CASE REPORT

Panhypopituitarism as a Presenting Manifestation of Neurosarcoidosis – A Rare Case Report

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Abstract

Sarcoidosis is a multisystem disease characterized by non-caseating granuloma that affects the nervous system occasionally. When neurosarcoidosis infiltrate the pituitary gland leading to panhypopituitarism, result can be devastating. We present here a case of 30-year-old lady who presented with fever and headache for 6 months along with prolonged period of amenorrhea and forgetfulness. She also had increased thirst and polyuria. Her hormone profiles were suggestive of panhypopituitarism. MRI of brain showed a contrast enhancing lesion in the sellar and suprasellar region along with nodular leptomeningeal enhancement . We retrogradely searched for the underlying reason behin`d this .Her MT was 0 along with ground glass opacity in both lung fields in HRCT chest which made the diagnosis of neurosarcoidosis most likely. We treated her with prednisolone to manage neurosarcoidosis and secondary adrenal insufficiency along with sequential hormone replacement with desmopressin and levothyroxine . Follow up MRI of brain done 3 months later showed near complete resolution of lesion along with significant clinical improvement.

Key words : *neurosarcoidosis, hypopituitarism, panhypopituitarism*

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Introduction

Sarcoidosis is a condition that triggers inflammation in various organs of the body , including the lungs, eye, skin and occasionally nervous system.[1] When sarcoidosis affects the nervous system, it is referred to as neurosarcoidosis, estimated to occur in approximately 5-15% of patients.[2] Pituitary involvement may be present in up to 5% of those cases and can manifest as hypothalamus, adenohypophyses dysfunction or arginine vasopressin deficiency in isolated fashion or variedly combined.[3] When neurosarcoidosis affects the pituitary gland, it can destroy or compress the gland, interfering it's hormone producing capabilities ultimately leading to a life-threatening condition.[1] Hypothalamic-pituitary neurosarcoidosis accounts for 1% of sellar masses and carriesa mortality rate approaching 10%.[4,5,6] We therefore present a rare case of neurosarcoidosis presenting with panhypopituitarism as it's first clinical manifestation.

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Case presentation

We present the case of 30-year-old lady with complaints of fever along with headache for 6 months and forgetfulness for 3 months. Fever was low grade, irregular with an evening rise of temperature along with global, dull aching headache without any blurring of vision or vomiting. She complained of forgetfulness for recent memory along with fatigability, constipation and cold intolerance for last 3 months. She had amenorrhoea for 18 months with hot flush, pallor and decreased libido. She also had polyuria and polydipsia. She had significant weight loss with anorexia. On general examination, patient was ill-looking, apathetic, pale, mildly anaemic with recorded temperature of 100°F. Nervous system examination revealed she had moderate dementia with MMSE score of 17. Other neurological examination does not reveal any abnormality. Examination of all other systems were unremarkable. Her routine investigations showed reduced haemoglobin along with raised serum sodium level . Hormone profile revealed reduced TSH, FSH, LH, ACTH, basal cortisol and IGF-1 along with raised serum prolactin . Her urine osmolarity was reduced whereas serum osmolarity was maintained. CSF study showed raised protein with negative gene xpert for M. tuberculosis. MRI of brain T1 and T1 contrast sequence revealed a contrast enhancing lesion in sellar and suprasellar region along with nodular leptomeningeal enhancement (Figure 1 & 2). HRCT chest showed ground glass opacity in multiple segments of both lung fields (figure 3) whereas bronchoalveolar lavage was unremarkable.

Table 1

Investigations			Reference range
Full blood count	Hemoglobin (gm/dl)	10	11.5-15.5
	White blood cells (× 10 ^ 9 / L)	13.01	4-11
	Platelets (× 10 ^ 9 / L)	245	150-450
	HCT (%)	30.9	36-46
	ESR (mm in 1st hour)	60	< 20
Renal function	S. Creatinine (mg/dl)	0.99	0.04 – 1.2
	Blood Urea (mg/dl)	4	15-40
Liver function	SGPT (U/L)	16	7-35
	ALP (U/L)	43	40-150
	HBsAGAnti-HCV	Negative	
HbA1C	HbA1c (%)	5	4.5-6.3
Serum electrolyte(mmol/l)	Sodium	149	134-144
	Potassium	3.5	3.3-4.6
	Chloride	111	98-106
	TCO2	24	23-27
Urine R/E		Pus cell: 2-3/ HPF, Albumin, RBC: nil	

Table 2

Test	Result	Reference range
Serum Calcium (mg/dl)	8.6	8.8-10.3
Serum Albumin (mg/dl)	4.0	3.5-5.6
Serum ACE (IU/L)	49	20-70
Serum LDH (IU/L)	222	120-246
Urine osmolarity (mOsm/kg)	71	500-850
Plasma osmolarity (mOsm/kg)	287	282-295
Serum TSH (IU/ml)	0.39	0.7 -4.17
Serum FT4 (pmol/l)	9.17	11.5- 22.7
Serum FSH (mIU/ml)	0.91	3.03-8.08
Serum Prolactin(mIU/ml)	1064.13	59-619
Plasma ACTH (pg/ml)	1.50	8.3-57.8
Basal Cortisol (nmol/L)	25	102-690
IGF-1 (ng/ml)	52	260-350
Urinary electrolyte (mmol/day)		
Urinary sodium	15	25-125
Urinary potassium	18	25-125
Urinary chloride	33	110-250
MT	0	
ANA	Negative	

Table 3

CSF study			Reference range
Cytology	Appearance	Clear	
	Total WBC count(/mm^3)	02	00-05
	Total RBC count(/mm^3)	00	
	Neutrophil (%)	00	
	Lymphocyte(%)	100	
Biochemical	Protein(mg/dl)	67.90	15-48
	Glucose(mg/dl)	59.76	40-70
	ADA (U/L)	2.10	< 10
Gene Xpert		Not detected	

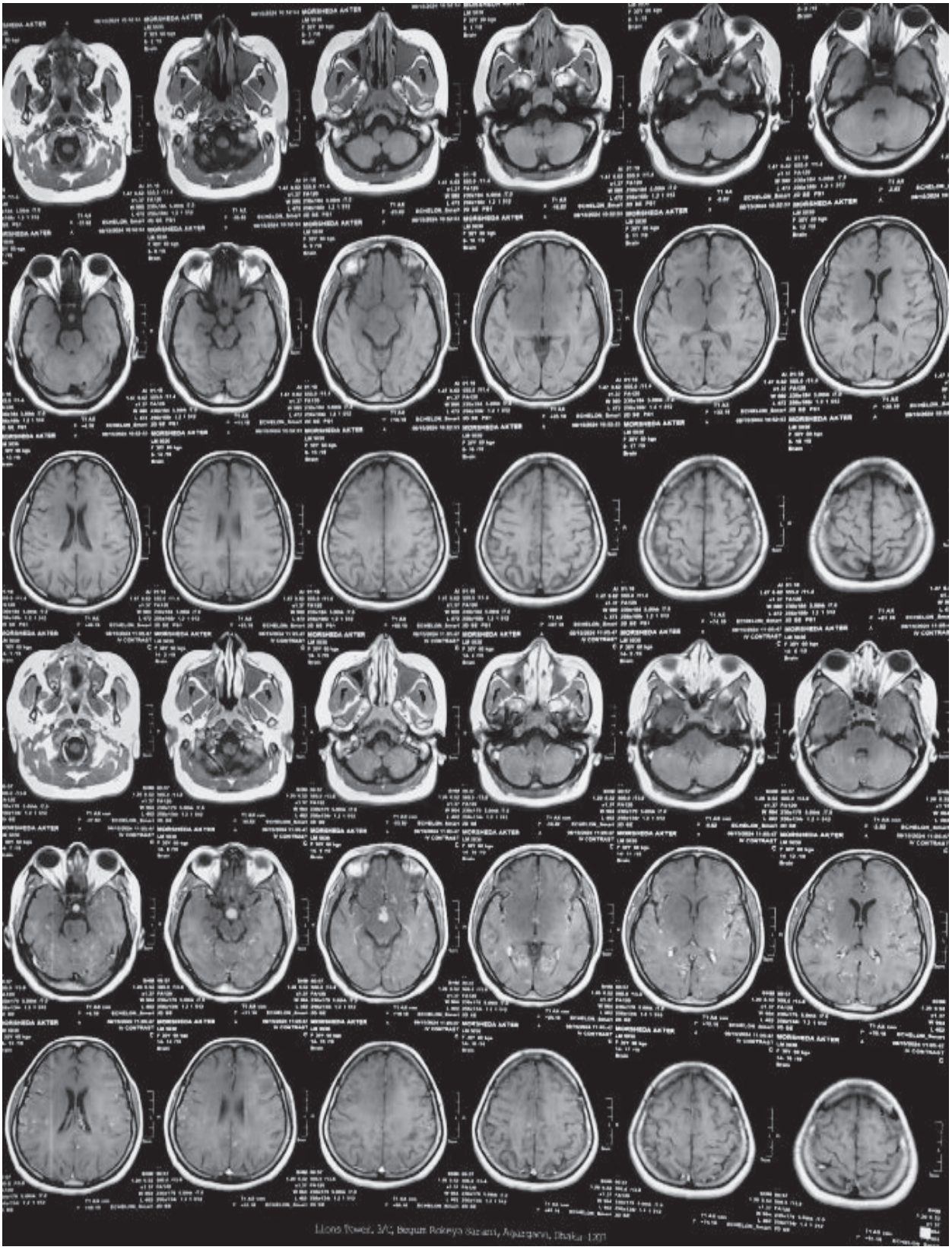

Fig 1: *MRI of brain multiple axial cut T1 and T1 contrast sequence shows a contrast enhancing lesion in sellar and suprasellar region along with nodular leptomeningeal enhancement*

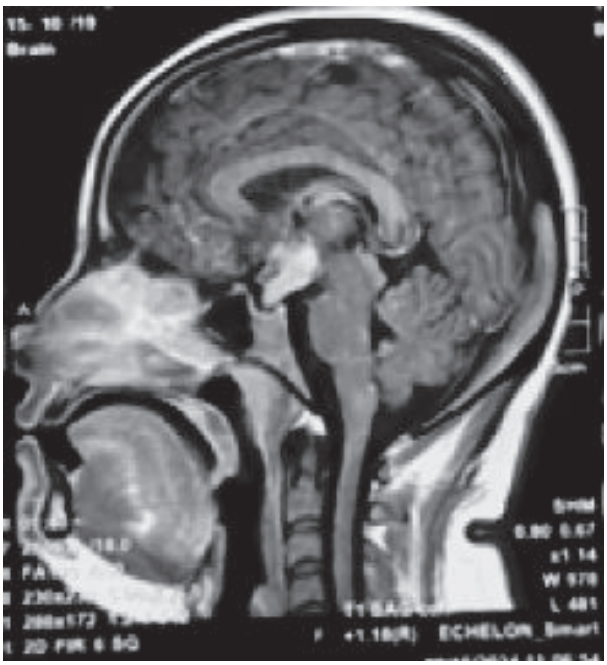

Fig 2a

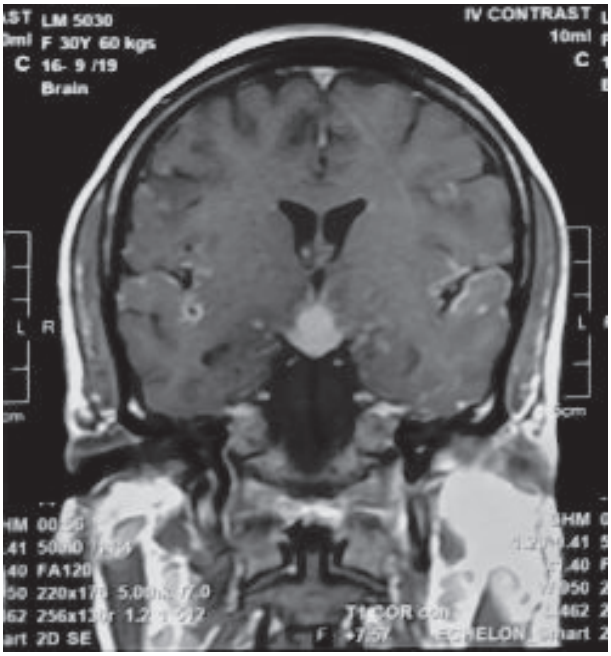

Fig 2b

Fig 2a and 2b showing MRI brain T1 contrast sagittal and coronal section respectively showing a contrast enhancing lesion involving pituitary stalk, pituitary gland, hypothalamus and subependymal portion of third ventricle along with nodular leptomeningeal enhancement

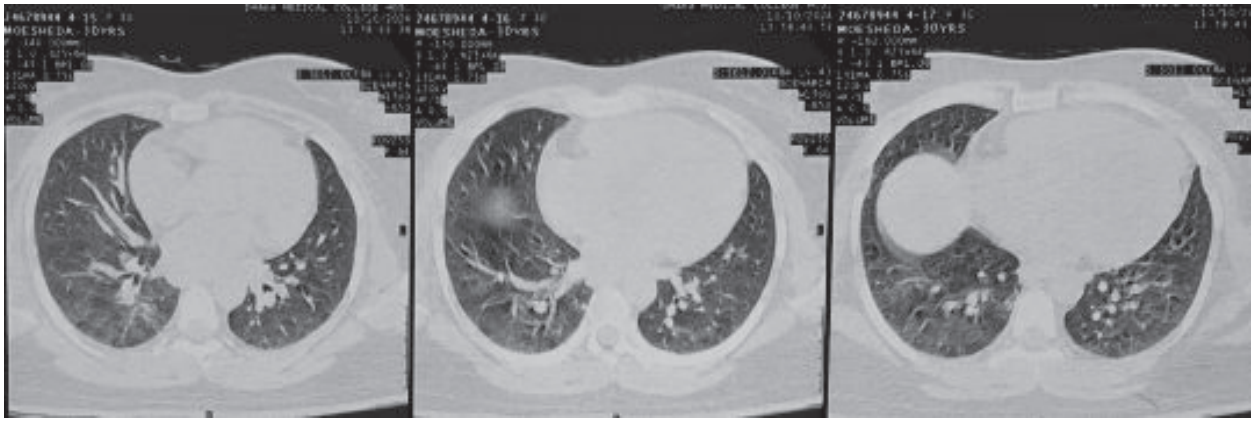

Fig 3 *showing HRCT chest axial section with ground glass opacities involving multiple segments of both lung fields*

On the basis of clinical features, suggestive finding in MRI brain and HRCT chest we diagnosed the case as neurosarcoidosis. We started prednisolone along with other hormone replacements which led to near complete resolution of lesion in follow up MRI brain along with normal s.sodium and TSH level after one month of treatment (Figure 4). Patient was deemed stable for discharge with the plan to schedule a follow-up appointment and reevaluate her pituitary hormones outpatient.

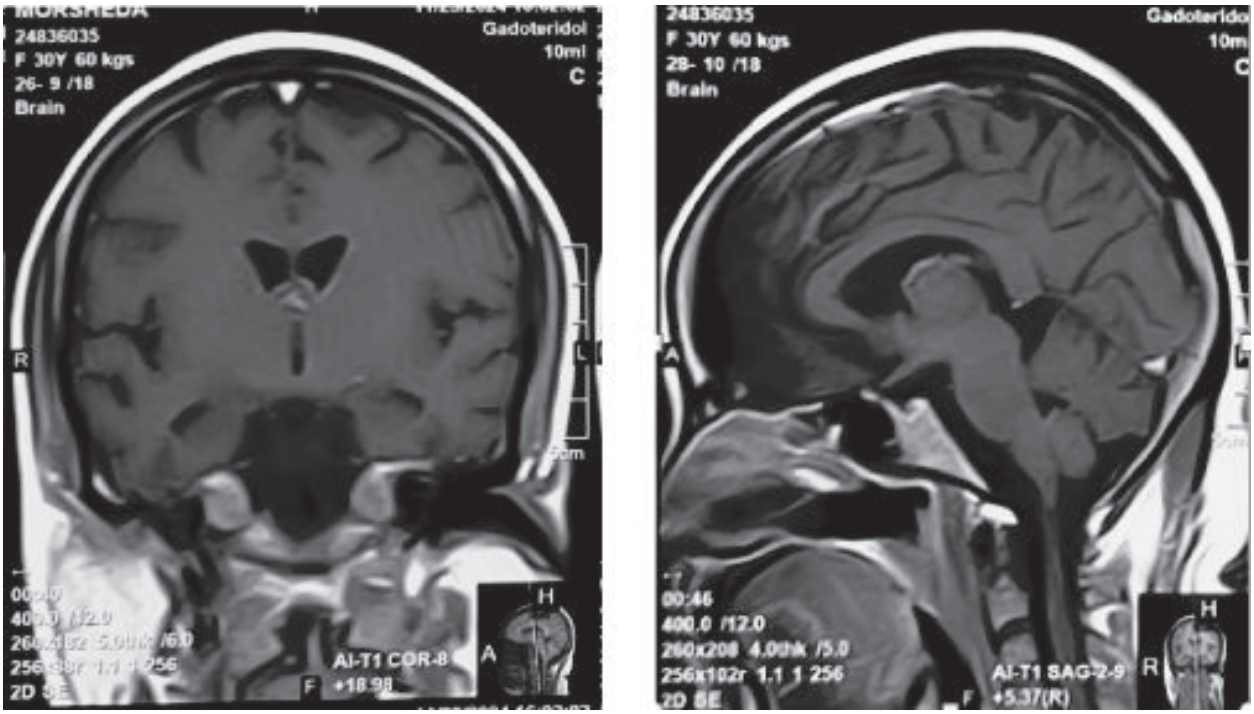

Figure 4 showing follow up MRI brain coronal and sagittal cut T1 contrast sequence showing near complete resolution of lesion after one month treatment with prednisolone.

Discussion

The symptoms of neurosarcoidosis vary depending on the specific anatomic structure affected by sarcoid lesion.[7] Approximately, 5-10% of patients diagnosed with sarcoidosis exhibit neurological symptoms. However, neurosarcoidosis comprises only 1% of all sarcoidosis patients.[8] Diagnosis of neurosarcoidosis on the background of panhypopituitarism is challenging. Occasionally, it may mimic a pituitary mass.[9] In this situation, it may be necessary to undergo biopsy to obtain histological confirmation. Though histological finding of non-caseating granuloma remains the hallmark of the disease, biopsy is not always practical or sufficiently safe as in our case. Neurosarcoidosis diagnosis primarily depends on factors beyond histology such as CSF results or MRI finding.[10,11] The most frequent abnormality observed is raised CSF protein level as in our case. 55% of patients show lymphocytosis in CSF[8] whereas it was normal in our case. MRI brain is very sensitive in detecting abnormality in neurosarcoidosis but it is non-specific.[1] However, it's worth noting that about half of the patients with hypothalamic-pituitary sarcoidosis may appear normal in radiological test.[12]

A literature review done by Ewelina N. et al showed gonadal insufficiency as the most frequent endocrinopathy (85.4%) followed by hypothyroidism (73%) , adrenal insufficiency (51.2%) and growth hormone deficiency (39%).[3] Hypoprolectinemia occurred in 43.9% patients and hyperprolactinemia was seen in 4.8% cases as observed in our case.[3] Clinically apparent HP dysfunction preceded the diagnosis of sarcoidosis in 13 out of 24 HP-NS patients described by Langrand et al.[5] Multiple reports indicated that vast majority of endocrinopathies persist even after resolution of symptoms.[5,13] Notably,Anthony et al found no correlation between neurological improvement radiologically and amelioration of endocrine deficiency.[6] Though beneficial effects of glucocorticoids on HP axis recovery has been proposed , restoration of pituitary function is rare.[14] For instance, on 4 year follow up of NS patients who achieved marked neuroimaging improvement following immunosuppression, only 8% recovered any pituitary function.[5]

In our patient ,there was near complete resolution of radiological finding along with normal thyroid profile and sodium level following one month of treatment with glucocorticoids. However, long term follow up is planned to see complete recovery of hormonal function.

Conclusion

Diagnosis of neurosarcoidosis can create a dilemma in patients presenting with panhypopituitarism. Early diagnosis and treatment is vital to salvage the pituitary function before irreversible damage occurs. Therefore, neurosarcoidosis should be always kept in mind while dealing with patients of panhypipituitarism**.**

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