



## Rapid visual field constriction in a patient with retinitis pigmentosa and pituitary adenoma

Hayder Al-Hasani<sup>a</sup>, Naheed W. Khan<sup>a</sup>, Kari H. Branham<sup>a</sup>, John R. Heckenlively<sup>a</sup>, Stephen E. Sullivan<sup>b</sup>, Lindsey B. De Lott<sup>a</sup>, Abigail T. Fahim<sup>a,\*</sup>

<sup>a</sup> Kellogg Eye Center, Department of Ophthalmology and Visual Sciences, University of Michigan, 1000 Wall Street, Ann Arbor, MI, 48105, USA

<sup>b</sup> Department of Neurosurgery, University of Michigan, 1500 E. Medical Center Drive SPC 5338, Ann Arbor, MI, 48109-5338, USA

### ARTICLE INFO

#### Keywords:

Retinitis pigmentosa  
Pituitary adenoma  
Chiasmal pathology  
Rapid visual field constriction  
Rapid visual acuity reduction  
Neuro-imaging

### ABSTRACT

**Purpose:** To report a case of pituitary adenoma in a patient with retinitis pigmentosa (RP) and consequent rapid constriction of the visual field in each eye, which is atypical for either of these pathologies.

**Observations:** A 45-year old male, with a long-standing history of RP, presented with rapid vision loss over 3 months. Examination revealed a severe drop in visual acuity and significant progression of concentric visual field constriction in each eye compared to 3 months prior. MRI revealed a pituitary macroadenoma compressing the optic chiasm. The patient underwent endoscopic trans-sphenoidal resection of the tumor and experienced partial recovery of visual acuity but not visual field.

**Conclusions and importance:** The visual field deficit in this patient was atypical for pituitary adenoma or optic neuropathy. The pattern was most consistent with RP, but the rate of progression was not. In a patient with chiasmal pathology in the setting of pre-existing retinopathy, visual field progression may not be limited exclusively to the bitemporal regions. Rapid constriction of the visual field in a patient with RP should prompt a work-up for alternative etiologies which includes neuro-imaging.

### 1. Introduction

Retinitis pigmentosa (RP) is a group of inherited retinal degenerative diseases involving progressive loss of rods and cones and subsequent blindness. It is the most common type of inherited retinopathy with a prevalence of 1:3500 to 1:4000 in the US and Europe.<sup>1,2</sup>

RP typically presents initially with nyctalopia (night blindness) followed by a gradual decline in peripheral vision, eventually leading to tunnel vision in late stages.<sup>1,3</sup> Visual field defects in RP start early in the disease course and typically follow one of three common patterns: progressive concentric constriction, arcuate scotomas that start superiorly and progress inferiorly, or mid-peripheral ring scotomas that progress both towards the center and the periphery.<sup>4</sup> Central vision and visual acuity are usually preserved until late stages unless patients develop cystoid macular edema or cataracts, which are treatable sequelae.<sup>1,5</sup> Progression of RP is slow over years to decades, and the visual field half-life can range from 4 to 15 years.<sup>6,7,8</sup>

On the other hand, visual field loss from pituitary adenomas progresses relatively more rapidly, over weeks to months. Visual field defects are typically bitemporal from compression of the chiasmal crossing fibers originating from the ganglion cells in the nasal retina,

and occasionally additional defects emerge from compression of the optic nerve.<sup>9</sup> However, other patterns like homonymous hemianopia and monocular defects have been described, depending on the site of optic pathway compression and the degree of displacement by the pituitary tumor.<sup>9</sup> Bilateral concentric constriction has not been described.

Here we report a patient with a longstanding diagnosis of RP that presented with rapid concentric constriction of the visual field and substantial drop in visual acuity in both eyes over a 3-month period that was associated with a pituitary adenoma complicating his precedent retinopathy.

### 2. Case report

A 45-year old man with a previous diagnosis of RP presented with rapid vision loss in both eyes over 3 months. He had a history of nyctalopia since his teens but was not diagnosed with RP until 1 year prior to this presentation. He denied headaches or other neurologic symptoms. On examination, his visual acuity had dropped to 20/100 OD and 20/150 OS compared to 20/30 OD and 20/40 OS 3 months prior. Pupil exam was normal with no afferent pupillary defect. Intraocular pressure was 13 mm Hg OD and 12 mm Hg OS. Slit lamp examination showed

\* Corresponding author. University of Michigan, 1000 Wall Street, Ann Arbor, MI, 48105, USA.

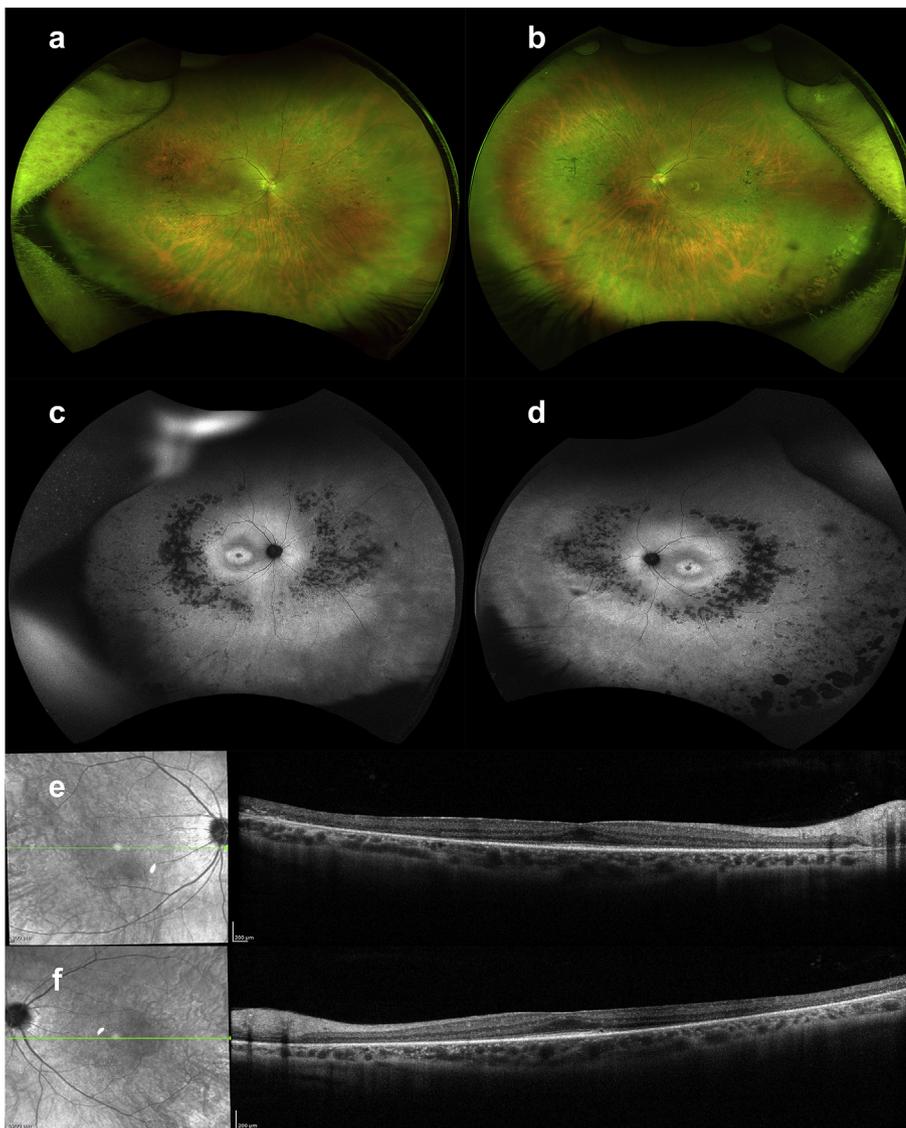
E-mail address: [ahreich@med.umich.edu](mailto:ahreich@med.umich.edu) (A.T. Fahim).

<https://doi.org/10.1016/j.ajoc.2020.100762>

Received 4 December 2019; Received in revised form 8 May 2020; Accepted 31 May 2020

Available online 02 June 2020

2451-9936/© 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



**Fig. 1.** Fundus examination and OCT images, showing RP disease findings. a. and b. are Optos ultra-widefield retinal imaging of right and left eyes respectively, one year after endoscopic trans-sphenoidal resection of the pituitary adenoma, showing attenuated retinal arterioles, mid-peripheral atrophy with mild bone spicules and inferotemporal cobblestone atrophy. The fundus exam was unchanged from his pre-operative exam. c. and d. are fundus autofluorescence images of the right and left eye respectively, also one year after surgery, showing perifoveal hyperfluorescent ring in macula and patchy hypofluorescence around posterior pole and inferotemporal periphery. e. and f. are spectral domain optical coherence tomography images of right and left eyes respectively, 3 months prior to presentation, showing a foveal island of preserved outer retina, surrounded by severe outer retinal atrophy with mild foveal hypoplasia.

normal anterior segments and posterior chamber intraocular lenses bilaterally. Fundus examination showed optic disc pallor with no disc edema, and mild peripapillary atrophy bilaterally. The cup to disc ratio was 0.05 OD and 0.1 OS. In both eyes, the macula had a blunt foveal light reflex, the retinal vessels were attenuated, and the mid-peripheral retina was atrophic with mild bone spicules (Fig. 1a–d). The fundus examination was unchanged compared to photos from 3 months prior.

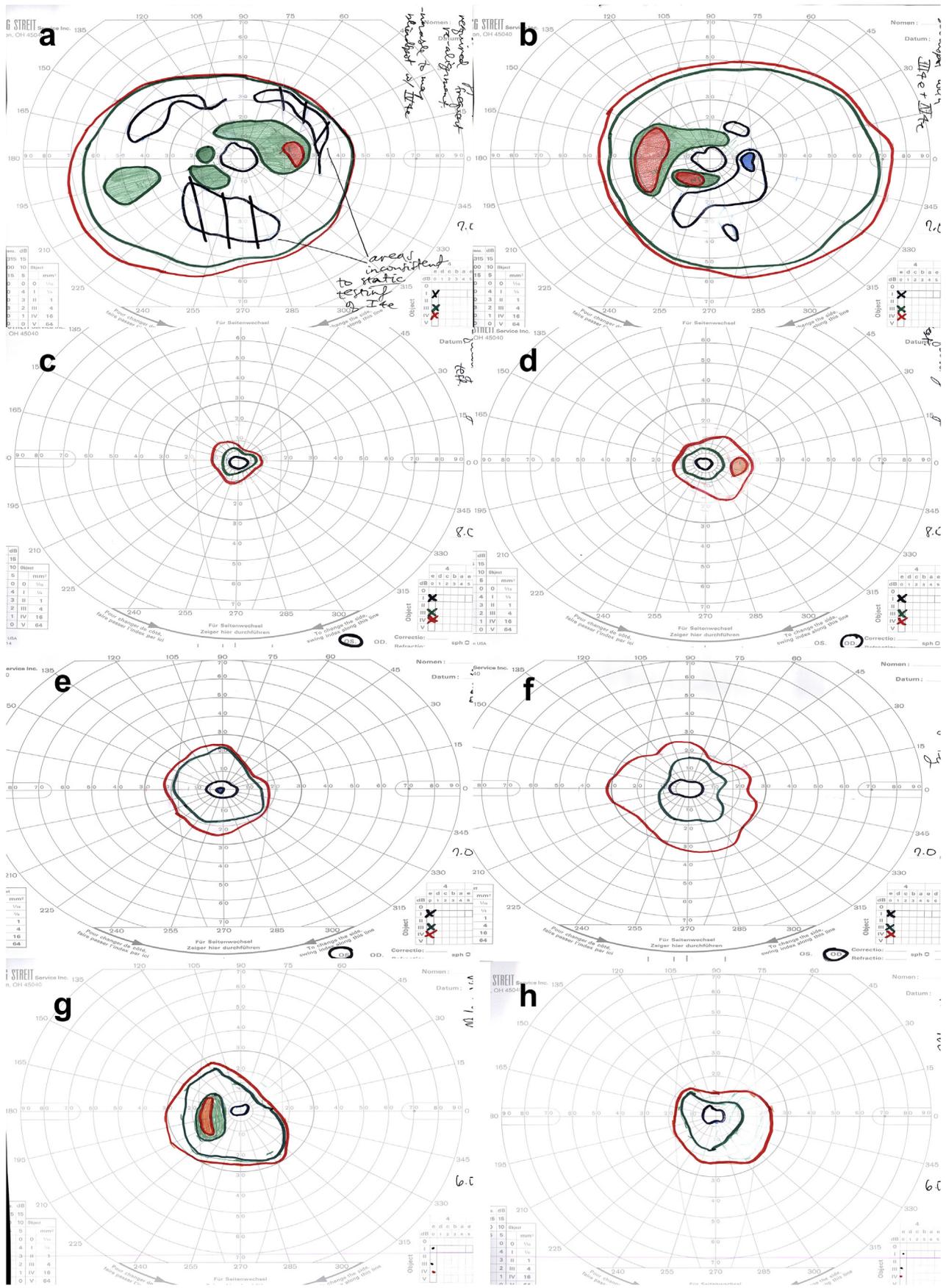
Goldmann visual field demonstrated significant progression of the patient's pre-existing concentric constriction of all isopters in both eyes since 3 months prior (Fig. 2a–d). Significant progression had occurred in all quadrants and was not more pronounced in the temporal hemifields. Optical coherence tomography findings were stable from 3 months prior, showing a foveal island of preserved outer retina surrounded by severe outer retinal atrophy with mild foveal hypoplasia in both eyes (Fig. 1e and f). Fluorescein angiography revealed significant window defects from retinal pigment epithelium (RPE) atrophy, peripheral non-perfusion in both eyes, and no vascular leakage. Previous full field electroretinography (ERG) results were already severely reduced and showed cone dysfunction, which precluded definitive assessment of further progression on repeat ERG.

Due to the rapid progression of his visual field and visual acuity in the setting of retinal degeneration, cancer-associated retinopathy (CAR) and non-neoplastic autoimmune retinopathy (AIR) were considered.

The patient declined testing for anti-retinal antibodies. Inflammatory work-up included angiotensin converting enzyme, human leukocyte antigen A29, fluorescent treponemal antibodies, and quantiferon gold, which were all normal. A trial of oral prednisone (1mg/kg/day) with a slow taper was started.

Although he had a previous diagnosis of RP, this had not been confirmed with genetic testing. Next generation sequencing was performed (Blueprint Genetics Retinal Dystrophy Panel, version 2) and revealed a pathogenic missense mutation of c.118C > T (p.Arg40Trp) in the *CRX* gene, which is associated with autosomal dominant RP.

Five weeks after starting prednisone treatment, the patient reported stabilization of his visual decline. His visual acuity was stable at 20/125 OD and 20/150 OS, and his visual field was improved in both eyes (Fig. 2e and f). At this time, computed tomography (CT) scan of his chest, abdomen and pelvis was performed to further assess for CAR. CT scan revealed a liver mass suggestive of hemangioma. Brain magnetic resonance imaging (MRI) showed a 38 × 26 mm pituitary mass with sellar/suprasellar extension, optic chiasm compression, and right cavernous sinus invasion, indicative of macroadenoma (Fig. 3). Endocrine evaluation revealed low total testosterone levels and otherwise normal serum levels of thyroid-stimulating hormone, free thyroxine, follicle-stimulating hormone, luteinizing hormone, prolactin, growth hormone, insulin-like growth factor 1, cortisol, and adrenocorticotropic hormone.



(caption on next page)

**Fig. 2.** Goldmann visual field (GVF) test. a. and b. are visual fields of left and right eyes respectively, 3 months prior to presentation, showing constriction of I4e (black isopter) with a few mid-peripheral islands, and multiple mid-peripheral scotomas of III4e (green isopter) and IV4e (red isopter) in each eye. c. and d. are visual fields of left and right eyes respectively, at the time of presentation, revealing a substantial concentric constriction of the visual field with all 3 isopters in both eyes. e. and f. are visual fields of left and right eyes respectively, after 5 weeks of prednisone, showing improvement of the visual field bilaterally. g. and h. are visual fields of left and right eyes respectively, one year after the surgery, showing stability in the left eye, with mild progression in the right eye. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

After the MRI was performed, the patient was referred to a neurosurgeon, who removed the tumor by stealth-guided intradural endoscopic transnasal resection 2 months after his initial presentation. Pathology confirmed the diagnosis of gonadotroph pituitary adenoma.

In the immediate post-operative period, visual acuity and visual fields remained stable. Color vision, tested with Ishihara color plates, was 2/11 on the right and 1/11 on the left, which was reduced from 1 year prior when color vision testing was 13/15 on the right and 14/15 on the left. One year later, the patient demonstrated partial recovery of visual acuity to 20/60 OD and 20/80 OS, while visual fields remained stable on the left and demonstrated mild progression on the right, consistent with the natural history of retinitis pigmentosa (Fig. 2g and h).

### 3. Discussion

The differential diagnosis of retinitis pigmentosa includes numerous non-inherited retinopathies, such as vitamin A deficiency, inflammatory and infectious retinopathies, and AIR.<sup>1,5</sup> Inflammatory and infectious causes include retinal vasculitis, end-stage birdshot chorioretinitis, acute zonal occult outer retinopathy, and congenital syphilis.<sup>1,5</sup> AIR includes CAR, melanoma-associated retinopathy, and non-paraneoplastic AIR.<sup>1,5</sup> While RP has a slowly progressive course, with sometimes no detectable progression over the course of a year, these other etiologies progress relatively quickly, over weeks to months. Any rapid visual deterioration associated with retinal degeneration or retinal electrophysiologic dysfunction should prompt a work-up to exclude other etiologies.

More importantly, although the concentric constriction of the visual field in this case harmonized with the conventional defect patterns seen in RP, the rate of progression did not.<sup>4,8,10</sup> In addition, this pattern of visual deficit departs from the customary bitemporal or mixed defects seen in pituitary adenoma cases as the visual field defect showed progression in all 4 quadrants of each eye.<sup>9</sup> Chiasmal pathologies may produce unconventional visual field defects when superimposed on a preceding retinopathy, because the neural tissue is already

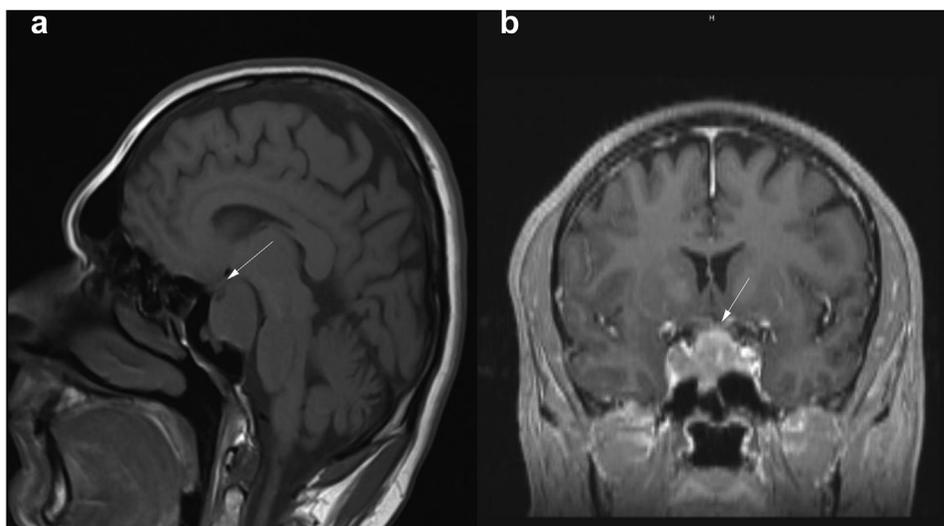
compromised.

The combined presence of both RP and pituitary adenoma with acromegaly has been reported previously by Smail et al.<sup>11</sup> and Cosemans I et al.<sup>12</sup> It was hypothesized that the pituitary disease process may cause atrophy of the pars intermedia with consequent reduction of melanocyte stimulating hormone, causing RPE dysfunction and retinal degeneration. In both reports, there is concentric visual field constriction in each eye without preferential loss of the temporal field. In another recent report, a patient of longstanding RP with concurrent pituitary adenoma was also described presenting with worsening visual acuity and visual fields, although serial visual fields were not shown.<sup>13</sup> However, he also expressed a relative afferent pupillary defect and a headache which suggested a neurological lesion that prompted a CT scan, and that patient declined treatment for his adenoma.

In those aforementioned reports, there was no documentation of visual fields prior to the diagnosis of pituitary adenoma, making this case report the first to document the pattern and rate of visual field loss first from RP alone and second from the addition of chiasmal compression. Furthermore, in the absence of any neurological signs and symptoms in this case, a high degree of suspicion was required due to the rapid rate of progression.

Pituitary abnormalities including enlargement, hypoplasia, and endocrine dysfunction, have also been reported in several patients with Bardet-Biedl syndrome, a form of syndromic RP.<sup>14,15</sup> Beyond these case reports there is no known association between pituitary tumors and RP.

After pituitary adenoma resection, the typical prognosis for visual recovery is excellent. The restoration of visual function has been described in three phases: the “early fast phase” (the first post-operative week), in which visual fields and visual acuity initially improve and may even normalize in some cases; the “early slow phase” (the first 6 months), in which the most dramatic improvement typically occurs; and the “late phase” (6 months–3 years), in which small residual improvement may still occur.<sup>16,17,18</sup> The early fast phase is attributed to initial recovery of conduction, while later stages might be explained by remyelination of affected fibers.<sup>17</sup> Recovery of visual fields is postulated to be influenced by patient age, degree of visual field defect pre-



**Fig. 3.** Brain MRI sections showing pituitary adenoma. a. and b. T1 weighted sagittal without contrast and T1 weighted coronal with contrast, respectively, showing a large pituitary adenoma compressing the optic chiasm (arrows).

operatively, volume of tumor, and expression of vascular endothelial growth factor and Ki-67 antigen by the tumor.<sup>19</sup>

In this case, the visual field had improved bilaterally after a 5 weeks trial of prednisone, which might be explained by the potential role of prednisone in partially modulating nerve compression symptoms.<sup>20,21</sup> Two weeks post-operatively, the visual fields did not improve beyond the level achieved by prednisone, and visual acuity did not improve at all. However, one year later, visual acuity in both eyes had improved significantly, while the visual field was stable in the left eye and mildly progressed in the right, which is consistent with the natural history of RP. Although the underlying RP limited visual field recovery in this patient, the remarkable improvement of his visual acuity suggests an encouraging prognosis for post-surgical outcomes in future similar cases. The low morbidity of trans sphenoidal resection and the potential for visual recovery support this approach even in cases of underlying retinopathy.<sup>22</sup>

#### 4. Conclusions

The visual field deficit in this patient was atypical for pituitary adenoma or optic neuropathy. The pattern was most consistent with RP, but the rate of progression was not. In a patient with chiasmal pathology in the setting of pre-existing retinopathy, visual field progression may not be limited exclusively to the bitemporal regions. Rapid constriction of the visual field in a patient with RP should prompt a work-up for alternative etiologies which includes neuro-imaging. Resection of pituitary adenoma, in the presence of concurrent retinal pathology, can still result in some recovery of vision and prevent further rapid decline.

#### Patient consent

The patient's consent to publish this case report was obtained and documented on file.

#### Funding

A.T. Fahim is supported by a National Institutes of Health K12 Award (K12EY022299).

#### Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

#### Declaration of competing interest

All authors have no conflict of interest with this report.

#### Acknowledgements

None.

#### References

- Fahim AT, Daiger SP, Weleber RG. Nonsyndromic retinitis pigmentosa overview. In: Adam MP, Ardinger HH, Pagon RA, eds. *GeneReviews*(®). 1993; 1993 Seattle (WA).
- Haim M. Epidemiology of retinitis pigmentosa in Denmark. *Acta Ophthalmol Scand Suppl.* 2002;1–34.
- Daiger SP, Bowne SJ, Sullivan LS. Perspective on genes and mutations causing retinitis pigmentosa. *Arch Ophthalmol.* 2007;125:151–158.
- Grover S, Fishman GA, Brown Jr J. Patterns of visual field progression in patients with retinitis pigmentosa. *Ophthalmology.* 1998;105:1069–1075.
- Fahim A. Retinitis pigmentosa: recent advances and future directions in diagnosis and management. *Curr Opin Pediatr.* 2018;30:725–733.
- Birch DG, Locke KG, Wen Y, Locke KI, Hoffman DR, Hood DC. Spectral-domain optical coherence tomography measures of outer segment layer progression in patients with X-linked retinitis pigmentosa. *JAMA Ophthalmol.* 2013;131:1143–1150.
- Berson EL, Sandberg MA, Rosner B, Birch DG, Hanson AH. Natural course of retinitis pigmentosa over a three-year interval. *Am J Ophthalmol.* 1985;99:240–251.
- Grover S, Fishman GA, Anderson RJ, Alexander KR, Derlacki DJ. Rate of visual field loss in retinitis pigmentosa. *Ophthalmology.* 1997;104:460–465.
- Lee IH, Miller NR, Zan E, et al. Visual defects in patients with pituitary adenomas: the myth of bitemporal hemianopsia. *AJR Am J Roentgenol.* 2015;205:W512–W518.
- Hamel C. Retinitis pigmentosa. *Orphanet J Rare Dis.* 2006;1:40.
- Smail JM. Primary pigmentary degeneration of the retina and acromegaly in a case of pituitary adenoma. *Br J Ophthalmol.* 1972;56:25–31.
- Cosemans I, Demaerel P, Wets B, De Hauwere B, Spileers W. Retinitis pigmentosa in association with acromegaly: a case report. *Doc Ophthalmol.* 1999;98:175–181.
- Taghipour M, Derakhshan N, Saffarian A, Ghanbari M. Undetected pituitary adenoma in a patient with retinitis pigmentosa. *Chinese Neurosurgical J.* 2019;5:20.
- Mujahid S, Hunt KF, Cheah YS, et al. The endocrine and metabolic characteristics of a large bardet-biedl syndrome clinic population. *J Clin Endocrinol Metab.* 2018;103:1834–1841.
- Guran T, Ekinci G, Atay Z, Turan S, Akcay T, Bereket A. Radiologic and hormonal evaluation of pituitary abnormalities in patients with Bardet-Biedl syndrome. *Clin Dysmorphol.* 2011;20:26–31.
- Kedar S, Ghate D, Corbett JJ. Visual fields in neuro-ophthalmology. *Indian J Ophthalmol.* 2011;59:103–109.
- Kerrison JB, Lynn MJ, Baer CA, Newman SA, Bioussé V, Newman NJ. Stages of improvement in visual fields after pituitary tumor resection. *Am J Ophthalmol.* 2000;130:813–820.
- Gnanalingham KK, Bhattacharjee S, Pennington R, Ng J, Mendoza N. The time course of visual field recovery following transphenoidal surgery for pituitary adenomas: predictive factors for a good outcome. *J Neurol Neurosurg Psychiatry.* 2005;76:415–419.
- Yu FF, Chen LL, Su YH, Huo LH, Lin XX, Liao RD. Factors influencing improvement of visual field after trans-sphenoidal resection of pituitary macroadenomas: a retrospective cohort study. *Int J Ophthalmol.* 2015;8:1224–1228.
- Goldberg H, Firtch W, Tyburski M, et al. Oral steroids for acute radiculopathy due to a herniated lumbar disk: a randomized clinical trial. *J Am Med Assoc.* 2015;313:1915–1923.
- Gabriel CM, Stevens JC, Bremner F, Brew S, Plant GT. Optic chiasm enhancement associated with giant aneurysm and yttrium treated pituitary adenoma. *J Neurol Neurosurg Psychiatry.* 2004;75:1343–1345.
- Agam MS, Zada G. Complications associated with transsphenoidal pituitary surgery: review of the literature. *Neurosurgery.* 2018;65:69–73.