CASE REPORT

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Acromegaly with Retinitis Pigmentosa

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Abstract

Acromegaly or gigantism is a disorder of excess growth hormone. The most common aetiology of acromegaly is Pituitary Adenoma which is easily detected on MRI. Visual disturbances are common in a macroadenoma due to compression of the optic chiasma. Unusual ocular findings like Rubeosus Iridis and Retinitis Pigmentosa are rarely described in this disorder. We hereby present a similar case with these findings in a patient with Pituitary Neuroendocrine tumour (Pit NET).

Key words: Pituitary neuroendocrine tumour (Pit NET), retinitis pigmentosa, acromegaly

Introduction

Pituitary Neuroendocrine tumours (Pit Nets) constitute around 12 % of all intracranial tumours[1]. Visual symptoms often accompany pituitary tumours due to chiasmal compression. Common symptoms are bitemporal hemianopia and Ophthalmoplegia[2]. Retinitis Pigmentosa is a hereditary degenerative disorder of the retina leading to vision loss and tubular vision. Association with functional pituitary tumours is rare with unclear aetiopathogenesis. Lawrence -Moon- Beidl Syndrome also has a similar association with Retinitis Pigmentosa and endocrine disorders such as obesity and hypogonadism. The literature is sparse regarding association of growth hormone secreting Pit NET and Retinitis Pigmentosa. Here we present a case with classical symptoms of pituitary macroadenoma with severe vision loss and retinal pigmentary changes.

Case Report

A 47-year-old male patient, resident of district Ratlam in Central India, presented to our institute with complaints of chronic headache, chronic cough and diminished visual acuity. On initial examination his vitals were within normal limits. Physical features favouring gigantism including frontal bossing, macroglossia, enlarged extremities and prognathism were obvious (Fig. 1 and 2). No prior history of diabetes, hypertension or any cardiac ailment was found.

Endocrine work-up revealed normal thyroid and gonadotrophin levels and surprisingly normal serum prolactin levels too. Growth hormone (GH) levels were significantly raised along with suppressed serum cortisol levels (Table I). Other laboratory parameters were within normal limits except HbA1c in prediabetes range. MRI revealed dumbbell shaped pituitary macroadenoma with dimensions 23 mm (SI) x 20 mm (AP) x 18 mm (TR) involving the sellar, suprasellar and left parasellar region. Superiorly the mass was casuing indentation of the optic chiasma and bilateral Internal carotids laterally (Fig. 3).

Ocular examination revealed bilateral inferolateral lenticular displacement along with Rubeosus Iridis. Fundus examination revealed primary pigmentary changes of Retinitis Pigmentosa (RP) (Fig. 4). Left eye had no vision and right eye had only tubular vision on visual field charting (Fig. 5).

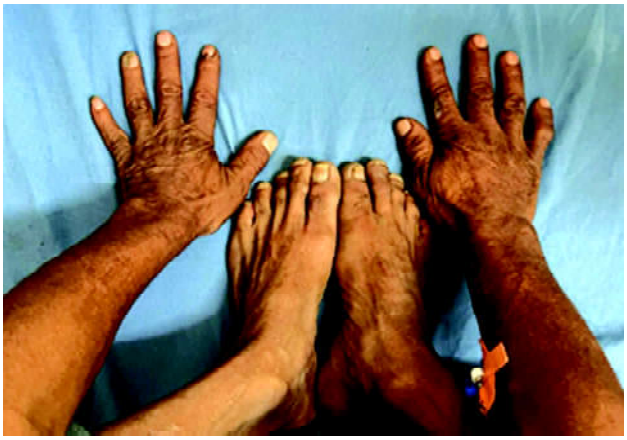

Fig. 1: *Coarse acral features of gigantism.*

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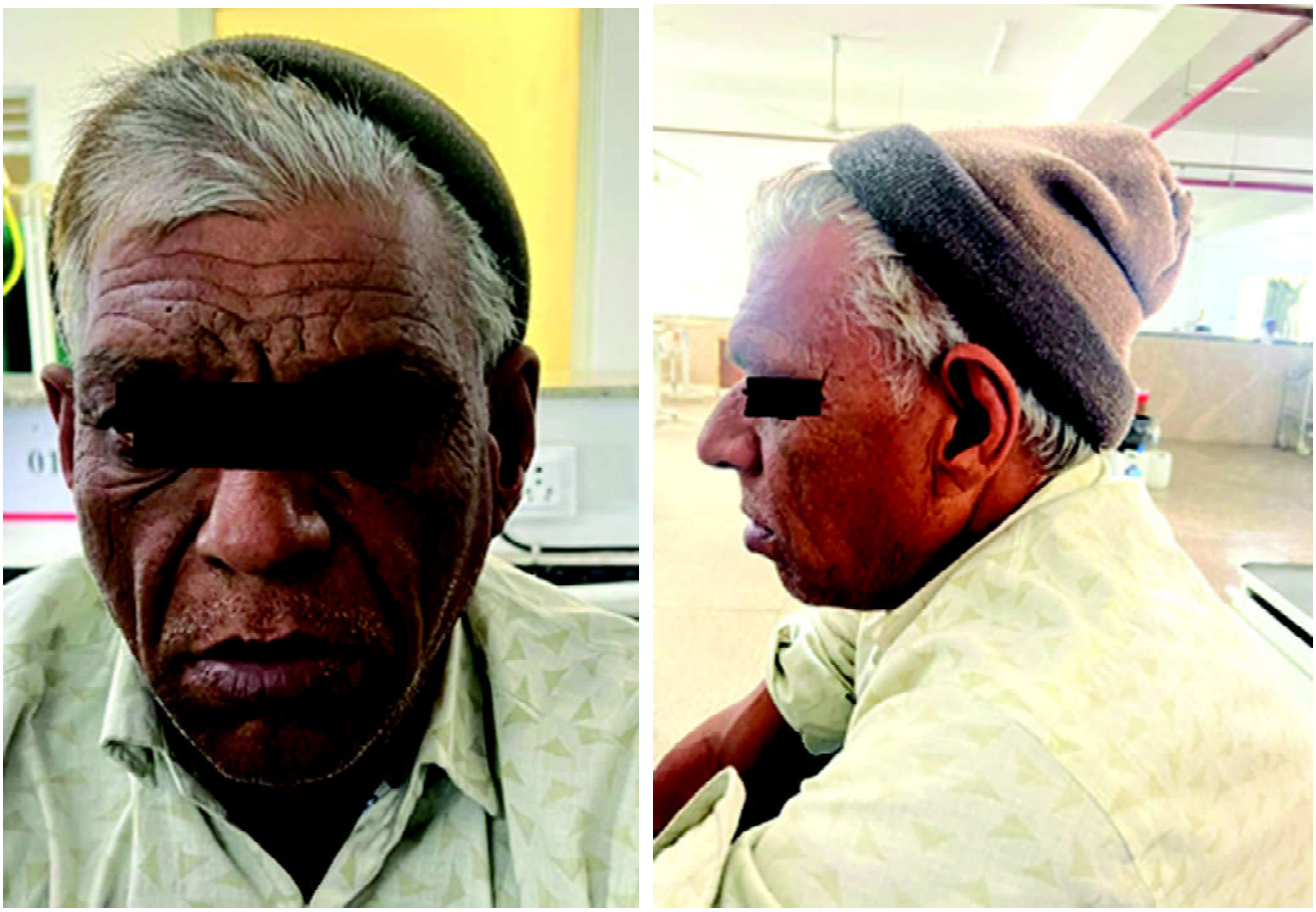

Fig. 2: *Facial features suggestive of Growth Hormone (GH) mediated soft tissue enlargement.*

Table I: Hormonal work-up of patient before and 1 month after surgery.

Parameter with Normal Reference Range	Pre-Operative	Post-Operative Day 30
Haemoglobin (>12 g/dL)	12.9	14.4
Total Leucocyte Count (4,000 - 11,000 cells/cumm)	4,500	10,730
Platelet Count (1.5 - 4 lac cells/cumm)	2.17	2.90
Serum Cortisol (140 - 690 nmol/L)	51.2 ↓	241
Growth Hormone (0.05 - 3 ng/mL)	24.7 ↑	13.3
Serum Prolactin (<20 ng/mL)	11 ↓	8.77
Testosterone (3.6 - 13.9 ng/mL)	1.88 ↓	Not performed
Estradiol (10 - 50 pg/mL)	5.2 ↓	Not performed
TSH (0.5 - 5 mIU/L)	0.58	0.71
T3 (0.8 - 1.8 ng/mL)	0.7	1.34
T4 (5 - 12 ug/dL)	8.18	9.75

He was advised for immediate neurosurgical intervention in view of imminent vision loss and referred to a specialist centre for the same. He underwent transsphenoidal pituitary adenoma resection soon afterwards and the tumour histopathology revealed a Pituitary Neuroendocrine tumour (Pit NET). Immunophenotyping and proliferative index could not be performed on the tissue sample. Post-operative hormonal levels on day 30 revealed significant reduction in GH levels and improvement in vision and symptoms (Table I). Fundoscopic findings were unchanged. However, patient was lost to follow-up and further assessment could not be done.

Discussion

Pituitary adenomas are among the commonest intracranial tumours. Often detected incidentally on routine MRI or CT imaging done for any non-pituitary indication or detected on autopsy. The peak incidence is from the fourth to the

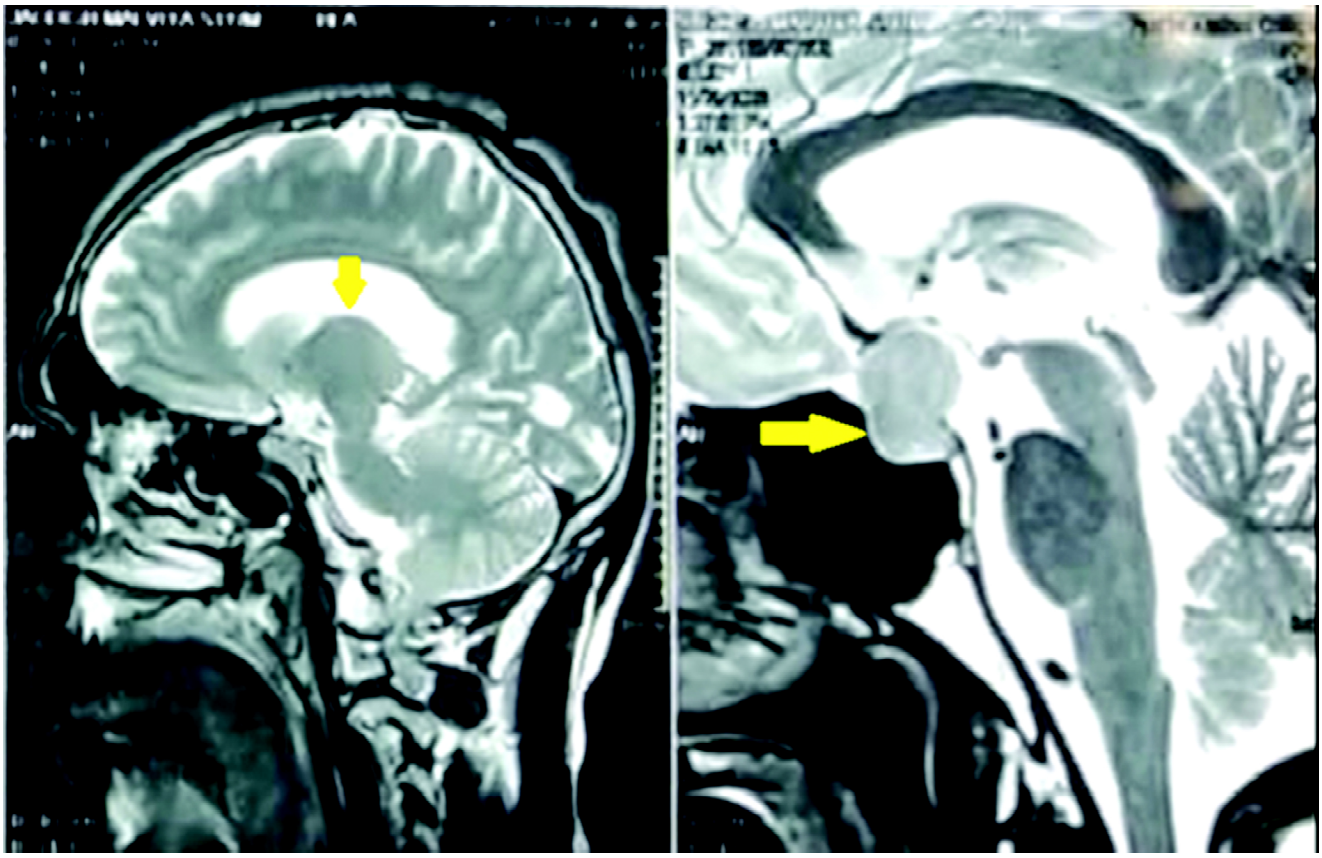

Fig. 3: *MRI pituitary showing Macroadenoma with suprasellar and parasellar extension and compression of Optic chiasma.*

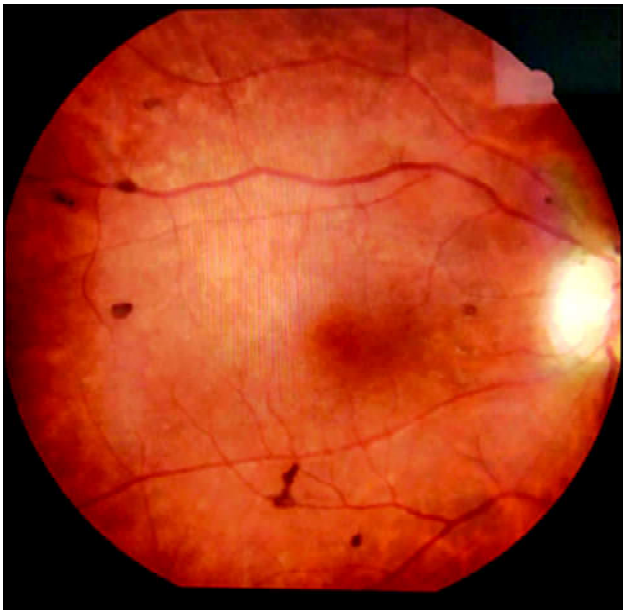

Fig. 4: *Fundus photograph with retinal degenerative and pigmentary changes.*

sixth decade of life with no specific gender predeliction[3]. A high index of suspicion should be kept for co-existent headache and visual symptoms as in our patient. These neurological symptoms are not characteristic of RP, thus point towards an intra-cranial pathology. However, there also were clear clues regarding excess GH in the form of acral and soft tissue enlargement as shown in Fig. 1 and 2. What was unusual in the case was the presence of retinal pigmentary changes in both the eyes along with visual field defects most likely due to chiasmal compression by the tumour.

Pituitary neuroendocrine tumour (Pit NET) is the third most commonly diagnosed intracranial tumour in the world[4]. In 2017, the International Pituitary Pathology Club proposed the use of the term "neuroendocrine tumour" rather than "adenoma" for adenohypophyseal tumours[5]. World Health Organisation (WHO) in 2022 revised the classification of pituitary tumours and a major nomenclature change was introduced by which pituitary adenomas were referred to as Pit NETs[6], Further, Pit NETs were classified into functioning or nonfunctioning tumours on the basis of hormone over secretion leading to conditions such as acromegaly, prolactinoma or Cushing's disease. 30% of all Pit NETs still remain nonfunctioning (nfPit NETs) which are the commonest and called as macroadenomas[3,7]. Somatotroph adenomas are classified as PIT1 lineage on histopathology

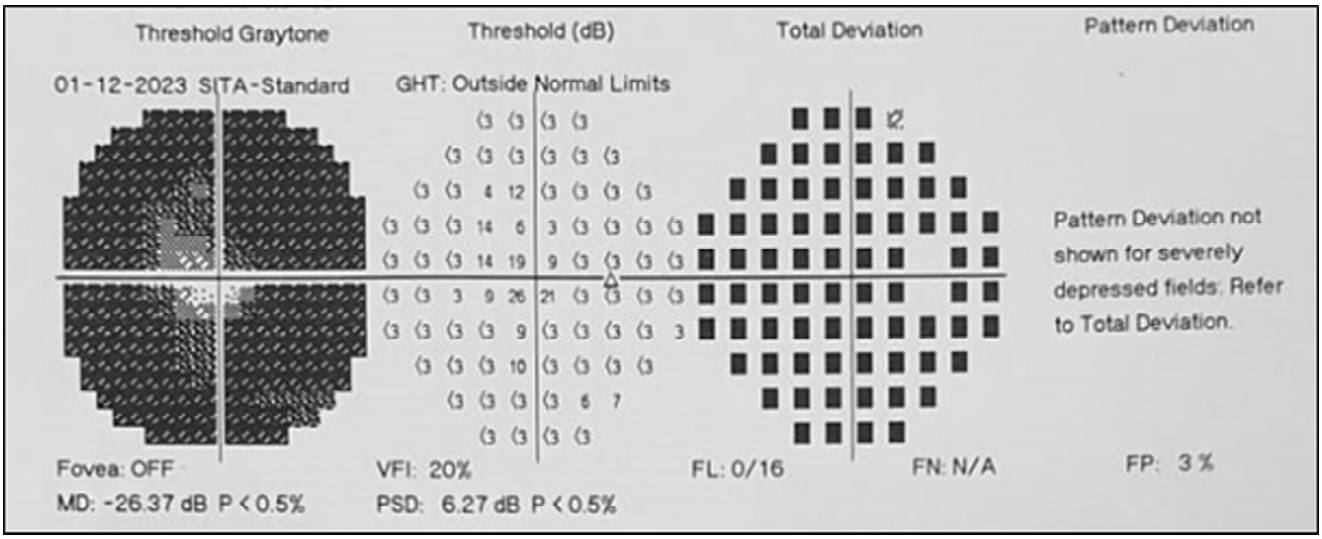

Fig. 5: *Perimetry showing restricted tubular vision in Right eye.*

and molecular biology (Fig. 3). Immunostaining for hormones including adrenocorticotropic hormone (ACTH), growth hormone (GH), prolactin (PRL), β-thyroid-stimulating hormone (β-TSH), β-follicle-stimulating hormone (β-FSH), and -luteinizing hormone (β-LH) can specifically determine the lineage of the tumour.

PIT 1 lineage

- Somatotroph tumour
- Lactotroph tumour
- Mammosomatotroph tumour
- Thyrotroph tumour
- Mature plurihormonal PIT 1 lineage tumour
- Immature PIT 1 lineage tumour
- Acidophil stem cell tumour
- Mixed somatotroph and lactotroph tumour

TPIT lineage

- Corticotroph tumour

SF 1 lineage

- Gonadotroph tumour

Tumours with no distinct cell lineage

- Plurihormonal tumour
- Null cell tumour

Fig. 6: *WHO 2022 classification of Pituitary Neuroendocrine tumours (PitNETs).*

Somatotroph (GH) adenomas/PitNETs are rare amongst all pituitary tumours[8]. This tumour typically arises from the adenohypophysis and is biochemically active, leading to acromegaly and gigantism. Due to excessive IGF-1 and IGFBP-3 levels, neovascularisation is often seen in various body tissues[9]. Similar changes are also seen in the eye as severe proliferative retinopathy and Iris neovascularisation[10]. It is a well-known clinical entity and was also seen in our patient as Rubeosus iridis. Retinal pigmentary changes have been described as an isolated entity and alongside many other endocrine disturbances as early as 1972 by JM Smail[11].

Retinitis pigmentosa (RP) is a hereditary retinal disorders with a worldwide prevalence of 1 in every 3,000 - 5,000 persons[12]. RP is a constellation of progressive visual dysfunction, restricted peripheral vision (tunnel vision) and loss of central vision in the elderly population[13].

What is not well described in existing literature are retinal changes in the form of pigmentary degeneration along with pituitary tumours. There are some scattered case reports of the same in patients with Acromegaly and Chromophobe adenoma[14]. Although tubular vision is a hallmark of RP, compressive effect of pituitary tumour may also lead to similar findings in visual field charting. Thus, fundoscopy plays an important role in ruling-out retinal involvement as a cause of vision loss and should be performed upfront.

We thus found this unusual association in our patient and felt the need for reporting it. It might also be an association by chance. Further, immunohistology studies and proliferative markers are needed to isolate the exact tumour phenotype which might answer some queries. These could not be performed in this subject due to financial constraints. Being a rare association, we must not subject every patient of RP to extensive imaging to rule-out Pituitary adenoma as it is not cost effective. However, every patient of PitNet must undergo a fundoscopic examination. Diminished visual acuity in this patient can be attributed both to the retinal changes and direct chiasmal compression. However, repeat perimetry

in post-operative follow-up is required to assess the same.

Conclusion

Pituitary macroadenoma causing Acromegaly and Retinal Pigmentary changes is an unusual finding. GH secreting pituitary tumours and retinal changes may be an association by chance or involvement of MSH secreting cells in pituitary. Detailed histologic examination of the pituitary tumour mass is may provide answers.

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