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Research Article

A Case of Hoffman Syndrome Masquerading as Pituitary Tumour

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ABSTRACT:
Hoffman syndrome, a rare presentation of hypothyroidism, is characterized by pseudo-hypertrophy and stiffness of muscles, myxoedematous features. Long standing hypothyroidism can cause pituitary hyperplasia which is difficult to distinguish with pituitary adenoma even with contrast MRI. We describe a case of a 48 years old male presenting as 'Hoffman syndrome' with reactive pituitary hyperplasia that mimicked a pituitary macroadenoma. After 20 days of thyroid hormone therapy, the patient had improvement of the muscular cramps. After 03 months of active therapy a repeat MRI was done which showed regression of size of the mass. In a case of primary hypothyroidism with a solid mass lesion of the pituitary gland, pituitary hyperplasia secondary to hypothyroidism rather than pituitary adenoma should be excluded to avoid unnecessary surgical intervention which has its own complications.

Keywords: Hypothyroidism, Hoffman syndrome, pseudo hypertrophy, Pituitary macroadenoma, Pituitary hyperplasia, Herculean, Thyroxine, Surgery, Myopathy.

INTRODUCTION

Hoffman syndrome, a rare and atypical presentation of hypothyroidism, is characterized by pseudo-hypertrophy and stiffness of muscles, myxoedematous features. Long standing hypothyroidism can cause pituitary hyperplasia which is difficult to distinguish with pituitary adenoma even with contrast MRI. We describe a case of a 48 years old male with long standing uncontrolled primary hypothyroidism presenting as 'Hoffman syndrome' with reactive pituitary hyperplasia that mimicked a pituitary macroadenoma.

CASE

A, 48 years-old man, known case of hypothyroidism (detected in 2005) with poor drug compliance presented with effort intolerance, generalized weakness, swelling of all four limbs progressive proximal muscular weakness with cramps and myalgia, dark pigmentation of face, increased hair fall, hoarseness in voice, increased body size, memory loss for 3 years. On clinical examination he was found to have macroglossia, infiltrated facies, hoarse voice and increased soft tissue mass all over body specially face, limbs & trunk. There was ichthyosis, dark pigmentation of face (Fig. 1), legs, oral mucosa & nails. Herculean appearance and pseudo-hypertrophy of muscles were observed (Fig 2 & 3). There was elongation of great toes (Fig 4) and dry fuzzy hair with alopecia (Fig. 5).

Fig 1. Showing ichthyosis and pigmentation of face

Fig 2. Showing pseudohypertrophy of shoulder muscles

Fig 3. Showing pseudohypertrophy of calf muscles

Fig 4. Elongation of great

Fig 5. Dry & fuzzy hair with alopecia

Neurological examination revealed proximal weakness of lower limbs (Grade 4-/5 Muscle Research Council [MRC]), global hyporeflexia, normal cranial nerves and normal fundus. Laboratorial investigation reveals (Table 1) increased serum levels of muscular enzymes, mild elevation of serum creatinine, dyslipidemia, raised levels of anti Thyroidperoxidase (566.70 u/ml- Normal: 35 u/ml), electrophysiological study showed normal test. DXA scan revealed increased body fat composition. Thyroid ultrasound showed reduced thyroid size with heterogeneous echogenecity and hypo-echoic areas consistent with autoimmune thyroiditis. Electrocardiography (ECG) revealed sinus bradycardia.

Table 1. Investigation reports.

Lab Parameters	Values
Bil Tot/bildir:	1.7 /1.3 mg/dl
Ser LDH	2151 (140 to 280 U/L
CPK	15860 (22 to 198 U/L)
TC/TG/LDL/HDL	206/818/126/37 mg/dL
Luteinizing Hormone	1.56 IU/L (2-18 U/L)
Follicle Stimulating Hormone	0.81 IU/L (1-18 U/L)
Prolactin	3.57 ng/ml (<20 ng/ml)
Thyroid stimulating Hormone	143.42 uIU/ml (0.5-6 uU/ml)
Anti TPO	566.70IU/ml
T3/T4	0.25ng/ml (0.75-2) ng/dL /<1 µg/ml (0.8 -2.8 µg/ml)
DXA Scan	% Fat-24.4
NCV Report (09.02.15)	Normal Study
MRI Brain (12.02.15)	Finding suggestive of Pituitary Hyperplasia (1.1x1.8x1.0 cm)

Two-dimensional echocardiography was normal. Nerve conduction study was normal. Electromyography showed small-amplitude motor unit potential –a myopathic pattern. Based on the above findings, a diagnosis of Hoffman's syndrome was made. This was followed by MRI brain which showed increased size of the pituitary gland (Fig. 6 & 7).

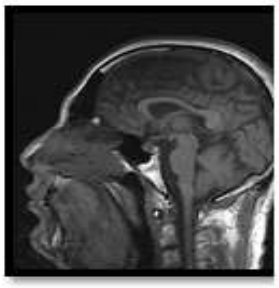

Fig 6. MRI brain T2 weighted image of sagittal section showing pituitary mass measuring 1.5x1.2 cm

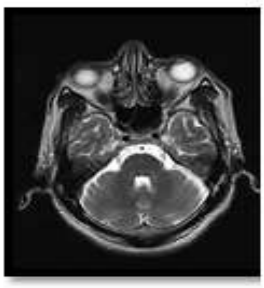

Fig 7. MRI brain T2 weighted image of axial section showing pituitary mass measuring 1.5x1.2 cm

A pituitary adenoma was less likely because of low levels of lieutinising and follicle stimulating hormone and normal prolactin. Pituitary hyperplasia secondary to hypothyroidism was a possibility and we managed the patient as pituitary hyperplasia secondary to long standing uncontrolled hypothyroidism with initial 100 µg/day and gradually increased to 200 µg daily which caused regression of the pituitary mass in 3 motnhs as evident by the repeat MRI brain and complete resolution of myopathic symptoms over 6 months.

DISCUSSION

Hypothyroidism associated neurologic symptoms appear late in the disease course (1). In our patient hypothyroidism was due to chronic autoimmune thyroiditis which is evident by presence of high levels of antiperoxidase (anti-TPO) and anti-thyroglobulin antibodies. Patients with hypothyroidism myopathies can have cramps, muscle weakness, atrophy or myasthenic syndrome, muscular pseudohypertrophy, myxedema and hyporeflexia (2). Myalgia can be as bad in severity as in polymyositis. Severe exercise can cause rhabdomyolisis in these patients too (2). Severe sodium loss is the reason behind myokymia in this case. The pseudohypertrophy is characterized by hypertrophy of muscles with loss of strength resulting in weakness. The exact mechanism is ill understood till date. It is named as Hoffman's syndrome as described first time by Hoffman in 1897. Similar presentation in children with cretinism is referred as Kocher-Debré-Sémélaigne syndrome. The speed of muscle contraction and relaxation depends on availability and clearance of calcium in the endoplasmic reticulum which follows a release, clearance and re-accumulation cycle. (Ianuzzo et al)(3). In hypothyroidism, due to decreased quantity of myosin adenosine triphosphatase (ATPase), velocity of both contraction and relaxation of a muscle are retarded and duration is prolonged. However, thyroxine does not interfere with the transmission of nerve impulses in the neuromuscular junction, sarcolemma or in peripheral nerves. It is postulated that changes in muscle fibers from type II (fast-twitching) to type-I (slow-twitching) fibers (4, 5), an increase in connective tissue, increase in the size and number of muscular fibers, accumulation of glycosaminoglycans in muscles cause hypertrophy in the muscles (5, 6) and reduced velocity of contraction and relaxation with prolonged duration (as explained above) result in weakness. The muscle fibers may show swelling, loss of normal striations, and separation by mucinous deposits (4). Thyroid myopathies can present like myositis characterised by raised creatinophosphokinase (CPK) level as seen in our case. The level of CPK gradually returned to half values in three weeks time in this patient. The myopathic effects of hypothyroidism need to be distinguished from those of a neuropathy, which may rarely complicate hypothyroidism. Prolongs twitch duration due to impaired calcium sequestration by sarcoplasmic reticulum is attributed to delayed relaxation of deep tendon jerks, which. However, the electrophysiological study was normal in this case. Pituitary hyperplasia, characterized by non-neoplastic growth

of one or more functionally different types of pituitary cells, may occur either due to physiologic stress (e.g pregnancy) or due to a pathologic process (7). In this case, thyrotrophic hyperplasia due to lack of feedback inhibition by thyroid gland is the reason for pituitary hyperplasia which can mimic pituitary adenoma and can cause compressive symptoms if large enough (8). MRI cannot distinguish between a pituitary hyperplasia and macroadenoma as was in this patient, where MRI impression was a macroadenoma. Meticulous history, clinical examination and extensive endocrine work up can distinguish between these two and should be treated with close follow up. High clinical suspicion of pituitary hyperplasia secondary to hypothyroidism corroborated with the treatment response with thyroxin and unnecessary surgery was avoided. Therefore, it is suggested that patients with pituitary enlargement on MRI associated with hypothyroidism should undergo extensive endocrine work up and given trial of hormonal replacement first. This can avoid unnecessary surgery (9).

CONCLUSION

In a case of primary hypothyroidism with a solid mass lesion of the pituitary gland, pituitary hyperplasia secondary to hypothyroidism rather than pituitary adenoma should be excluded to avoid unnecessary surgical intervention which has its own complications.

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