DIAGNOSIS NOT TO BE MISSED: PRIMARY HYPERPARATHYROIDISM

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Summary

A 67-year-old lady with history of recurrent renal stones presented with polyarthritis, multiple bone pain and chronic duodenal ulcer. Her skeletal problem was initially attributed to osteoarthritis, gouty arthritis and osteoporosis. The diagnosis of primary hyperparathyroidism was suspected six years later by a high serum calcium level detected on routine screening; and was confirmed by an elevated serum parathyroid hormone level and the finding of a parathyroid adenoma on neck exploration. The challenge of diagnosing this potentially treatable disorder in the presence of multiple pathology in old age was discussed.

Case Report

A 67-year-old lady was referred to our out-patient clinic in 1987 for dizziness, malaise, epigastric pain and arthritis. She was a retired textile factory worker. She had been operated for renal stones in 1975 and 1982 and subsequently she had a left nephrectomy in 1983. She had polyarthritis affecting her knees, ankles and finger joints, as well as low back pain since 1973. She had been consuming a lot of analgesics for her joint pain but she could not tolerate non-steroidal anti-inflammatory drugs. Physical examination showed a left thyroid nodule, Heberden's nodes over terminal interphalangeal joints, bilateral knee crepitus and abdominal surgical scars. She had no uraemic symptoms or signs. Initial investigations in 1987 revealed hypochromic microcytic anaemia (Hb 8.5 g/dl) with normal white cell and platelet counts. The ESR was 38 mm/h, and tests for rheumatoid and antinuclear factors were negative. The alkaline phosphatase was raised at 172 iu/l while the rest of liver function test was otherwise normal. Renal function was mildly impaired(serum urea 12.1 mmol/l, creatinine 175 μmol/l). X-ray of her knees and ankles revealed only changes of osteoporosis and osteoarthritis. Subsequent investigations for the cause of her anaemia revealed chronic duodenal ulcer and gastritis, as well as Haemoglobin H disease, while bone marrow examination was normal.

During her follow-up in our clinic, she had on-and-off joint pain affecting her finger joints and knees for which she was treated as osteoarthritis of hands and knees with analgesics. She also had several episodes of severe acute ankle arthritis with raised serum urate acid level and gouty arthritis of ankles was diagnosed. She had intermittent backache and multiple bone pain, for which she was treated symptomatically as osteoporosis. In 1993 she was found to have hypercalcaemia (serum calcium 3.5mmol/l, phosphate 0.8mmol/l, albumin 37g/dl) on routine screening. Hospital admission was arranged for management and investigation of her hypercalcaemia. Myeloma screen was negative. Thyroid function tests were normal. Chest X-ray was unremarkable. X-ray hands(Figure 1) revealed marked osteoarthritic changes

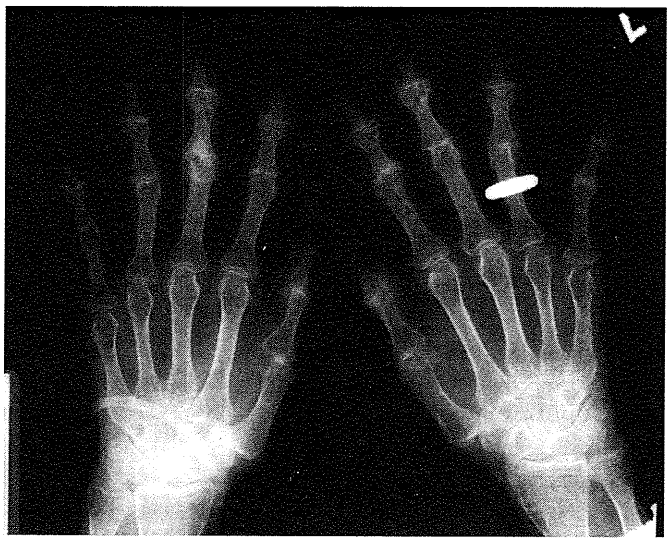

Figure 1. X-rays of hands showing marked osteoarthritic changes in the interphalangeal joints with narrowing of joint spaces.

and skull X-ray showed decreased bone density with no abnormal calcification. There was metabolic acidosis (bicarbonate 13.8mmol/l) with an increased serum chloride of 121mmol/l. Parathyroid hormone level was markedly elevated at 145.6pmol/l(normal reference: 1.16-5.67pmol/l). A diagnosis of primary hyperparathyroidism was made. CT scan and ultrasound study of the neck were performed, showing multinodular goitre affecting mainly

the left lobe of thyroid with intrathoracic extension but otherwise no definite parathyroid mass was detected.

She subsequently had a neck exploration by our surgical colleagues on 19.5.1993. A left inferior parathyroid adenoma was found and excised; a left hemithyroidectomy was also performed. Histology showed parathyroid adenoma and thyroid colloid nodule. Her serum calcium level returned to normal and she is now symptom-free.

Discussion

Primary hyperparathyroidism is an important cause of hypercalcaemia. The underlying pathology includes adenoma(83%), hyperplasia(15%) and carcinoma(less than 1%)[1]. The overall incidence varies from 0.1-0.4%[2,3], with a female predominance(female:male 4:1)[2,3]. Over the last two decades, the reported incidence of primary hyperparathyroidism has been increasing because of the widespread use of autoanalyzer for plasma calcium measurement[4], so that patients who are either asymptomatic or have minimal symptoms can be picked up early by a routine plasma calcium measurement[5].

The present case illustrates that primary hyperparathyroidism can be easily overlooked. This 67-year-old lady did present with a symptom-complex of recurrent renal stones, duodenal ulcer and multiple bone pain, which on retrospective review was highly suggestive of primary hyperparathyroidism. Although only 5% of renal stones are due to primary hyperparathyroidism, the incidence rises to 12-15% in case of recurrent renal calculi[6]. Peptic ulcer is a known complication of hypercalcaemia and could be due to gastric acid secretion or of gastrin formation by hypercalcaemia or parathyroid hormone[7]. Although the present case did not demonstrate the classical radiological features of fibrocystic disease of bone described by Von Recklinghausen, the bone pain experienced by the patient is still significant and is the presenting feature in many patients with primary hyperparathyroidism[6]. In fact, increased awareness of the condition in recent decades has led to earlier diagnosis before the occurrence of severe bony complications. Radiological signs of the skeleton are far less common nowadays[5], and may be limited to osteoporosis only.

It took six years to diagnose primary hyperparathyroidism for this lady. Why is it so? It may be difficult to recognise mild hyperparathyroidism when symptoms are subtle or absent, but to label this present case as "asymptomatic" hyperparathyroidism is incorrect, as symptoms though non-specific, were definitely present. Disorders such as peptic ulceration, impaired renal function, renal stones, and bone pain are so commonly seen in elderly patients that they may be regarded as due to multiple pathologies rather than due to a single underlying disease. On the other hand, the principle of multiple pathology in dealing with elderly patients should also alert one to the possibility of alternate or additional explanations to a single symptom. Thus, while her ulcer pain may be related to the use of non-steroidal anti-inflammatory drugs(NSAIDs); it can also be due to hypercalcaemia. Likewise, osteoarthritis and osteoporosis are common in old age and certainly both of these are present clinically and radiologically in this patient so that her joint and bone pain have all along been attributed to these, and primary hyperparathyroidism as an important cause of bone pain and secondary osteoporosis has been overlooked until the detection of hypercalcaemia on routine screening. The significance of the mildly elevated alkaline phosphatase at the initial presentation of this patient has also been ignored. Therefore, a high index of suspicion is required especially for physicians looking after elderly patients.

Could this be a case of tertiary hyperparathyroidism? Unfortunately, previous calcium or phosphate results were not available for us to definitely exclude this diagnosis, but it is very unlikely. First, the renal function was only mildly impaired and the patient did not have the uraemic symptoms seen in those chronic renal failure patients with tertiary hyperparathyroidism. Second, one would expect the osteodystrophy to be more severe in cases of tertiary hyperparathyroidism, but this patient only has osteopenia and there was no evidence of osteitis fibrosa cystica or any metastatic calcification in soft tissue or arterial walls. Third, the operative findings revealed only one abnormal left inferior parathyroid gland(adenoma) while the other three glands appeared normal with no sign of hyperplasia.

Confirmatory diagnosis of primary hyperparathyroidism is simple: persistent hypercalcaemia with an inappropriately high serum parathyroid hormone concentration is considered to be the most accurate and cost-effective laboratory diagnostic test[4]. Operative intervention for cure is the current and acceptable treatment for symptomatic primary hyperparathyroidism while some asymptomatic cases can be conscientiously surveillanced[4]. However, a high index of clinical suspicion is essential for this treatable disease to be diagnosed. As symptoms are often subtle, non-specific or even absent especially in elderly patients, plasma calcium measurement as a screening test becomes an important diagnostic tool in geriatric practice. Primary hyperparathyroidism is not a condition for clinicians to "wait for"; it is a disease that we should "hunt".

References

1. Whitman ED, Norton JA. Endocrine surgical diseases of elderly patients. Surg Clin N America 1994;74:127-44.
2. Christensson T. Primary hyperparathyroidism: pathogenesis, incidence and natural history. Prog Surg 1986;18:34-44.
3. Heath H III, Hodgson SF, Kennedy MA. Primary hyperparathyroidism: incidence, morbidity, and potential economic impact in a community. N Engl J

Med 1980;302:189-93.
4. Potts JT Jr, Ackerman IP, Barker CF, et al. Diagnosis and management of asymptomatic primary hyperparathyroidism: Consensus Development Conference Statement. Ann Intern Med 1991;114:593-7.
5. Bilezikian JP. Guidelines for the medical or surgical management of primary hyperparathyroidism: To operate or not to operate. In: Bilezikian JP, Levine MA, Marcus R(eds). The Parathyroids: Basic and Clinical Concepts. New York: Raven Press Ltd., 1994:567-74.
6. Bilezikian JP, Silverberg SJ, Gartenberg F et al. Clinical Presentation of Primary Hyperparathyroidism. In: Bilezikian JP, Levine MA, Marcus R(eds). The Parathyroids: Basic and Clinical Concepts. New York: Raven Press Ltd., 1994:457-70.
7. Clark OH. Hyerparathyroidism. In Clark OH(ed). Endocrine surgery of thyroid and parathyroid glands. St Louis, Toronto, Princeton: Mosby Co., 1985:172-240.

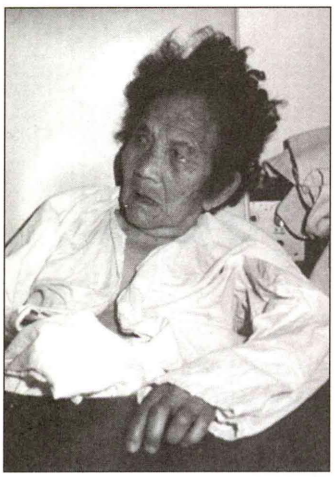

Figure 1

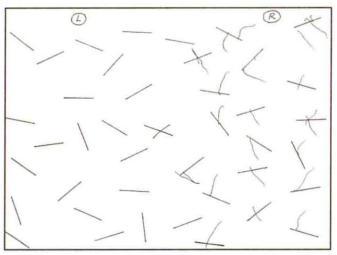

Figure 2

Figure 3

THROUGH THE LOOKING GLASS

The diagonal patient and perceptual neglect

The patient shown in Figure 1 slumped to one side diagonally, leaving an exposed triangle on the back of the chair, a sitting posture which Professor Bernard Issacs identified as a predictor of long-stay[1]. This is the characteristic posture of the patient with perceptual neglect: the trunk, head and eyes all turned away from the affected side. Perceptual neglect is the tendency to ignore spatial surroundings on the side contralateral to the side of cerebral damage; the afflicted has a distorted image of her own body and of her surroundings. Unilateral neglect can be readily detected by the Albert's test[2,3] in which the patient is asked to cross out lines ruled on a sheet of paper; the central line being crossed by the examiner as a demonstration. Our patient left 55%(22/40) of lines uncrossed on her left side(Figure 2) and this indicates severe left-sided neglect. A functional equivalent of this in everyday activity is leaving half of the plate unfinished and yet she would ask for more! Moreover, the eyes of a diagonal patient would not be parallel to the horizon so that it would be difficult for her to relate to food normally during eating. Perceptual neglect has been found in 49% of non-dominant hemisphere strokes and 25% of dominant hemisphere strokes in the early stages[3]. The distress to patients with neglect is best shown by the self-portrait(Figure 3) of a stroke victim upon recovery. It may be further aggravated if such patients are mistakenly labelled as "poorly motivated" or "demented". I remember attending a psychogeriatric session in which a patient appeared indifferent to the questions of a psychogeriatrician. Subsequently, a therapist noted that the patient had right-sided neglect. CT later revealed a left-sided brain tumour. Retrospectively, the psychogeriatrician understood the reason for the lack of response from the patient; he was all along sitting on the right side of the patient! That patient actually had trimodal neglect[4](visual, auditory and tactile neglect occurring together). Well, beware of the fallacy of the golden rule "examine a patient on his right side" when assessing patients with right-sided neglect. Adams[5] identified neglect as an important prognostic factor in determining functional recovery from stroke and successful discharge back home. Similarly, the Albert's test score(percentage of lines left uncrossed) was identified as a significant predictor of both mortality and functional activity six months after stroke[3]. In strokes, family members and even health profession tend to focus on motor paralysis and ignore perceptual deficits. Because perceptual neglect carries important functional and prognostic significance, it deserves much more attention from all those caring for stroke patients.

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References

1. Issacs B. The Challenge of Geriatric Medicine. Oxford, New York, Tokyo: Oxford University Press 1992:174,187.
2. Albert M. A simple test of visual neglect. Neurology 1973;23:658-64.
3. Fullerton KJ, McSherry D, Stout RW. Albert's test: a neglected test of perceptual neglect. Lancet 1986;i:430-2.
4. Heilman KM, Pandya DN, Geschwind N. Trimodal inattention following parietal lobe ablations. Trans Am Neurol Assoc 1970;95:259-61.
5. Adams GF, Hurwitz LJ. Mental barriers to recovery from strokes. Lancet 1963;ii:533-7.