SHORT REPORT

Pseudopseudohypoparathyroidism and spinal cord compression

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Abstract

A 42 year old Greek male with pseudopseudohypoparathyroidism presented with difficulty in walking and with lower limb weakness. His physical signs included short stature, thick neck, short fourth metacarpals and metatarsals, and a spastic paraparesis. Serum calcium and phosphate and parathyroid concentrations were normal. Myelography demonstrated compression of the cervical and lumbar cord in association with local bony abnormalities.

This case documents the previously unreported complication of spinal cord compression in a patient with pseudopseudohypoparathyroidism. The metabolic abnormalities are discussed in the light of the current understanding of calcium metabolism.

Case report

The patient, a 42 year old Greek businessman, presented with a three year history of back discomfort associated with difficulty in walking. He also complained of stiffness in both legs and some weakness of the left leg that although initially mild had progressed over the years. His presentation for review was

precipitated by the development of paraesthesiae in the sole of the right foot. He also had some mild upper limb weakness at night but had no other symptoms. In particular there was no sphincteric disturbance and sexual function was normal. At the time of review he was on no medications although he had had a course of betamethasone some years earlier on the basis that he might have multiple sclerosis.

He was otherwise well with no significant past history. In retrospect he felt that his grandmother had shared his general physical features and particularly the appearance of his hands. He smoked cigars but was a non-drinker.

On examination he had a short stature with a rounded face and thick neck. He was alert and cooperative with a mild scoliosis and a spastic gait. Cranial nerve examination was normal except for a brisk jaw jerk. In the upper limbs the fourth metacarpals were short bilaterally (fig 1) but otherwise neurologically normal. In the lower limbs the fourth metatarsals were short bilaterally (fig 2). Tone was increased bilaterally with a clasp knife phenomenon and there was a marked pyramidal pattern of weakness. The lower limb reflexes were brisk with ankle clonus and bilateral extensor plantar responses. There was a reduced light touch and pinprick sensation in the lower limbs from L2 to S1. General examination was otherwise unremarkable.

The serum electrolytes including the calcium (2.65 mmol/l) and phosphate (1.13 mmol/l) levels were normal as was renal function, serum albumin and alkaline phosphatase activity. The plasma parathyroid hormone (PTH) level was 3.6 pmol/l (Reference range: 0.9-5.4 pmol/l) and a parathyroid hormone stimulation test demonstrated a blunted response of urinary cyclic adenosine monophosphate (cAMP). The urine cAMP response to intravenously infused human PTH (200 IU in human albumin 4.0% w/v in 0.9% saline, 60 ml) went from a control level of 0.45 (nmol urine cAMP/ μ mol creatinine) to a peak of 1.12 at 90 minutes. This contrasts with an expected normal increase of 10-20 fold. Urine mucopolysaccharides were normal. CT scan of the brain was normal, in particular, there was no suggestion of calcification in the basal ganglia. MRI scan of the brain was normal. Myelography demonstrated on the plain films a variably affected vertebral column with structural changes in the thoracic spine consisting of short pedicles and large laminae (fig

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Figure 1 Plain radiograph of the patient's hands demonstrating shortened fourth metacarpals.

Figure 2 Plain radiograph of the patient's feet demonstrating shortened fourth metatarsals.

3). After dye injection the cord was seen to be compressed posterolaterally by the posterior joints and associated ligaments some of which were ossified. Compression of the cervical and lumbar cord and cauda equina were also seen in association with local vertebral abnormalities.

Discussion

This case has the classic findings of short fourth metacarpals and metatarsals, normal serum calcium, phosphate and PTH levels diagnostic of pseudopseudohypoparathyroidism, with the added unusual feature of spinal cord compression resulting in a spastic paraparesis. Indeed the widespread bony abnormalities in a syndrome said to have questionable if any metabolic defect are themselves remarkable.

Hypoparathyroidism is characterised by an abnormally low serum calcium and high phosphate levels. In its idiopathic form it is due to primary failure of the parathyroid gland to secrete PTH. Many secondary causes have been described and the key biochemical feature is a low or absent PTH level. Pseudohypoparathyroidism is a rare hereditary disorder that is due to a deficient end-organ response to circulating PTH.¹ The syndrome is characterised by neuromuscular irritability resulting from low serum calcium. Symptoms include seizures, muscle cramps and poor vision due to cataracts. Ectopic calcification is a common problem and is usually seen in the subcutaneous tissues and in the cerebellum and basal ganglia.² These latter features are not usually seen in pseudopseudohypoparathyroidism but have been described.³ Skeletal abnormalities in pseudopseudohypoparathyroidism include short stature, round face, thick-set build and bony abnormalities, particularly short metacarpals or metatarsals or both, probably

Figure 3 Myelogram demonstrating both the affected vertebral column (see text) and a filling defect in the thoracic region.

due to premature closure of the epiphyses. The diagnosis of pseudohypoparathyroidism is established by the finding of a raised plasma PTH level and an absent urinary cAMP response to exogenous PTH.

Pseudopseudohypoparathyroidism is the even rarer occurrence of the skeletal abnormalities without any obvious biochemical defect, that is, normal calcium, phosphate and PTH levels. The patient described fits this phenotype with normal biochemistry and the classic bony features in the hands and feet with the added unusual feature of spinal cord compression. In pseudopseudohypoparathyroidism this latter feature has been seen in children but only as an isolated cervical lesion.⁴ Compression of the spinal cord has been reported in hypoparathyroidism^{5,6} and reviewed for pseudopseudohypoparathyroidism.^{7,8} Interestingly Alam and Kelly⁷ commented that the

bone in their case was not soft and suggested a role for ectopic calcification involving spinal ligaments in producing the cord problems. Our patient had both bony problems and ligamentous involvement with perhaps both contributing to the cord compression. The response to exogenous PTH in our patient strongly suggests a partial biochemical defect. The presence of myelographic abnormalities at the cervical, thoracic and lumbar levels supports the view that this patient's problem was a generalised bony defect. While similar changes are seen in Paget's Disease he had none of the biochemical or radiographic features of that condition.

The basis of this defect is generally considered to be in the G-protein second messenger system that couples the PTH/PTH-receptor interaction with its intracellular mechanisms.⁹ A blunted response to PTH and hypocalcaemia are usually regarded as essential features of pseudopseudohypoparathyroidism although temporary normalisation of the serum calcium may be seen.¹⁰ The basis of the metabolic defect in pseudopseudohypoparathyroidism is not totally understood. Originally thought not to be associated with resistance to PTH,³ it has recently been suggested that there may be partial resistance to PTH and that the normocalcaemia at the time of diagnosis may be a temporary phase.¹⁰ The patient we describe had at least two other estimates of calcium over a period of years that were also normal in spite of his continuing bony problems. These observations suggest that there may indeed be a partial metabolic defect in pseudopseudohypoparathyroidism. Unfortunately, there is no specific therapy for this variant of the problem. Moreover the presence

of cervical, thoracic and lumbar disease makes operation very difficult.

In summary, a case of pseudopseudohypoparathyroidism is described in which the classical skeletal features of thick short stature and short fourth metacarpals and metatarsals with normal biochemistry are seen. The clinical presentation with multiple level spinal cord compression is unusual for the problem and represents a previously unreported adult complication of this rare and interesting group of disorders.

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