Neuroanatomical Changes and Visual Cognition in a Teenager with Cerebral Infarction – A Familial Case Study of POEMS Syndrome

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Research Article

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Abstract

Symptoms of cognitive and motor impairments are the most important factors when considering children with cerebral infarction and polyneuropathy, organomegaly, endocrinopathy, myeloma protein, and skin changes (POEMS) syndrome.

Purpose

What factors are important between POEMS Syndrome and ischemic stroke? Are there novel diagnostics for reducing stroke incidence in POEMS Syndrome?

Method

An observational study comprised 100 patients without CT or MRI and 340 multilingual participants with CT and MRI. All relevant behavior and demographic information were recorded. Per the familial history of POEMS Syndrome, we selected one teenager with cerebral infarction and visual cognition.

Result

A few studies have used a representative sample of children with cerebral disorders in which all patients were investigated separately. Occasionally, severe motor impairment in children is often suggested but not investigated, while cognitive impairment was evident among this populace. Thus, it is advised and required to conduct long-term neuropsychological studies that consider not just interventional studies but also very young cohorts with severe speech and movement disorders alongside visual cognitive issues as failure in the evaluation may overestimate the prevalence of mental disorder.

Conclusion

The endocrine system's role in neurocognition and neuroplasticity behavior is distinct. Clinical educators must maintain the multifaceted interplay between gender, hormones, dosage, exposure time, and brain structure. These complex implications are moving the field of neuroendocrinology with exciting new concepts.

Introduction

POEMS syndrome, which is referred to by various names such as osteosclerotic myeloma, Crow-Fukase syndrome, or Takatsuki disease, is an uncommon paraneoplastic syndrome with systemic manifestations. Multiple symptoms, including organomegaly, skin changes, monoclonal gammopathy, and polyneuropathy characterize it. Clonal plasma cell dyscrasia is often associated with these symptoms. [1, 2]. The less common complication of POEMS Syndrome is arterial or venous thrombosis. But sporadically, ischemic stroke has also been reported.

The relationship between POEMS syndrome and ischemic stroke, despite much research, remains elusive, with many aspects still not fully understood. [6–11]. POEMS syndrome also includes additional significant manifestations such as Castleman's disease, sclerotic bone lesions, papilledema, thrombocytosis, polycythemia, pulmonary hypertension, clubbing, weight loss, thrombotic diatheses, vitamin B12 deficiency, and extravascular volume overload. [1, 3–5]. The precise mechanisms responsible for the development of POEMS syndrome remain uncertain, one of the essential diagnostic criteria for POEMS syndrome is the excessive production of vascular endothelial growth factor (VEGF). [1]. In the past few years, ischemic stroke has emerged as a noteworthy manifestation of POEMS syndrome, receiving increased recognition. Studies indicate that the risk of experiencing an ischemic stroke within five years for individuals with POEMS syndrome is estimated to be 13.4%. [12]. Several studies have documented the presence of a multi-vessel anomaly.[13–16], but cerebral vasculopathy's pathogenesis is unclear. In this report, we present the case of a young female diagnosed with POEMS syndrome who experienced acute neurological deficits during her treatment.

The rationale of the study

POEMS syndrome is related to polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes and remains poorly understood [18]. These may enhance neuroplasticity in peri-infarct regions and the hippocampus to improve motor and visual cognitive outcomes [17]. Hence, cerebral infarction in POEMS syndrome is not as uncommon as previously believed, as numerous cases and case series have been subsequently reported [36]. Before establishing the novel diagnostic criteria for POEMS factors, nearly all cases of cerebrovascular involvement in POEMS syndrome were associated with the condition. [37]. The observed phenomenon has been consistently noted in patients diagnosed with POEMS syndrome. [36, 37], a disease with many similar pathological features, such as elevated VEGF. We could benefit more if we associated these traits and considered the pathological findings of POEMS syndrome. We proffer the following: what factors are essential between POEMS Syndrome and ischemic stroke?

Method

An observational study comprised 100 patients without CT or MRI and 340 multilingual participants with CT and MRI. All relevant behavior and demographic information were recorded. Per the familial history of POEMS Syndrome, we selected one teenager with cerebral infarction and visual cognition.

Behavior Measurements

The Bilingual Aphasia Test (BAT) is a widely administered and validated tool designed to assess aphasia in bilingual or multilingual individuals with aphasia, readily available in 74 language versions. These include Farsi, Balochi, Luri, Talysh, East Mazandarani, Gilaki, Azari, and Arabic. Further, the BATs for Luri, Balochi, Farsi, Kurdish, and Azari (Luri, Balochi, Azari, Gilaki, Talysh, Eastern Mazandarani, Arab, and Farsi) were followed by **Paradis et al**. [19–26]. We designed the test to evaluate the reader's word recognition skills, allowing participants to use lexical and non-lexical techniques (i.e., eye tracking,

handiness, simple commands, mental skills, complex commands, naming, pointing, and repetition tasks). All participants had to employ ten non-words in addition to words from the Farsi, Balochi, and Luri, Azari languages. There were different words and non-words along the visual-linguistic axis.

Case

AB is a right-handed, literate, 14-year-old bilingual (L1: Luri, L2: Farsi) with a high growth hormone level and an unnatural height and weight. The patient had eaten more than usual during dinner which was followed by a sudden headache. The headache worsened with time, and she was taken to the hospital. The patient was admitted to the hospital post-diagnosis of a left temporal intracerebral hematoma. She was followed up on days 1, 3, and 7, where the patient presented with global aphasia. There was difficulty repeating highly grammatical sentences on days 1, 3, and 7, and there was a full decline in speech and motor clarity in both L1 and L2. Cooperation with difficult orders and pointing duties in any language was not observed as day 7 drew near. Her neurological status deteriorated, and she was subsequently transferred to another hospital for recovery and rehabilitation. Unfortunately, the treatments and interventions were not effective, and was diagnosed with brain death. However, we had the opportunity to examine the patient's level of cognition and any anomalies in the conscious state (Fig. 3). These variables corresponded to BAT actions such as pointing, following simple instructions, raising the eyes, and elevating the hands. The patient received dexamethasone, vitamins B1, B6, B12, and Mannitol during her hospital admission. In consultation with the medical personnel and the patient’s family, a clinical decision to harvest the patient’s organs for donation was reached and agreed upon. Corresponding imaging analyses and patient anatomy are depicted in Fig. 2. Investigating the patient's mother and sister led us to learn that the patient's mother had two miscarriages following her second delivery, as well as psychiatric issues and asthma. The patient's sister had enlarged heart valves, excessive body hair, a pituitary microadenoma (measuring 4 mm) alongside sleep and hormonal disorders (Table 1), eyelid weakness, sporadic dry eye, and vague pain (Figs. 4 to 9). The sister’s polycystic ovarian syndrome (PCOS) was being managed with hormonal therapy alongside other medications (i.e., Dupbaston 10mg; Hair. vit; Flavian 100 mg; Cetirizine 10mg; Lexie 5mg, Fin Oscar 5 mg). The mother and the sister were transferred to Shiraz University of Medical Sciences for further analysis and management.

Table 1
This test was investigated by Pediatric Endocrinology and Metabolic specialist.

Test	Result	Flag Unit	Normal Range
FBS	83	Mg/dl	Normal:70–99 Impaired fasting glucose:100–125 Diabetes:>126
SGPT	9	U/l	0–40
Sodium (ISE)	137	mEq/Litr	135–145
Potassium (ISE)	4.2	mEq/Litr	3.5–5.5
17-OH-progestrone	1.7	Ng/mL	Follicular phase:0.3-1.0; Luteal phase:0.2–2.9; After ACTH stimulation:<3.0; Pregnancy (3rd trimester):1.8–20.0
Estradiol (ECLA)	**55.05**	Pg/ml	Children girl (1-10y):6.0–27.0; Follicular phase:12.5–166; Ovulate phase:85.8–498; Luteal phase:43.8–211; Post menopause:<54.7: Pregnancy:215–4300
FSH (ECLA)	5.36	Miu/ml	< 10 years:0.68–7.1; Follicular phase:2.5–10; Ovalatory:3.4–33.0; Luteal phase:1.5–9.1; Post menopause:23.0–66.0
LH (ECLA)	27.76	Miu/ml	< 10 years:0.03–3.9; Follicular phase:0.5–12.5; Midcycle:16.6–104.0; Luteal phase:0.5–18.0; Post menophase:16.0–66.0
Prolactin	**33.9**	Ng/ml	Female:4.5–30.4; Post menophase:3.1–25.7
DHEA-S	1.3	Mic g/ml	0.03–5.88
Cortisol Morning	20.35	Mic g/dl	5.0–25.0
ACTH	40.54	Pg/ml	7.2–63.6
Testosterone	0.43	Ng/ml	Follicular phase: Nd-1.18 Midcycle: 0.21–1.04 Luteal phase: ND-1.19 Ovulatory: 0.65–1.19 Post menopausal: ND-1.1

Discussion

A complete understanding of the association between POEMS syndrome and ischemic stroke has yet to be achieved [6, 7]. Even with the novel consensus diagnostic criteria, it is still a rare and challenging condition to diagnose. Following a systemic diagnostic workup, our patient was diagnosed with POEMS syndrome. Initially, she responded positively to the therapy; however, her condition deteriorated during the active phase of the disease, eventually leading to coma. The current study concerns cognitive impairment and visual cognition corresponding to the familial history of POEMS syndrome. As previous studies have stated, the positive effects of growth hormone on cognitive function post-stroke and the impact on ischemic stroke and motor function remain unclear. [34,35;37,38]. Therefore, most children exhibit motor deficits, while cognitive and behavioral outcomes may be predicted by lesion characteristics on MRI [29, 34, 35]. Thus, for all observational and experimental models for children, it is essential to consider how well the model performs in both men and women, especially when gender differences have identified a specific disorder, such as depression or stroke. These studies have elucidated that the female brain responds to steroid hormones differently than the male brain. Also, it is paramount to consider comparing the effects on neuroplasticity and neurobehavior in both males and females, where the interest lies in models demonstrating sex differences in drawbacks, etiology, or management [30–32, 35, 38]. Patients diagnosed with POEMS syndrome have consistently exhibited a similar phenomenon [8, 36], a disease that shares many similar pathological features. We speculated that the neurological complication in our patient, an adolescent female who should be at least considered a stroke per her clinical presentation and neurological deficits, was not a mere coincidence. However, the underlying pathophysiological mechanism of this unique complication in POEMS syndrome remains elusive and requires further investigation, primarily due to the rarity of the syndrome itself. The cerebral thrombotic event during the active phase of the disease can be attributed to several factors. Elevated levels of circulating pro-inflammatory cytokines, along with a hypercoagulable state induced by hyperfibrinogenemia and the angiogenesis occurring within the vessel wall adventitia due to VEGF [6, 5], contribute to the pathogenesis of chronic inflammation in cerebral vessels. These mechanisms collectively increase the vulnerability to ischemic stroke or transient ischemic attack (TIA).

Conclusion

The pathophysiological mechanism and prognosis of ischemic stroke in patients with POEMS syndrome is unclear. We investigated the clinical features and long-term outcomes of patients and their families with POEMS syndrome and ischemic stroke [37]. On the contrary, we might argue that the endocrine system has a different role in neurocognition and neuroplasticity. Clinical educators need to pertain an understanding of the complex relationships between gender, hormones, dosage, exposure time, and brain structure. These multifaceted complications and their novel ideas may ultimately enhance the science of neuroendocrinology. [33, 34, 35, 38, 18]

Future Purposes

We, amongst the medical community and other researchers, will all acquire comprehension and understanding from this effort regarding how to manage and prevent these disorders in an individual with symptomology of endocrinopathy, gigantism, and organomegaly. This management permits patients, or those displaying these signs, to undergo therapy before substantial health issues, as we observed with this patient.

Declarations

Data availability statement:

The data that supports the findings of this study are available in the article

Acknowledgments:

The first author (Afshangian) began this international endeavor between the years 2014 and 2020. We have gathered data on 100 patients without CDs and 340 individuals with CDs and MRIs. I paid for everything, along with my family. No colleges assisted in this study. However, I am grateful for their support in recruiting study participants. An ethical code in the Department of Neurology and Neuroscience under multicenter supervision authorized the preparation of this project (Shiraz University of Medical Sciences). The Department of Speech Therapy and Rehabilitation at the Universities of Medical Sciences in Zahedan, Tabriz, Tehran, Yasuj, Guilan, Mazandaran, and Ahvaz are additional centers involved in this initiative. If editors request it, we can deliver letters of support. Various brain damage discipline teams have collaborated in this study.

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Ethical Clearance:

An ethical code approved the preparation of this paper and project (IR.SUMS.REC.1395. S878.) The Shiraz University of Medical Science.

Competing Interests:

The authors report no competing interests

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Figures

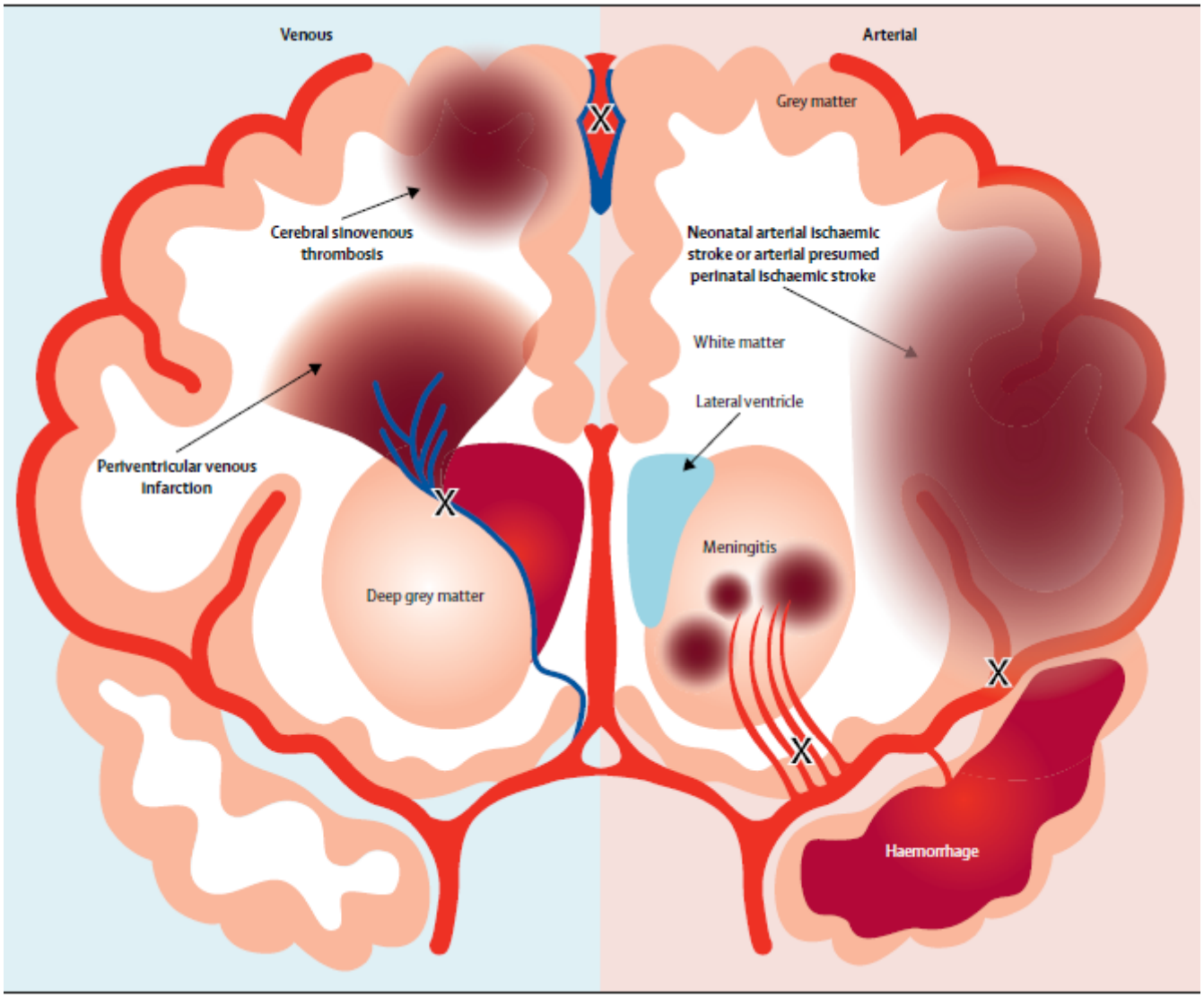

Figure 1

Sinus thrombosis presents as occlusion of the superior sagittal sinus with adjacent venous infarction, periventricular venous infarction with intraventricular hemorrhage, and subsequent medullary vein compression with periventricular white matter venous infarction. X demonstrates an area of vessel occlusion for adjacent stroke [17]

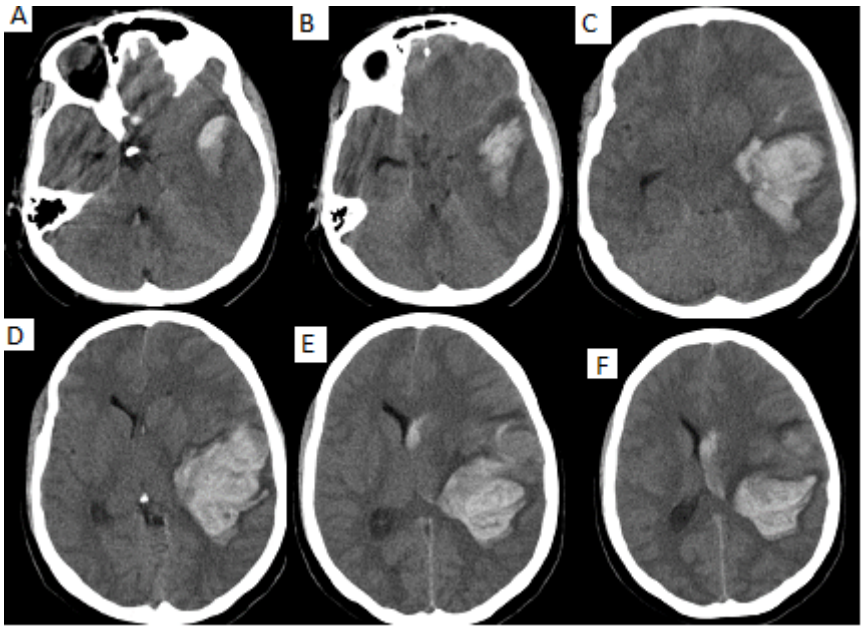

Figure 2

Consequent axial CT scan: Left temporal hematoma opening into the lateral ventricle and obliterating basal cisterns, compressing lateral ventricles, and shift of midline to the right due to the mass effect.

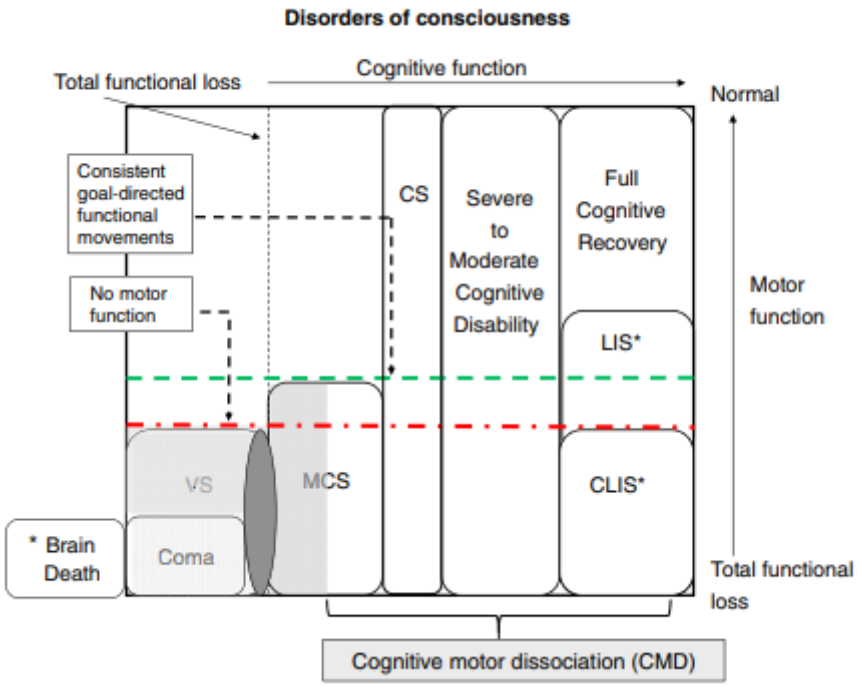

Figure 3

Clinical disorders of consciousness can be classified along two axes, which contrast the level of motor function preservation with the extent of cognitive function impairment. The condition of brain death indicated by an asterisk is not a disturbance of consciousness but rather the death of neurons throughout the brain. Patients with motor cognitive dissociation are identified by a light gray area that includes coma,

vegetative state (VS), and the left half of the minimally conscious state (MCS) region (CMD). Cognitive-motor dissociation, denoted by the inverted parenthesis, raises significant uncertainty regarding the underlying cognitive capacity in individuals affected by such conditions. The functional equivalent of coma and vegetative states, characterized by unconscious brain states with no observable behavioral signs of consciousness or motor and cognitive function, is depicted in the lower left portion of the image (vegetative state differing from the coma by the presence of blinking eyes - open periods or eye tracking, vision tracking). The dark gray ellipse indicates the transition zone between the coma/vegetative state and the minimally conscious state, and there may be behavioral fragments there [27,28,39,40].

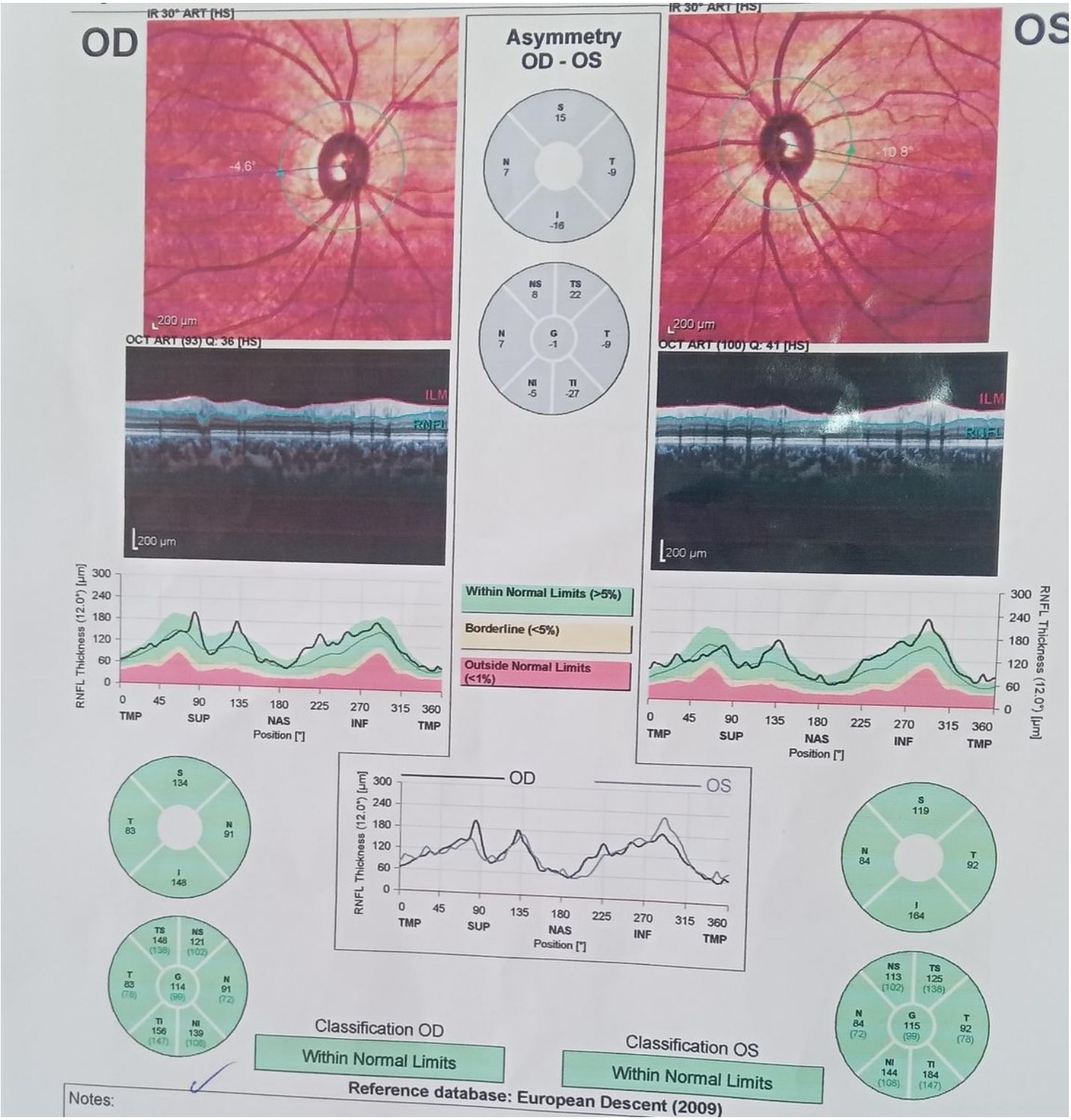

Figure 4

Visual acuity corresponding to Asymmetry OD-OS. optic nerve head regular OCT aspects for classification OD and OS

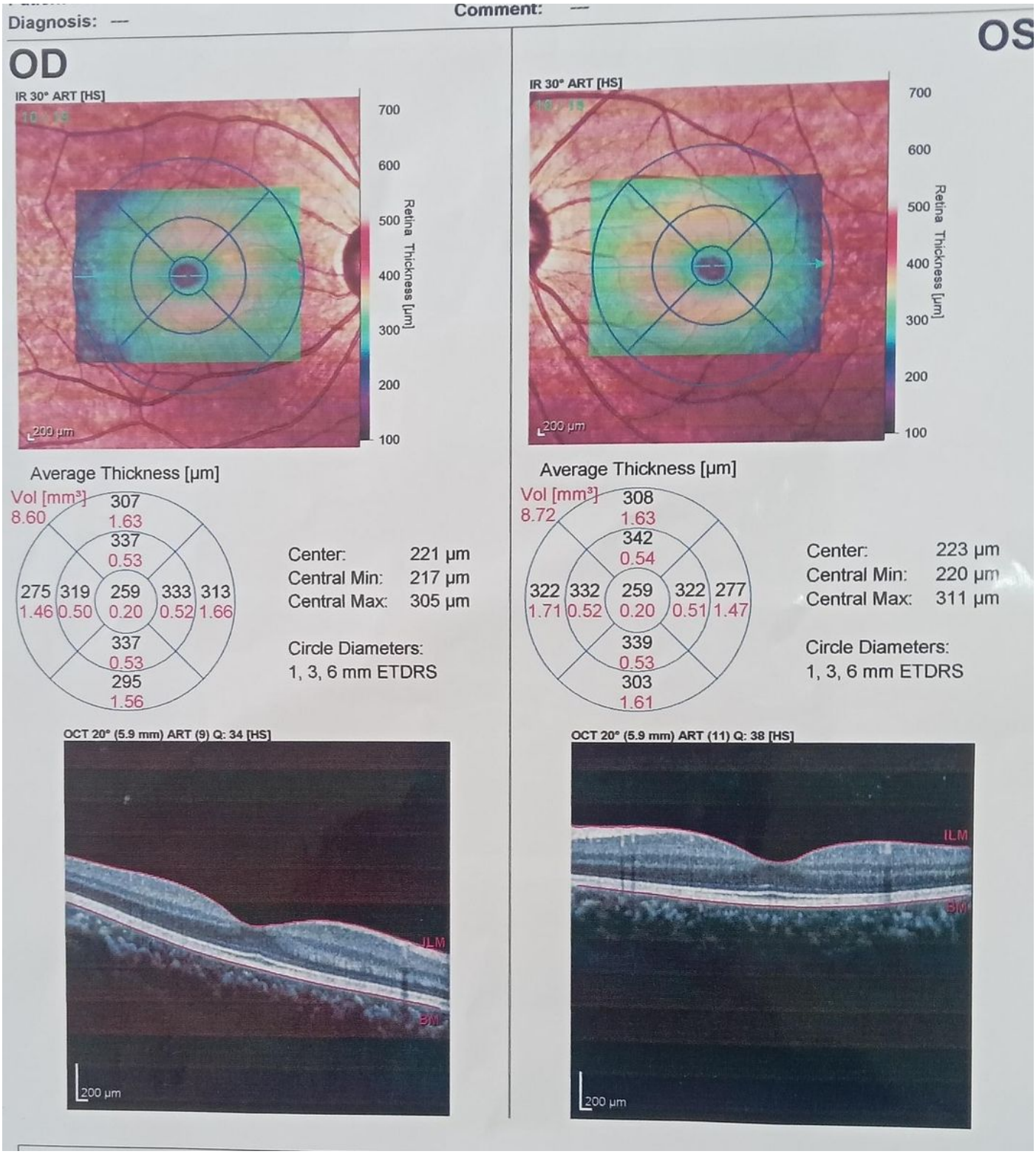

Figure 5

Optical coherence tomography of the retinal nerve fiber layer showing a borderline thickness in both eyes

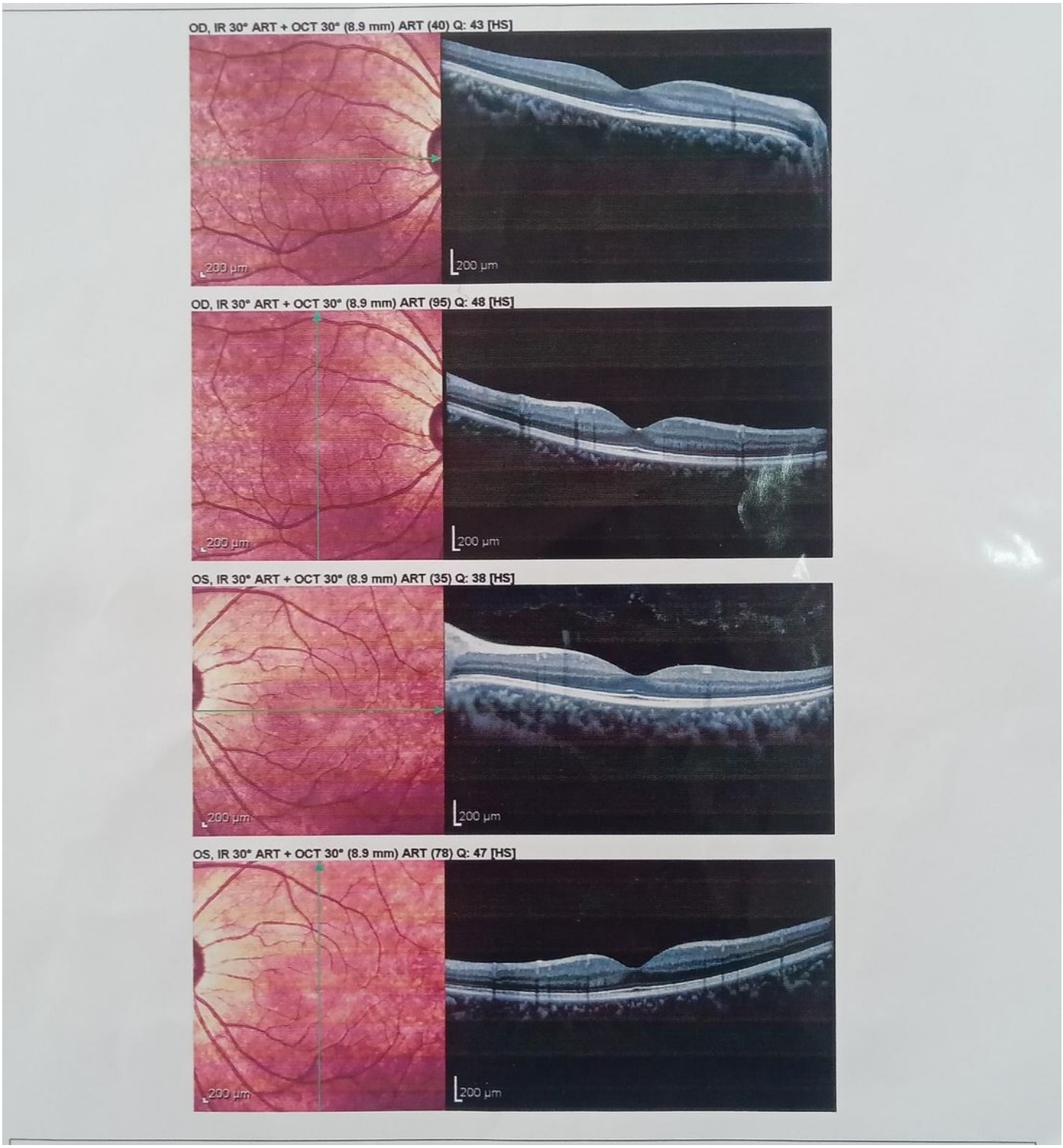

Figure 6

Figures 4, 5 and 6. optic nerve head regular funduscopic aspect 5) optical coherence tomography of cell inner plexiform layer showing a bilateral, 6) Nerve fiber layer showing a borderline thickness in both eyes; (ILM and RPE retinal; Nerve fiber layer; Macular OCT to layer)

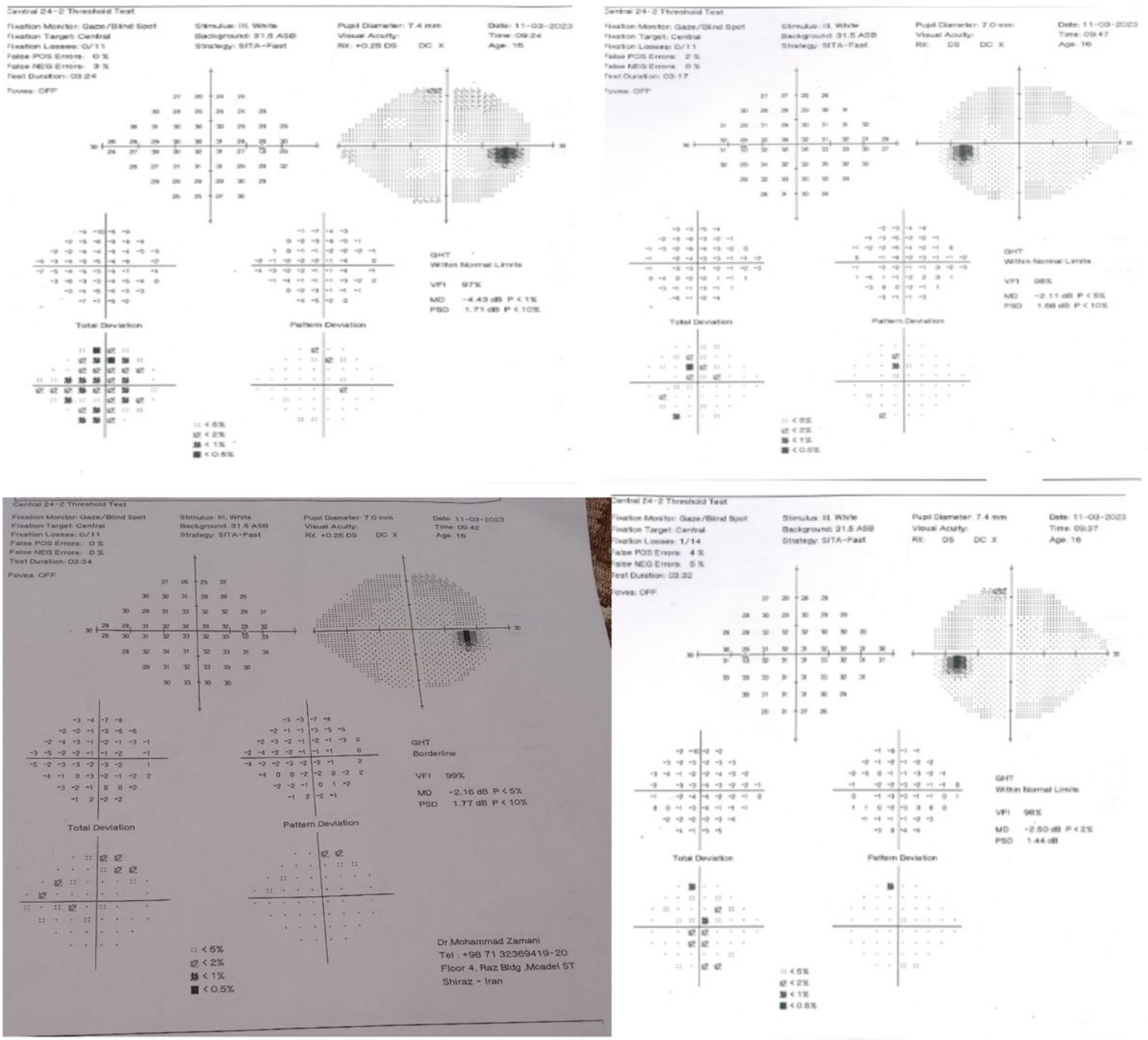

Figure 7

Peripheral vision of the visual fields of the sister 1) right eye of the patient. 2) the left eye of the patient 3) the right eye and 4) the left eye. At the first evaluation, there was a very weak threshold in the fixations and Gaze/blind. Such as detailed objects. After drug therapy and hormone therapy, the fixations of both eyes were clear and a central-Centro cecal visual field was normal.

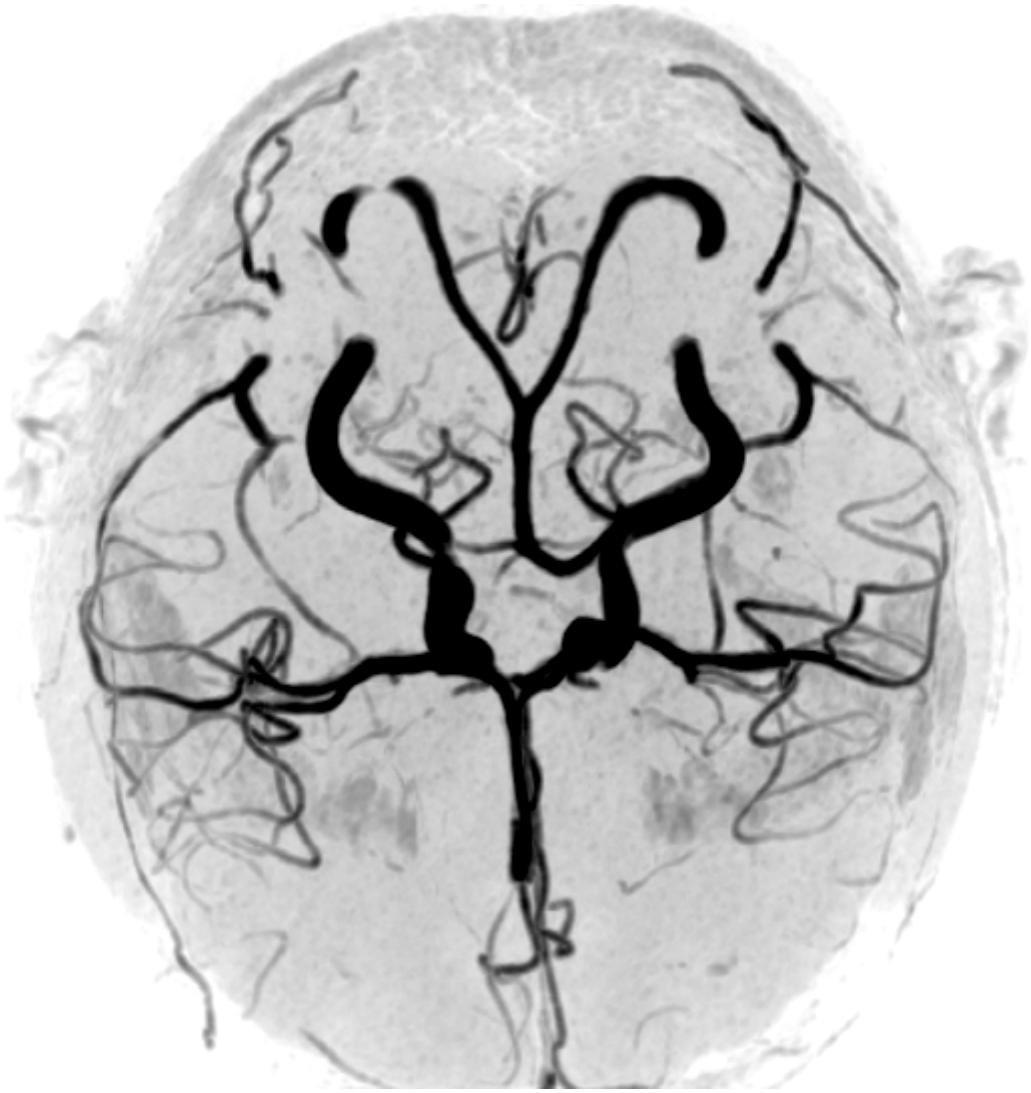

Figure 8

Neuroanatomical and brain changes after improving hormone or hormone disorder. The cranial vascular system appears normal.

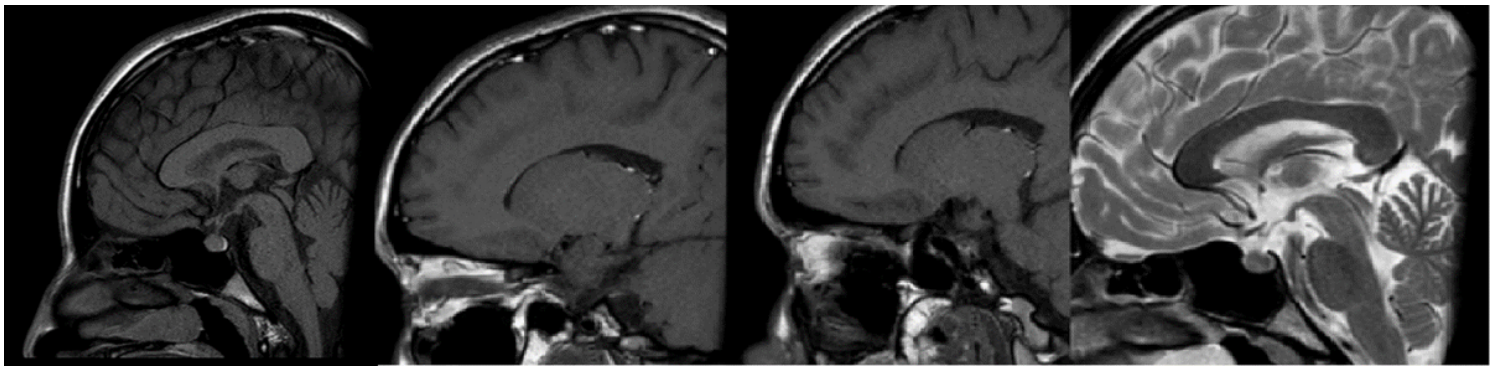

Figure 9

Multiplanar MR images of the brain with special attention to the pituitary gland before and after injection of intravenous contrast, including dynamic post-contrast images are taken.

Evidence of microadenoma 4 mm Rt. The side of the posterior adenohypophysis is seen