

Case Report

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Primary Hyperparathyroidism in 9/11 First Responders

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ABSTRACT

Primary Hyperparathyroidism is an unfortunate consequence in 9/11 first responders that is being overlooked. Survivors of that tragic day may have to live with a long list of comorbidities, however, hyperparathyroidism due to parathyroid adenomas is a well-known outcome.

Heightened awareness of the disease and its prevalence should promote a lower threshold for suspicion in 9/11 first responders, leading to frequent screening and appropriate management of the disease before they become poor surgical candidates. Currently, the World Trade Center Health Program does not recognize hyperparathyroidism as a condition of concern. We aim to raise awareness for the screening for hyperparathyroidism in the 9/11 survivor and responder population. This is a case report of a 90-year-old male who was found to have asymptomatic hypercalcemia that was overlooked and presented years later to his primary care physician with complaints of recurrent kidney stones and new-onset paroxysmal A. fib in the setting of newly diagnosed hyperparathyroidism which is likely secondary to 9/11 ground zero occupational exposure for over 2 years. This case report has the objective to encourage clinicians to include hyperparathyroidism in the differential diagnosis of 9/11 first responders.

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Background

Primary hyperparathyroidism (PHPT) is a disorder of one or more of the parathyroid glands [1]. The parathyroid gland(s) becomes overactive and secretes excess amounts of parathyroid hormone (PTH) [1]. As a result, the blood calcium rises to a level that is higher than normal called hyperkalemia. An elevated calcium level can cause many short-term and long-term complications [1]. Although recognition of normocalcemic PHPT (normal serum calcium with elevated PTH concentrations; no secondary cause for hyperparathyroidism) is increasing, data on the clinical presentation and natural history of this phenotype are limited [2]. Ground Zero dust contained many known carcinogens such as soot, benzene, cement, asbestos, heavy metals, and combustion products from jet fuel (polycyclic aromatic hydrocarbons and dioxins) [3]. EDCs and the toxic dust clouds, and asbestos from the collapse of the two office towers put 9/11 survivors and responders at increased risk of head and neck cancers. The very same exposures may also be culprits in the hyperplasia leading to parathyroid adenomas [4].

Case

90-year-old Southeast Asian male with a past medical history of hypertension, hyperlipidemia, coronary artery disease (CAD), benign prostate hyperplasia and, a history of 9/11 occupational exposure at ground zero for over 2 years, presented to the primary care office for routine screening and evaluation in 2019 to establish care. Patients complained of recurrent kidney stones,

worsening weakness, generalized pain, and new-onset CAD. Patients reported worsening generalized weakness and fatigue with symmetric pain in bilateral shoulders, upper extremities and lower extremities. He brought with him previous medical records which were significant for elevated serum calcium levels since at least 2014. Despite this, the patient had multiple office visits between specialists and primary care physicians where hypercalcemia was not documented. Patient was evaluated with serum calcium and PTH levels and referred for age-appropriate osteoporosis screening. The patient was found to have a serum calcium of 10.7. Dual-energy X-ray absorptiometry (DEXA scan) showed osteoporosis of multiple sites and -2.80 T score at the left femoral neck. Soon after establishing care, he developed chest pain and underwent percutaneous coronary intervention (PCI) with placement of 2 stents. He had no prior cardiac history.

Table 1: Calcium levels ref range 8.6-10.2

Date	Serum Calcium	Serum	Vit D 25 hydroxy	PTH intact
6/10/20	10.3			183
8/13/2019	10.7		7.2	
7/29/20	10.7	2.0		
8/1/2020	10.3			
10/23/20	8.7	2.5		150.6
3/21/21	10.9	2.5		163.6
6/15/21			54	

Surgical removal was indicated, however, his cardiologist advised him not to undergo surgery because of high risk due to his recent history of cardiac stent placement. Cinacalcet was considered, however, due to the patient's bone disease being in the osteoporotic range, a bisphosphonate would be the drug of choice. The patient was subsequently medically managed with alendronate for hyperparathyroid bone disease. Over the course of the next year, the patient went on to have a transient ischemic attack and developed new-onset paroxysmal atrial fibrillation with new-onset congestive heart failure all likely secondary to primary hyperparathyroidism that was overlooked.

Discussion

First responders and survivors of that tragic day were exposed to heavy amounts of carcinogens following the collapse of the two towers. First responders who participated in the cleanup process that concluded in July 2002 had prolonged exposure to those carcinogens [4]. People at the highest risk include first responders, firefighters, search and rescue workers, clean-up workers, survivors and residents [5]. Those with the highest exposure showed the highest risk of cancer" indicating a possible "dose dependent" risk [4]. This dose dependent exposure relationship may lead to certain survivors and responders not acquiring a cancerous head and neck mass but an adenoma such as a parathyroid adenoma as in our patient.

Contrary to prior research, new evidence shows occupational exposure-related diseases stemming from 9/11 will peak by 2041 [5]. Incidence of many cancers beginning 20 years after 9/11 and to peak about 40 years after 9/11. It is a looming health problem that is underestimated right now by the general public" [5].

The only definitive therapy for hyperparathyroidism is surgery. Indications for surgery include any clinical symptoms, vertebral fractures, DEXA confirmed osteoporosis, a serum calcium one above the upper limit, a GFR <60, a 24 hour urine for calcium >400, or nephrolithiasis. "Observational studies report a marked reduction in formation of kidney stones after successful surgery [3,5]. Furthermore, over a 10-year follow-up period, all patients with a history of nephrolithiasis who did not choose to have parathyroidectomy had progression of disease" [6]. Nephrolithiasis has been a mainstay indicator for patients. In patients where nonspecific symptoms take precedence, the distinction between asymptomatic and symptomatic has not always been clear. The mainstay focus is to identify symptomatic patients to slow down disease progression via surgery. "Although parathyroidectomy improves bone density and may have modest effects on some quality-of-life symptoms, long-term, observational data and short-term, randomized trial data demonstrate that a large subgroup of patients with asymptomatic PHPT can be followed safely without surgery because they do not have disease progression"[6]. Alternatively, poor surgical candidates, such as those over the age of 50, can be managed with medical therapy.

Cinacalcet can be used in patients whose surgical indication is mainly severe hypercalcemia. It is not the drug of choice for patients with a bone density in the osteoporotic range. For individuals with osteoporosis, alendronate with estrogen and progestin is indicated. "Bisphosphonates and estrogen plus progestin, which inhibit bone resorption and can increase bone density and possibly lower serum calcium concentrations in patients with hyperparathyroidism" [6].

Poor surgical candidates should also avoid thiazide diuretics, lithium therapy and prolonged bed rest. Physical activity should be encouraged. A low calcium diet may lead to a further

increase in PTH secretion and can exacerbate hypercalcemia and hypercalciuria. Moderate calcium consumption, under 800 mg per day, is recently recommended when the serum calcitriol is high. Vitamin D levels should be maintained at 400-800 IU daily to prevent PTH secretion and bone resorption [6].

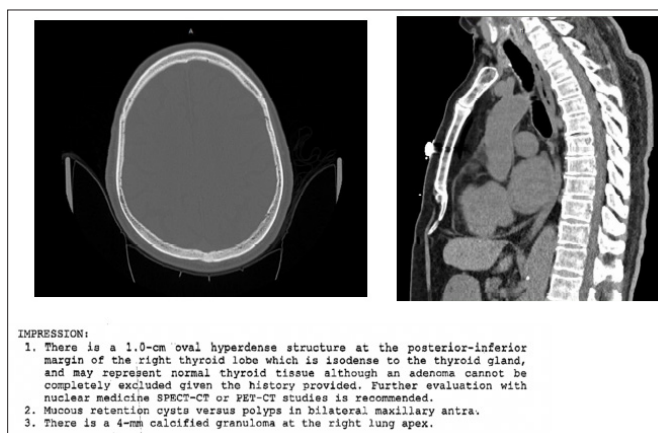


Table 2: WHO Criteria for BMD Classification

Diagnosis	T-Score
Normal	-1.0 or higher
Osteopenia	Between -1.0 and -2.5
Osteoporosis	-2.5 or lower
Severe osteoporosis	-2.5 or lower plus fragility fracture

Our patient falls in the category of Severe osteoporosis. Pt sustained a coccyx fracture while riding a rickshaw while visiting Southeast Asia approximately 3 years ago.

Conclusion

Hyperparathyroidism is less frequently screened even in the general population. Parathyroidectomy is considered a low risk minimally invasive same-day surgical procedure for most patients. This generally low risk surgery is all it takes to cure hyperparathyroidism in most patients and prevent the unfortunate sequelae that follows chronically elevated calcium. "Individuals with laboratory evidence of abnormal calcium and parathyroid hormone regulation should be evaluated for parathyroidectomy regardless of age because all ages can be successfully treated"[7]. This is especially important as the 9/11 workers grow older and their list of comorbidities grows, making them less ideal surgical candidates. "People older than 75 get parathyroid disease. Importantly, these people are excellent candidates to have parathyroidectomy since the high calcium makes many of their other problems worse, and fixing it can make a huge difference in their overall health. People in this group often have heart problems related to high calcium (like atrial fibrillation)" [7]. our patient is now not a surgical candidate. He could have been a candidate for parathyroidectomy a decade earlier and led to significantly decreased morbidity [8-13].

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