

On the 7th day of hospitalization, the patient had an altered mental status with generalized tonic-clonic seizures lasting for 1 min.

Laboratory examinations

Her serum calcium level was 15.8 mg/dL.

Imaging examinations

Electroencephalography showed repetitive seizures localized in the bilateral posterior region that were more prominent on the left side. Brain magnetic resonance imaging showed bilateral cortical and subcortical edema of the occipital lobes suggesting PRES lesions (Figure 1).

FINAL DIAGNOSIS

The final diagnosis of the presented case was PRES due to uncontrolled hypertension and hypercalcemia.

TREATMENT

Her high BP was controlled using intravenous nicardipine, while the hypercalcemia was treated using normal saline, elcatonin, and zoledronic acid.

OUTCOME AND FOLLOW-UP

After two days of treatment, she had a BP of 130/91 mmHg and a serum calcium level of 10.1 mg/dL. Moreover, her mental status improved. After regaining consciousness, she experienced a partial visual field defect for a few days because of the occipital lobe involvement of PRES.

After the patient regained consciousness, fluorodeoxyglucose-positron emission tomography (FDG-PET) imaging was performed to evaluate the cancer status. FDG-PET imaging suggested right large breast cancer with extensive metastatic lesions, including the left breast, right axillary lymph node, and multiple bones (Figure 2). In addition, a biopsy for histopathological examination of the breast lesion, confirmed invasive ductal carcinoma.

DISCUSSION

The pathophysiology of PRES remains unclear, but there are two leading theories. First, when the blood pressure exceeds the upper limit of cerebral blood flow autoregulation, cerebral hyperperfusion occurs, and the blood-brain barrier breaks, allowing interstitial extravasation, which may cause vascular leakage and vasogenic edema[1]. The posterior brain areas are particularly susceptible to hyperperfusion due to the lack of sympathetic innervation. The second theory suggests that the syndrome is triggered by endothelial dysfunction, caused by circulating endogenous or exogenous toxins. The excessive release of pro-inflammatory cytokines results in endothelial activation, enhancing the release of vasoactive agents, and increasing vascular permeability and edema formation, which can also cause hypertension[1].

In this case, the patient had uncontrolled progressive hypertension after admission. Her systolic BP reached ≥ 180 mmHg. Her elevated BP was one of the leading causes of PRES.

Another consideration was her high calcium level, associated with her advanced breast cancer and multiple bone metastasis. Hypercalcemia is common in breast cancer patients, especially those with advanced-stage and multiple skeletal metastases[3]. The intervention of osteoclasts is the main mechanism of hypercalcemia in patients with extensive osteolytic bone metastases[4]. Excessive osteoclast activation, resulting from RANKL/RANK interaction and malignancy-secreted cytokines, leads to enhanced bone resorption and hypercalcemia.

Although the precise mechanism remains unclear, the pathophysiology of PRES can be correlated with increased calcium levels. Hypercalcemic conditions impair endothelial function by inhibiting the

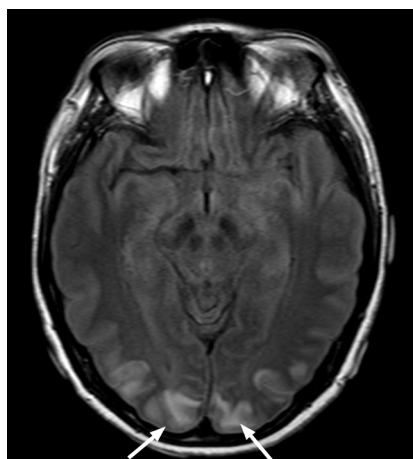


Figure 1 Brain magnetic resonance imaging showed T2 fluid-attenuated inversion recovery hyperintensities in the occipital cortex.

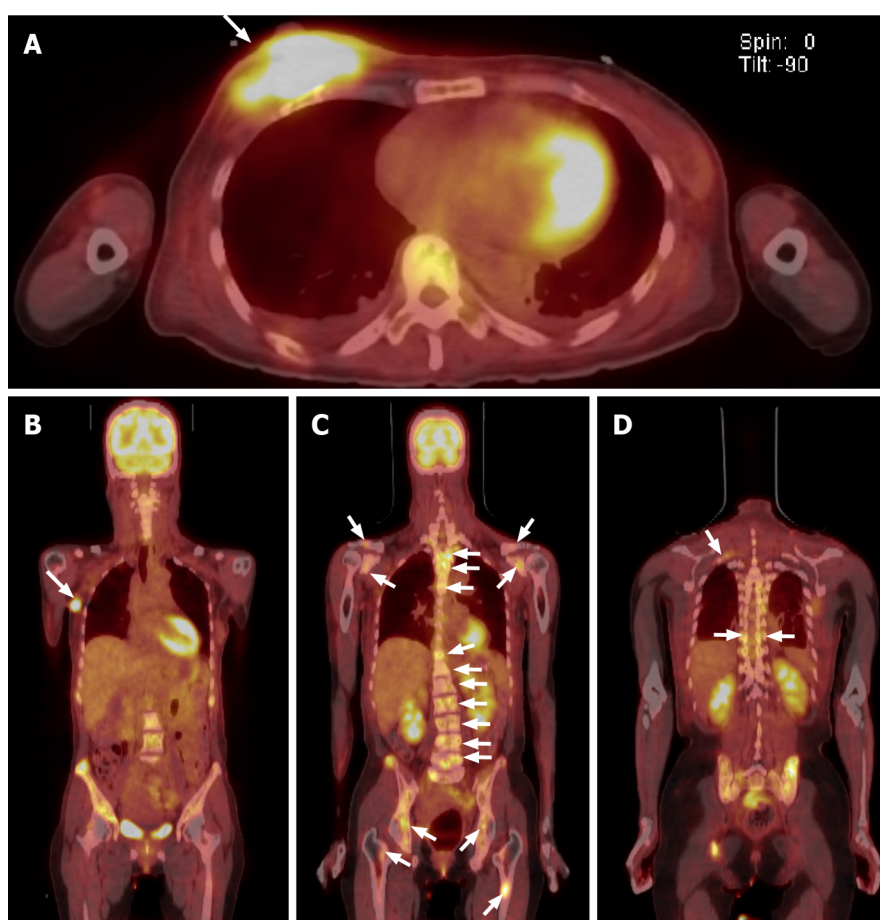


Figure 2 Fluorodeoxyglucose-positron emission tomography showed high uptake. A: Both breasts; B: The right axillary lymph node; C: Both clavicles, scapulars, pelvic bones, femurs, entire spines; D: The sternum, and ribs.

activation of nitric oxide released from endothelial cells. This has a vasodilating effect and increases systolic blood pressure[5]. In this case, the patient's high blood pressure was not controlled by antihypertensive drugs but was controlled after hypercalcemia was corrected. Another hypothesis is that hypercalcemia-induced hypomagnesemia results in hypertension. Based on the antagonism between calcium and magnesium, and the vasodilating properties of magnesium elevated calcium levels lower magnesium concentration. Thus, a magnesium deficit contributes to the development of vasoconstriction. The patient had slight hypomagnesemia (0.72 mmol/L, reference value 0.77-1.03 mmol/L). Based on this, the excessive calcium level of the patient made her vulnerable to developing PRES.

PRES has been reported in cancer patients who have undergone chemotherapy of targeted agents[6, 7]. However, herein we focused on the pathophysiology found in advanced cancer in a case of PRES in an untreated breast cancer patient.

CONCLUSION

This was a rare case of PRES caused by hypertension and hypercalcemia. Although hypercalcemia is a rare cause of PRES, it can, directly and indirectly, result in uncontrolled hypertension, which can lead to PRES. Thus, it is essential to recognize diseases that induce hypercalcemia because PRES has been associated with severe consciousness disturbances and can be fatal. A prompt diagnosis is essential for adequate treatment.

FOOTNOTES

Author contributions: Jeon HR, and Song CH designed the research study; Jeon HR, Song CH, and Lee SJ wrote the manuscript; all authors have read and approve the final manuscript.

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