Clinical Schizophrenia & Related Psychoses

Bilateral Putaminal Haemorrhage and Blindness in Times of the Coronavirus Pandemic and Dysbiosis: Case Report and Literature Review

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Abstract

Background: Bilateral putaminal haemorrhage (BPH) is a rare medical event caused by methanol intoxication, metastasis, bleeding disorders, and amyloid angiopathies. However, many other conditions can cause BPH and are discussed in this manuscript.

We reviewed the literature using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist. We searched for publications on BPH, but we did not find any publications reporting reversible bilateral blindness and bilateral ring putaminal haemorrhage.

Case report: A 34-year-old male patient is admitted to the neurology ward on a referral from a regional hospital. The patient complained of sudden-onset bilateral blindness lasting one day, with no other associated symptoms. MRI confirmed symmetrical bilateral putaminal haemorrhage.

Conclusion: To the best of our knowledge, this patient is the first one presenting bilateral putaminal haemorrhage and spontaneous and partial reversible prequiasmatic blindness reported in the medical literature.

After a wide searching of available medical literature and detailed discussion, we concluded that our reported case is an atypical presentation of BPH, and blindness of unknown cause probably related with COVID-19, until proven otherwise.

Our review of the medical literature concluded that MRI is the best investigation to assess basal ganglia pathologies due to its superior contrast resolution. Nonetheless, CT has a relevant role in detecting calcification; SW-MRI has poor accuracy, but when only one study is possible, SW-MRI is the best choice.

We also concluded that in times of COVID-19 pandemic, all neuro-ophthalmological presentation (even with PCR negative) must be excluded from the extended list of clinical manifestations of SARS-CoV-2 infection-related and keeping in mind that most patients do not have respiratory symptoms.

Based on revised articles, we have hypothesised that in times of coronavirus pandemic, peoples under severe and prolonged stress are more prompt to develop abnormal microbiome composition and dysfunctional immune system facilitating the acquisition of SARS-CoV-2 infection and an associated vascular damage-causing cerebrovascular diseases which aggravate neuroinflammation. Same mechanism explains the presence of optic neuritis.

Further research is warranted to confirm a potential association between ICH/blindness/SARS-CoV-2 infection and the role played by microbiomes.

Keywords: Bilateral putaminal haemorrhage • Bilateral blindness • Partial reversible prequiasmatic blindness • MRI in bilateral haemorrhage stroke • Methanol intoxication • Microbiome • COVID-19 • Optic neuritis

Abbreviations: DD: Differential Diagnosis, BL: Bilateral, BG: Basal Ganglia, WM: White Matter, WD: Wilson Disease, GP: Globus Pallidus, HD: Huntington Disease, PKAN: Pantothenate Kinase-associated Neurodegeneration, GM: Grey Matter, UL: Unilateral, CSF: Cerebrospinal Fluid, anti-CV2/CRMP5: Collapsing Response Mediator Protein 5, SWI-MR: Susceptibility-Weighted Magnetic Resonance Imaging, HIV: Human Immunodeficiency Virus, CT: Computed Tomography, DWI: Diffusion-Weighted Imaging, FLAIR: Fluid-Attenuated Inversion Recovery, dAVF: Dural Arteriovenous Fistula, PCNSL: Primary Central Nervous System Lymphoma, NF-1: Neurofibromatosis Type 1, ODS: Osmotic Demyelination Syndrome, CPM: Central Pontine Myelinolysis, EPM: Extra Pontine Myelinolysis, MRI: Magnetic Resonance Imaging, CJD: Creutzfeldt–Jakob Disease, ADEM: Acute Disseminated/Demyelinating Encephalomyelitis, AHEM: Acute Haemorrhagic Encephalomyelitis, MOG: Myelin Oligodendrocyte Glycoprotein, rCBV: Relative Cerebral Blood Volume, AIDS: Acquired Immunodeficiency Syndrome, PRES: Posterior Reversible Encephalopathy Syndrome, PCR: Polymerase Chain Reaction, ULH: Unilateral Haemorrhage, TP the putamen, SW-MRI: Susceptibility-Weighted Magnetic Resonance Imaging, RNA: Ribonucleic Acid, DNA: Deoxyribonucleic Acid

Introduction

The putamen (TP) is the outer part of the lentiform nucleus (which also includes the globus pallidus) in both cerebral hemispheres; together with the caudate nucleus, it forms part of the corpus striatum, and all the regions mentioned above are components of the basal ganglia. TP is involved in cognitive function, language articulation, motor control, and addiction [1-3]. As we will discuss later, putamen lesions are present in different pathological processes, such as Parkinson's disease (PD), Alzheimer's disease (AD), bipolar disorder (BD), Huntington's disease (HD), Lewy body disorder (LBD), and Wilson disease (WD).

Some authors postulate that the putamen nucleus modulates the motor and sensory aspects of pain [4]. The entire posterior region of TP connects with the supplementary motor cortex and the primary motor cortex in the precentral gyrus. In contrast, the anterior part connects with motor association areas of the frontal cortex [5,6].

On the other hand, other authors have reported that the basal ganglia participate in purely motor activities and are involved in more complex goal-directed behaviours such as motivation, cognitive functions, and emotion

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[1]. Therefore, some degenerative and vascular disorders involving the corpus striatum can cause PD, psychiatric diseases, and an inability to identify fearful facial expressions [3,7].

Perforating branches from the middle cerebral artery and the anterior cerebral artery (ACA) constitute the lenticulostriate arteries, which supply TP with blood, and the mechanism for cleansing waste from TP depends on the glymphatic system, meningeal lymphatic vessels, perivascular drainage pathways, and the olfactory/cervical lymphatic drainage path in combination with cerebrospinal fluid (CSF), among other mechanisms [8-14].

TP's primary afferent pathways as part of the striatum are the thalamus, the cortex, and substantia nigra. In addition, the efferent pathways target the globus pallidus (GP), the substantia nigra pars compacta, and the substantia nigra pars reticulata [1].

Putaminal volume is essential, and volume defects can lead to several neurological and psychiatric disorders. Some investigators have confirmed that volumetric changes in TP are related to its physiological state and may differ according to age [3, 15]. TP is the basal nucleus most affected by intraparenchymal cerebral haemorrhage secondary to arterial hypertension and with the poorest prognosis due to the initial extravasation size [16]. Other authors believe that this elevated frequency of hypertensive bleeding is related to the lenticulostriate arterioles' corkscrew-like anatomical pattern, leading to increased luminal pressure along with the presence of fibrinoid necrosis and the subsequent formation of a Charcot-Bouchard aneurysm with a predisposition to rupture [16,17]. Nevertheless, the combination of micro-atheroma and lipohyalinosis causes a high frequency of ischaemic infarction in this vascular territory [16].

Bilateral putaminal haemorrhage (BPH) is a rare medical event caused mainly by methanol intoxication, metastasis, bleeding disorders, and amyloid angiopathies [17]. However, many other conditions causing BPH will be discussed below.

The volume of TP is related to several diseases, such as Gilles de la Tourette syndrome [18], bipolar disorder [19], and attention-deficit-hyperactivity conditions [20]. At the same time, other authors found a decreased volume of TP in Williams syndrome [21], attempted suicide [22], major depressive disorder [23], autism and schizophrenia [24], cognitive and motor impairment secondary to putaminal haemorrhage [17] and BPH/ necrosis caused by methanol intoxication [25,26], among other conditions.

Since the first detection of the virus, more than 231,415,298 people have been confirmed worldwide, and more than 4,741,801 have died as of September 24, 2021.

This article's aim is to answer the following research questions: how often have bilateral putaminal haemorrhage and associated partially reversible blindness been reported in the medical literature? Can intracranial cerebral haemorrhage (ICH) and associated blindness be related to SARS-CoV-2 infection? Moreover, this article contains a case report.

To review the medical literature, we used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

We searched for BPH publications, bilateral basal ganglia haemorrhage stroke, reversible bilateral blindness, COVID-19 Neuro-COVID optic neuritis, microbiome to answer the previous research questions using the procedure mentioned below and presented our case.

Literature Review

Literature search strategy

We performed a systematic review based on the PRISMA statement and searched the literature from January 1, 2010, to July 1, 2021. In the initial search, we included all studies in English, Spanish, and Portuguese that reported bilateral putaminal haemorrhage*, bilateral blindness*, and bilateral basal ganglia haemorrhage stroke* (search terms). We also reviewed the following databases for published studies: Medline, Embase, Scopus online databases, Google Scholar, Science Direct, Scielo, LILACS, Web of Sciences, and the Cochrane Library; we searched those databases to identify also articles on bilateral intraparenchymal haemorrhage* bilateral putaminal haemorrhage and blindness associated to COVID-19. In addition, all articles on reversible bilateral blindness* OR asymptomatic bilateral putaminal haemorrhage* OR bilateral basal ganglia haemorrhage* were included, where * is the PubMed wildcard for the beginning or end of a word.

Study and cohort selection: We select case reports, case series, cross-sectional studies, clinical trials and observational cohort studies reporting putaminal haemorrhage and bilateral blindness patients during the initial search. Later we progressively s excluded all duplicate studies, and those publications were not meeting inclusion criteria because they reported only putaminal haemorrhage separately or articles reporting prechiasmatic blindness or visual agnosia/ cortical blindness alone, and some were written in different languages apart from English, Spanish or Portuguese, and other abstracts without translation.

Finally, we focus on studies on reversible bilateral prechiasmatic blindness.

Between January 1, 2010, and July 1, 2021, our literature search yielded 989 publications. After removing duplicate articles, we retained 551 unique records. After considering the title and abstracts, we kept 149 items; we then screened the full text. Most of the publications combined bilateral blindness and putaminal haemorrhage secondary to methanol intoxication. We did not find publications related to reversible bilateral blindness and associated bilateral ring putaminal haemorrhage of unknown cause. See Appendix A for a flow diagram of the studies included in this review.

A place for flow diagram

Case presentation: On a referral from Mthatha Regional Hospital, a 34-year-old male patient came to the level III hospital and was admitted into neurology ward on September 19, 2020. The patient complained of acute ocular movement-induced pain, central dark points in the visual field, bilateral clouding vision one day ago and sudden loss of vision upon arrival to accident and emergency department accompanied by no other associated symptoms.

There was not previous antecedent of neurological disease, known allergies, one-time surgical treatment, tobacco or alcohol consumption, and chronic medication use. The patient also had no history of high blood pressure; decreased low-density lipoprotein cholesterol; low serum triglyceride levels; medication side effects; intoxication with substances such as cocaine, ephedrine, heroin, amphetamines, cyanide, methanol, and carbon monoxide; or confirmed SARS-CoV-2 infection. Because we had not suspicion of COVID-19 plus other logistic problems we did not repeat the PCR. The patient's general examination and vital signs were normal.

Our patient was fully conscious and well oriented on examination, with no meningeal signs on nervous system examination. Examination of the cranial nerves revealed no abnormalities.

According to gonioscopy, the anterior chamber was profound, no new vessels were observed in the iris or angles, and all quadrants of the curve were open in both eyes. Intra-ocular pressure was 15 mmHg on the right and 16 mmHg on the left by Goldmann applanation tonometry. A slit-lamp examination confirmed no signs of uveitis.

The laboratory investigations performed on the day of admission were as follows: see the following table 1.

Table 1. The laboratory investigations performed on the day of admission.

White cell count	7.10 x 109/L	3.9-12.6 x 109/L
Hb	10.4 g/dL	12-15 g/dl
Platelets	356 x 109/L	186-454/L
Sodium	140 mmol/L	136-145 mmol/L
Potassium	4.4 mmol/L	3.5-5.1 mmol/L
Chloride	102 mmol/L	98-105 mmol/L
Urea	7.1 mmol/L	2.1-7.1 mmol/L
Creatinine	68 µmol/L	48-90 µmol/L
Calcium	2.23 mmol/L,	2.15-2.5 mmol/L
Magnesium	0.83 mmol/L,	0.63-1.05 mmol/L
Phosphate	1.48 mmol/L	0.78-1.42 mmol/L
C-reactive protein	1 mg/L	<10 mg/L
Erythrocyte sedimentation rate	16 mm/hr	0-10 mm/hr
Total protein	74 g/L	60-78 g/L
Total bilirubin	<3 µmol/L	5-21 µmol/L
Alkaline phosphatase	92 U/L	42-98 U/L
Aspartate transaminase	23 U/L	13-35 U/L
Alanine transaminase	18 U/L	7-35 U/L
Total cholesterol	4.78 mmol/L	<4.5 mmol/L
HbA1C	5.1%	<7%
INR	1.01	1
D-dimer	0.8 mg/L	0.00-0.25 mg/L
Rheumatoid factor	7IU/ml	<20IU/L
Ceruloplasmin serum	28 mg/dL	20-35 mg/dL
Vitamin B12	136 pmol/L	145-569 pmol/L
Thyroid stimulating hormone	0.78 MIU/L	0.27-4.2 MIU/L
Anticardiolipin antibody	Negative	
Protein S	40 IU/dL	55-123 IU/dL
Protein C	100 IU/dL	70-130 IU/dL
Angiotensin-converting enzyme	30 IU/L	8-53 IU/L
Anticardiolipin antibody	Negative	
Anti-streptolysin O titre	88 IU/ml	<200 IU/L
Toxoplasmosis gondii IgG antibody	Positive	
Cytomegalovirus IgG antibody	Positive	
Rubella IgG antibody	Positive	
Rubella IgM antibody	Negative	
Cytomegalovirus IgM antibody	Negative	
C3	1.5 g/L	0.9-1.8 g/L
C4	0.4 g/L	0.1-0.4 g/L
Anti-nuclear antibody	Negative	
Anti-double-stranded DNA antibody	Negative	
PH	7.38	7.35-7.45
PaQ	92 mmHg	75-100 mmHg
Anion gap	8	12.
HCO$_3$	23	22-26 mQ/L
Anti-RNP antibody	Negative	
PCR	Negative	
CSF (viral panel) (antigens: NCC, cryptococcus, toxoplasmosis, neurosyphilis), Oligoclonal IgG band.	Negative	

Toxicology investigations confirmed no alcohol, drugs, or toxic substances in blood. His maximum D-dimer, erythrocyte sedimentation rate (ESR), and CRP levels were 15,941 ng/mL (normal 0–230), 76 mm (normal 0–20), and 27.00 mg/dL (normal 0.50–1.00), respectively. Here, raised suspicion of COVID-19 was present but in absence of respiratory manifestation no PCR test was done.

Ultrasound of the abdomen showed unremarkable findings. Lumbar puncture yielded the following results: Opening pressure, 19.1 cm H2O. CSF: Poly, 0; Lymph, 2; Glucose, 4.9; Protein, 0.34; normal lactate level.

He underwent MR imaging within 12 h of the time of hospital admission. It was performed using a 3-tesla MR imaging system (Magnetom Vision, Siemens Medical Systems, Erlangen, Germany), including T1- and T2-weighted imaging, fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC), and susceptibility-weighted imaging (SWI).

The following brain MRI scans were taken axial FLAIR, DWI-ADC, and T1WI pre-and post-contrast; coronal T2WI, and sagittal T1W1 pre-and post-contrast.

Brain imaging revealed symmetrical, bilateral lesions in the posterior putamen with high FLAIR-T2W and T1W signal and restriction on DWI, suggesting sub-acute haemorrhage (specifically, BPH). In addition, the lesions demonstrated peripheral enhancement in the coronal, sagittal, and axial views (Figure 1).

globus pallidus and caudate nucleus, bilateral optic radiations and bilateral globes were normal. We report a subtle increase in signal in the optic nerves bilaterally probable secondary to optic neuritis. There was no abnormal enhancement, and the dural veins were enhanced naturally. V4 and the basal cistern were patented, with no midline shift or hydrocephalus. The paranasal sinuses and mastoid air cells showed no abnormalities.

MRI scans were taken of the whole spine, including sagittal T1WI and T2WI.

Findings: At the cervicothoracic level, we observed that the brainstem and posterior fossa structures were typical. The craniocervical junction was normal as well. Lordosis was maintained. The bone marrow and intervertebral discs were normal and the signal intensity of the CSF and spinal cord as well. The study did not show disc herniation, spinal stenosis or neural foraminal narrowing, and the spinal cord showed no abnormal signs that would account for the patient's symptoms.

In the lumbar spine, we observed five lumbar-type vertebrae. Lordosis was maintained. The conus medullaris at T12-L1 level. The disc at L4-5 was desiccated. The marrow and CSF signals were standard. There was

moderate, multilevel, broad-based disc herniation at L4-5 and L5-S1, along with facet arthropathy and associated annular fissuring at L4-5, resulting in moderate spinal stenosis and mild bilateral neural foraminal narrowing. The Erector spine, psoas muscles and bladder were within normal parameters. This patient developed mild flulike symptoms and dysgeusia nine days after initial presentation and was under suspicion of COVID-19, but the nasopharyngeal swab PCR test was negative.

The cardiac ultrasound showed no abnormalities. Therefore, the patient was admitted and received the following treatment: Prednisone (60 mg po daily), Vitamin B12 supplementation (1000 µg IM daily), Aspirin (150 mg daily), Enoxaparin (40 mg s/c daily), Simvastatin (20 mg daily), Pyridoxine (50 mg daily), Thiamine (100 mg daily).

The patient underwent rehabilitation for two weeks and was discharged home after spontaneously recovering 50% of his prior visual acuity. Four weeks later, his visual acuity recovered utterly, and his fundus abnormalities resolved with an additional four-week course of prednisone with no pulmonary involvement.

We performed a systematic review of most of medical publications related to this topic following the PRISMA statement looking for case report, case series and cohort group. We checked almost all available literature published in English, Spanish and Portuguese on BPH, bilateral blindness, spontaneous partial visual acuity recovery, COVID-19 optic neuritis, and bilateral haemorrhage stroke dysbiosis related. Unfortunately, we only found the scarcest report, as seen in the flow diagram of selected articles.

It would be extremely difficult task to undertake in-depth discussion of all disorders affecting BP in this clinical-demographic-pictorial review. Therefore, we focus our discussion on the most typical presentations, MRI findings, demographic features, and bibliographic research findings. Although, we as clinicians did not expect these MRI findings because our patient never presented basal ganglia symptomatology.

diseases cause BPH, as shown in Figure 2; some of these pathological processes are relatively common, while others are scarce. Amongst those is methanol intoxication (MI). This type of poisoning is found after the ingestion of industrial liquids containing methyl alcohol. Patient complaints range from disturbance of visual acuity to bilateral blindness (as our patient), followed by other clinical manifestations secondary to the metabolism of methanol to formic acid by alcohol dehydrogenase, leading to severe metabolic acidosis, bilateral blindness, and brain damage if the patient survives. A combination of BPH and frontal and insular white matter lesions are usually seen in MI [27,28]. In these cases, visual damage is permanent, which differs from our patient's condition. However, the combination of TP and caudate nucleus haemorrhage is more commonly seen in other metabolic disorders, including uraemic encephalopathy (UE) [29].
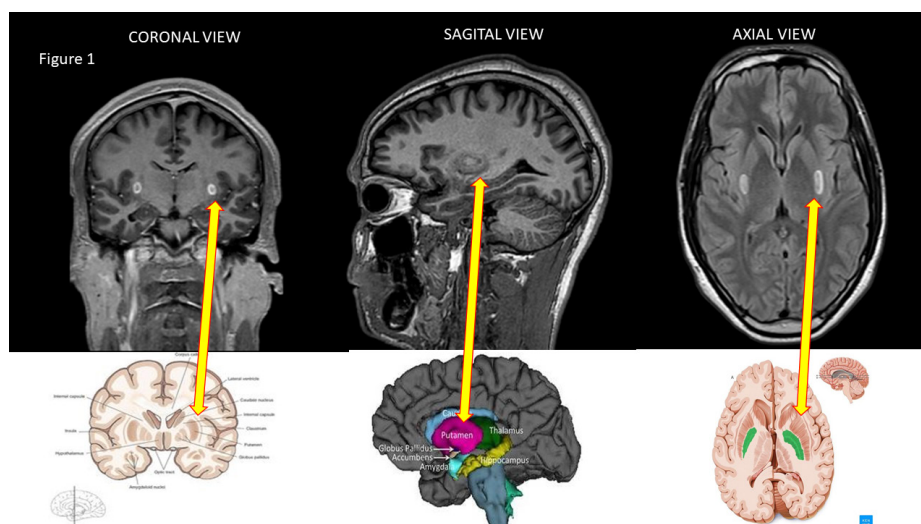

Figure 1. Coronal/Sagittal/Axial MRI views: shows a symmetrical bilateral posterior putaminal haemorrhage with mild contrast enhancement and its graphical illustration.
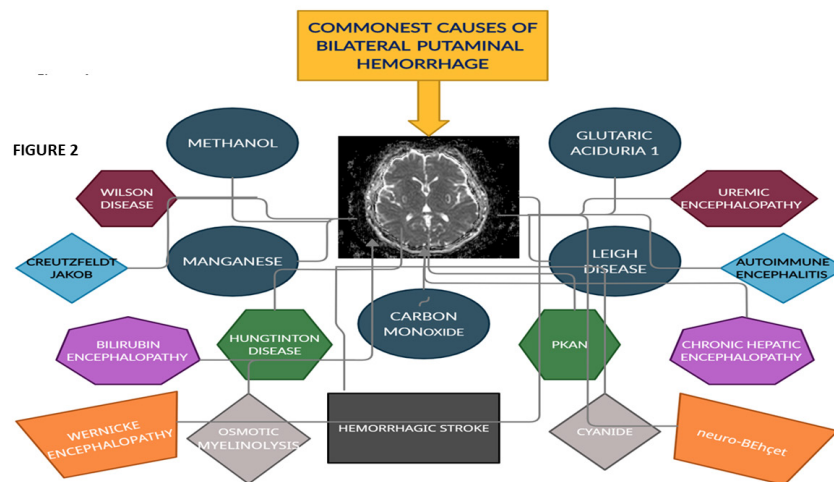
Figure 2. List of most common causes of putamen haemorrhage, as discussed in this report.

In patients presenting with uraemic encephalopathy, swelling of the lentiform nucleus with hyperintensity on T2-weighted and FLAIR magnetic resonance images (MRI) can also be observed like some images observed in our patient but without globus pallidus involvement.

In some patients with UE, MRI shows the lentiform nucleus separated by three lines called a lentiform fork, and there is no contrast enhancement [30]. This sign can be observed in patients with metabolic acidosis due to other causes, such as metformin-associated encephalopathy [31].

Sometimes hypertensive bilateral haematoma leads to BPH, but an association with bilateral blindness (chronic papilloedema?) has never occurred in our region, and simultaneous bilateral thalamic haemorrhages or hypertensive basal ganglia haemorrhage is usually asymmetric [32,33]. These haematomas usually dissect the brain parenchyma with scarce associated tissue necrosis and cavity formation plus haemosiderin staining, producing a peripheral region of low signal on MRI images and accentuation on GRE T2SW-MRI or SW-MRI images. In addition, around the haematoma, there can be a thin layer of contrast enhancement around the lesion [34].

One common aetiology of gaseous intoxication in humans worldwide is carbon monoxide (CM) poisoning due to the incomplete combustion of carbon-based fuels. Soon after inspiration, CM binds to haemoglobin (with 250-fold stronger affinity than O_2), leading to hypoxia, subsequent dysfunction of mitochondrial respiratory activity, and increased oxygen free radical production. To differentiate this feature from our patient's condition, we noted that the patient had no history of CM inhalation. We also observed other clinical and immunological features, such as the absence of GP damage with typically reduced diffusivity in regions including the thalamus, cerebellum, hippocampus, and substantia nigra [35]. Despite, figure 1 showed bilateral round hyperdense lesions with a mild enhancing response, which resembles the typical image seen in CM cases on MRI studies; in our case no history of CM was documented. If difficulties arise in differential diagnosis, it is important to keep in mind that CM preferentially damages the GP.

Taking into consideration that sub-acute necrotising encephalopathy (Leigh syndrome) affects only children with high lactate levels in the CSF, it is easy to perform early differential diagnosis (DD) between this disorder and our patient's condition (Figure 2). This pathological process is characterised by a progressive neurodegenerative mitochondrial disease leading to developmental milestone delays, ataxia, and feeding difficulties. MRI findings also help support DD because, apart from putaminal lesions, there are lesions in the midbrain, pons, subthalamic nucleus, caudate nucleus, dorsomedial thalamus, substantial nigra, the dentate nucleus of the cerebellum, and periaqueductal grey matter due to cytotoxic oedema [36, 37]; all these additional lesions were absent in our case. A lack of associated blindness is another strong point for final DD.

As shown in Figure 2, another cause of BPH is glutaric aciduria type 1. This condition is a genetic (autosomal recessive) metabolic disease commonly seen in children causing post-vaccination epilepsy leading to macrocephaly, extrapyramidal involuntary movements, and psychomotor disorder. However, MRI studies show a typical frontotemporal atrophy pattern, delayed myelination, and subdural effusion with reduced diffusivity [38, 39], which is quite different from the MRI findings in our patient apart from the clinical manifestations.

Because it is listed in Figure 2, we include kernicterus (KS) in this discussion of the DD of BPH. Bilirubin encephalopathy (KS) appears in neonates, and an MRI study shows bilateral atypical T2 hyperintensity in both the subthalamic nucleus and globus pallidus [40]. Our case did not meet the criteria for this neurological disorder. Among other metabolic causes of BPH, we considered Wilson disease (WD), also known as hepatolenticular degeneration. This condition is a genetic disorder caused by mutation of the ATP7B gene leading to abnormal transport and deposition of copper in some organs (including the brain), a Kayser-Fleischer ring in the iris, low ceruloplasmin levels, extrapyramidal signs, and abnormal behaviour. MRI investigation confirms hyperintensity of the midbrain without the involvement of the substantia nigra, red nucleus and superior colliculus, forming a pathognomonic sign known as the "face of the giant panda". On the other hand, other changes have been reported in the thalamus, globus pallidus, and caudate nucleus [41-43]. These signs differ vastly from our case apart from his clinical features.

Discussion

QAetiology of BPH is a neuro-Behçet syndrome (NBS), as listed in figure four. NBS is an uncommon, chronic disorder affecting the inner lining of the genitalia, mouth, and small blood vessels in young patients leading to skin lesions, recurrent genital and mouth ulcers, and neurovascular complications, including intraparenchymal haemorrhage. In our experience, it is usually seen unilaterally. Patients can also present uveitis and retinitis, which may cause bilateral blindness with or without arthritis and peripheral vascular disorder [44]. The combination of bilateral blindness and intracerebral haemorrhage should be considered in the differential diagnosis, but our case did not present any clinical manifestations of the neuro-Behçet syndrome as we described before [44].

Our patient did not present the classical triad of progressive (15-20 years) cognitive, motor, and psychiatric manifestations typically seen in patients with Huntington disease, a genetic autosomal dominant neurodegenerative process of the striatum. Therefore, prominent MRI abnormalities (atrophy) are seen in the bilateral striatum and are most prominent in the head of

the caudate nucleus, causing dilatation of the anterior horn of the lateral ventricles and flattening of their lateral shape ("boxed-out" sign) along with an increased intercaudate distance (> 20 mm) and diffuse cerebral atrophy (more in the frontal lobes), which can be confirmed by volumetric MRI [45,46].

Creutzfeldt-Jakob disease (CJD) is a fatal and swift progressive neurodegenerative disorder characterised by ataxia, myoclonus, cognitive decline, and behavioural abnormalities. Approximately 85%–90% of cases are classified as sporadic CJD, for which no aetiology can be identified. Genetic or familial CJD, caused by four common mutations and many other rarer mutations in the prion protein gene [47-61].

Due to the high incidence/prevalence of HIV/AIDS in our region, CNS cryptococcosis (granulomas, gelatinous pseudocysts, meningitis) is a frequent pathological process [62] that should be discussed in this report.

The combination of bilateral blindness (chronic papilloedema) and basal ganglia deep grey matter lesions seen in cryptococcosis must be distinguished from our case. The clinical features and MRI findings serve to differentiate it. Sometimes CT brain studies show only dilatation of the ventricular system or no abnormalities at all. On MRI, hyperintensities on FLAIR and T2-weighted images can be observed in the deep grey matter with contrast enhancement and surrounding oedema [63,64]. Our case did not present cryptococcosis.

After toxicology screening, we did not find trace of toxins, venoms, and poisons in our patient. However, we consider discussing cyanide poisoning (Cp) because it has several clinical presentations, including early asymptomatic presentations [65]. In addition, Cp has been noted to occur in different scenarios and can be secondary to inhalation, skin contact, ingestion, and whether it is intentional or accidental, being the primary threat to military personnel and civilians worldwide [66].

Clinical features include confusion, vertigo, headache, metabolic acidosis, palpitations, hyperventilation, respiratory failure with swift progression to hypotension, bradycardia, shock, coma, and cardiorespiratory arrest [67].

All the previously mentioned clinical manifestations differ from our case, and the MRI findings are also different (extensive lengthening of repetition time (TR), high signal and restricted diffusion in the GP and hippocampal formation bilaterally). In addition, in some cases, MRI confirmed TR signal changes in the ventrolateral thalamus, cingulate gyrus, posterior putamen and head of the caudate nucleus in both cerebral hemispheres [68], which is quite different from our case.

Pathology to be differentiated from our case, is osmotic demyelination syndrome (ODS), which is classically associated with a swift adjustment of hyponatraemia. However, it can result from many electrolyte abnormality corrections, which are frequently seen in chronically deteriorated patients. ODS's clinical features include cognitive disturbances and tetraparesis plus typical lesions on brain MRI due to central pontine and extra pontine myelinolysis (CPM/EPM) [69-70].

We considered other causes of BPH and visual disturbances while processing our DD, but we did not include them in this discussion because they are exceedingly rare in our setting or because they differ markedly from our case in MRI features or clinical manifestations. Among these pathological processes are: metastasis, bleeding disorders, amyloid angiopathies, germinomas, lysosomal storage disorders such as Tay–Sachs and Sandhoff diseases, but primarily Krabbe disease and neuronal ceroid lipofuscinosis. Also, toluene toxicity/solvent abuse, metronidazole-induced encephalopathy, acute hyperammonaemia encephalopathy, acute disseminated encephalomyelitis, acute necrotising encephalitis, artery of Percheron stroke, deep cerebral venous thrombosis, haemorrhagic presentations of dural arteriovenous fistulas, diffuse midline glioma with H3K27M mutant, bilateral BG gliomas, primary CNS lymphoma, tubulinopathies (including the microlissencephaly subtype),

neurofibromatosis type 1, primary familial brain calcification (Fahr disease), Cockayne syndrome, carbonic anhydrase deficiency type 2, Labrune syndrome, Coats plus syndrome, ethylene glycol intoxication, vigabatrin-associated MRI abnormalities, acute disseminated encephalomyelitis, acute haemorrhagic encephalomyelitis (Hurst disease), viral encephalitis (mainly Flaviviridae {Japanese and West Nile}, Epstein–Barr), tick-borne encephalitis, cerebral toxoplasmosis, hypoxic-ischaemic encephalopathy, and status marmoratus ("état marbré").

We will briefly discuss posterior reversible encephalopathy syndrome (PRES) because it may be increasing gradually in incidence or may simply be diagnosed increasingly often because it is a better-known pathological process. The combination of cerebrovascular lesions and visual loss is also observed in PRES, and cortical blindness has been reported [71]. The presence of partial reversible prequiasmatic blindness and ovoidal BPH is sufficient to establish the difference. Nevertheless, during the coronavirus pandemic, it is essential to remember that PRES is a neurological complication of COVID-19 pneumonia [72-76].

For other hand , more than 50 % of cases of MI are caused by inhalation, dermal exposure, accident or suicidal attend or ingestion of a large variety of windshield products, organic solvents, commercial paint thinners, washer fluid, shellac varnish, photocopying fluids, eau de cologne, perfumes, gasoline antifreeze ("dry gas") or fraudulent adulteration of alcoholic beverages causing early or late visual disturbance secondary to destruction of optic nerve fibers and pigmented retinal epithelial cells, leading to visual field defects. It ranges from cloudy/blurred vision to "snowfield vision" or permanent bilateral blindness and bilateral putaminal necrosis/haemorrhage due to elevated anion gap metabolic acidosis from the production of lactic and formic acids or secondary to anoxia and acidosis [77]. On visual assessment, pallor of the optic disc, hyperemia, central scotoma, afferent pupillary defect, and papilledema, which are reported as characteristic findings [78] which never happened in our case.

During the current coronavirus disease 2019 pandemic in Iran, there has been a relevant increase in methanol-induced morbidity and mortality, being the most significant prevalence of methanol mass poisoning in Iran's history because methanol is cheapest, more available than ethanol and consumption of fraudulent home-made alcohol [78-80]. However, there are no similarities between Iranians reported patients and our patients. Other information to be considered is when our patient developed clinical manifestation, all liqueur stores in this country were closed, and alcohol consumption was managing as a crime.

Apart from BPH followed by blindness, another sensory disorder like deafness was reported after BPH [81-84]. It is well known that cortical deafness (CD) is an uncommon presentation of types of auditory disorder due to bilateral subcortical interruption of acoustic radiations or bilateral damage of auditory cortices. Recently, Gwak and collaborators using diffuse tension imaging (DTI) confirmed that CD preceded by BPH is caused by anatomical damage of the acoustic radiation on both cerebral hemispheres. In their case, that dysfunctional connectivity between sensorimotor and intrinsic auditory networks was documented by DTI and resting-state functional MRI, being the first case reported in the medical literature [85]. Last year, Min and colleagues studied the capacity of DTI in predicting motor outcome in twelve patients presenting putaminal haemorrhage measuring clinical outcome at baseline, three weeks, twelve weeks months, and twenty-four weeks after the initial treatment and they found on the side of the lesion a remarkable higher value of fractional anisotropy (FA) in the group of patients with a better outcome, and they concluded that modifications in the FA ratio on diffusion can be a predictor of good motor recovery after BPH [86].

Intracerebral haemorrhage in times of coronavirus pandemic: From the first description of SARS-CoV-2 transmission at the beginning of the pandemic in Wuhan, different theories have been proposed including it laboratory source. Our hypothesis on SARS-CoV-2 transmission is graphically summarized in Figure 3.
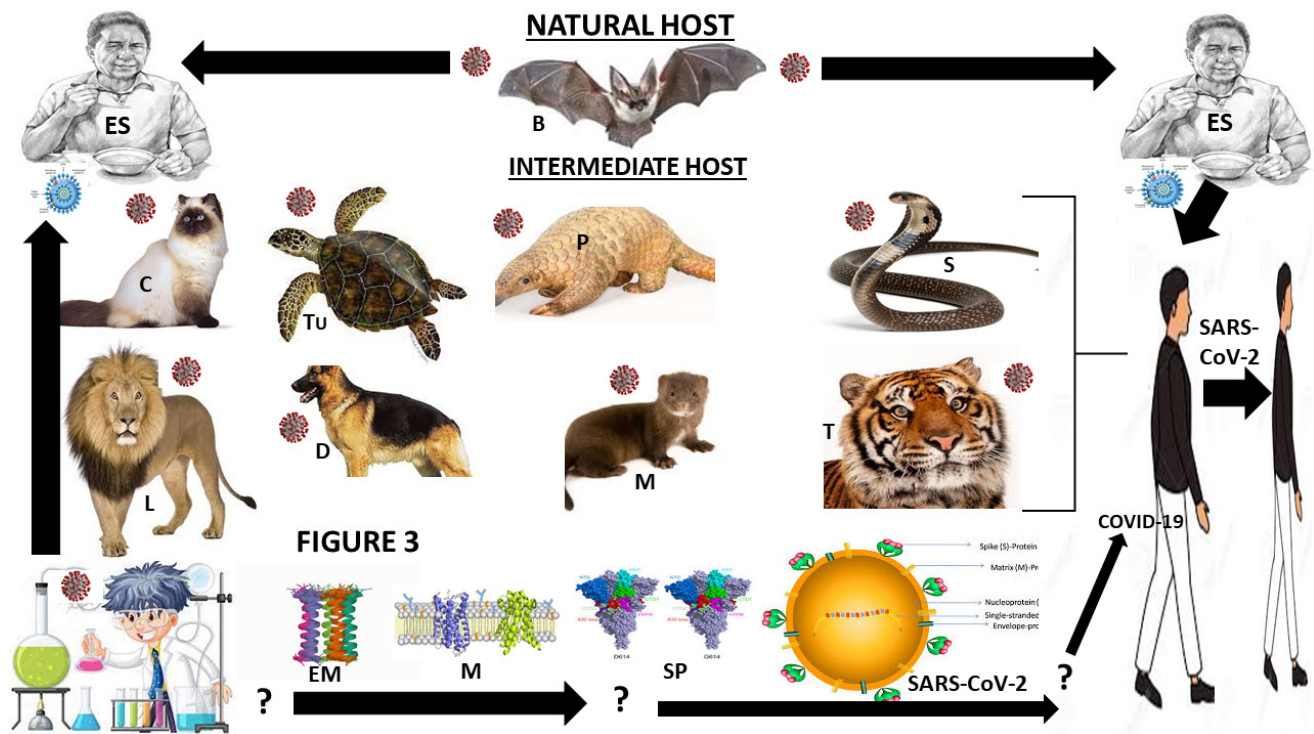
Figure 3. Graphical representation of SARS-CoV-2 transmission from natural host, intermediate host to human beings. B-bag, C-cat, D-dog, EM-envelop membrane, ES-eating bag soup, L-lion, M-matrix, M-mink, P-pangolin, S-snake, SP-spike protein, T-tiger, Tu-turtle.

During the current pandemic, many COVID-19 patients remain free of symptoms and signs, while many other are PCR-negative. Therefore, to confirm the infection by SARS-CoV-2 in 100% of cases would be extremely difficult to reach.

Anticoagulation therapy is part of the treatment in COVID-19 patients, and the risk of hemorrhagic stroke has been well documented [87]. However, because our patient never received anticoagulant medication, we will not discuss this issue now.

On the other hand, Abbas and other authors analysed 19 patients presenting ICH and SARS-CoV-2 from four tertiary-care cerebrovascular centres. From the total of the case, 63% presented intraparenchymal haemorrhage and other subarachnoid haemorrhage or subdural haematoma. The mortality rate was 59%. Finally, they proposed a possible pathophysiological mechanism to connect ICH and COVID-19 [88-89] that makes sense. In case of COVID-19 and ICH, we have hypothesized that the direct damage on the blood vessel caused by SARS-CoV-2 attached to the ACE2 receptor present in the wall of arterioles can cause breaking of the wall vessel. We will comment on it later on because now we are going to review the relationship between blindness and SARS-CoV-2.

Neuro-blindness in times of coronavirus pandemic: Authors like Macovei believe the current pandemic has a long-lasting collateral eye health effect with an increased risk of permanent vision impairment and blindness [90]. At the same time, other authors report different experiences on ophthalmological manifestation related to the COVID-19 pandemic worldwide [91,92]. More than 15% of the global population (1-billion people) has a disability, according to WHO [93], and visual impairment is a significant cause of disability across the world. Before the current pandemic, 441.5-million people suffered visual impairment, 36 million had blindness, and 217 million presented low vision [94]. Based on these data, some investigators calculated that the total amount of patients with an ophthalmological impairment will be triplicated by 2050 [95] knowing the neurotropic effect of SARS-CoV-2 and the prolongation of the current pandemic. Even at the time of this writing it continues to grow, there is a lack of proper neuro-ophthalmological care in COVID-19 times including delayed diagnosis and improper management. Therefore, we have hypothesised that the prevalence of COVID-19 neuro-ophthalmological sequels will increase many times more by the same year.

During the ongoing pandemic in some countries, the eye health system has been excluded from the list of essential health care services in parallel with the COVID-19 response, and now it is not yet confident what will happen with eye care services. Therefore, the real possibility of establishing the incidence of people's eyesight pathologies during the current pandemic will be unknown [96-97], even the devastating consequences of the undiagnosed or untreated neuro-ophthalmic disease. Fortunately, some developed countries have a chance to integrate telemedicine into the neuro-ophthalmologist's practice implementing tele-neuro-ophthalmology to improve this situation while other combat the effects and aftereffects of this COVID-19 pandemic with scarce resources. This disruptive innovation will raise a better future of telemedicine in neuro-ophthalmology [98], but it will not happen in most places, including almost all developing countries.

Authors like Azab and collaborators aimed to report a 32-year-old male patient presenting post-COVID-19 optic neuritis. Thus, they made the first meta-analysis for the published similar case reports worldwide. According to their results, post-COVID optic neuritis and retinal complications are neurological manifestations of the SARS-CoV-2 infection being more frequent in female patients' left eyes, leading to unilateral or bilateral blindness [99].

As has been well documented, optic neuritis is an autoimmune inflammatory disorder commonly associated with another demyelinating disease like multiple sclerosis and neuromyelitis optical spectrum disorder associated with COVID-19 or not, leading to a swift drop of visual acuity and ocular movement-induced pain [100]. The first anatomical damage is characterised by demyelination and inflammation of the optic nerve, as shown in figure 4, where the mechanism of systemic T-cell activation causing an immunological antigen-antibody reaction [101] is graphically represented.
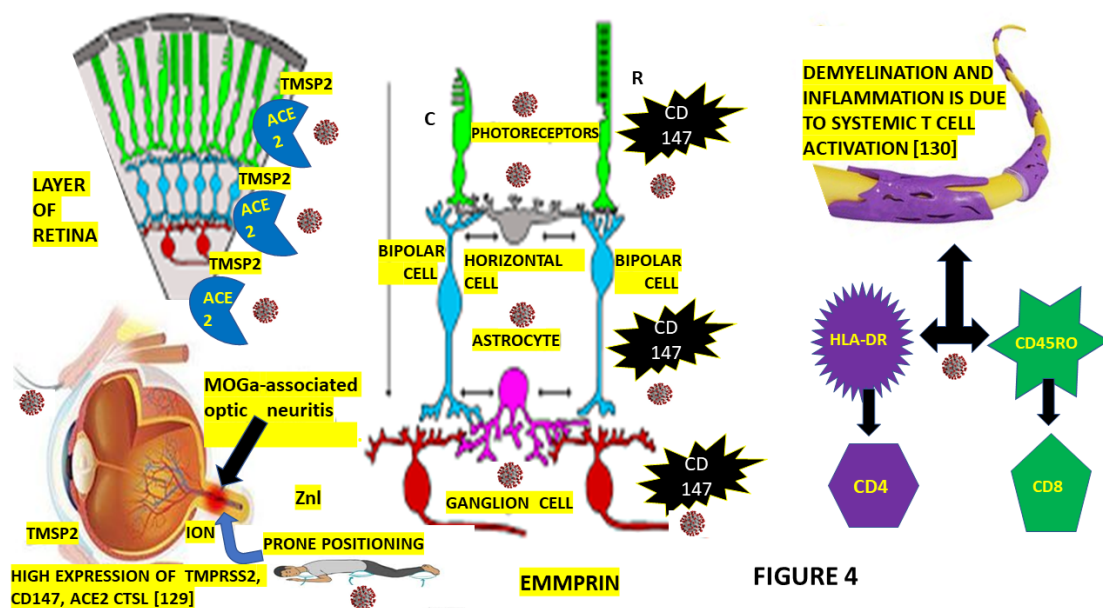
Figure 4. Shows a graphical representation of demyelination and swelling of optic nerve fibres due to systemic T-cell activation and increased expression of HLA-DR and CD45R0 on CD4 and CD8 T cells. EMMPRIN- extracellular matrix metalloproteinase inducer (CD147/Basigin2), HLA-DR- human leukocyte antigen – DR isotype, CD45- transmembrane protein tyrosine phosphatase, receptor type, CD45RO- single marker for human memory T cells, MOGa-myeline oligodendrocyte glycoprotein antibody, Znl-zonulin receptor.

In our patient, the suspicion of optic neuritis is based on the clinical features of pain in the eyes, decreased visual acuity, the MRI study and confirmed findings in the fundoscopic examination.

On the other hand, the current pandemic causes a disproportionate impact on the visually impaired peoples leading to a high risk of re-infections [102], aggravating the visual impairment apart from the confirmed damage of the macula, leading to permanent blindness. In these COVID-19 cases, simplified anti-vascular endothelial growth factor therapy and priority therapy for those at the highest risk of irreversible vision loss, is potent recommended [103].

It is well known that SARS-CoV-2 cause neuronal damage from the augmented release of the proinflammatory cytokine, chemokine, TNFα, macrophage inflammatory protein 1, interferon γ and from leukocytes infiltration, activated astrocytes and activated microglia [104]. Everybody agrees that SARS-CoV-2 infection causes a remarkable dysregulation in the balance between Th1 and Th2 lymphocytes, decreasing CD4+T and CD8+T cells by direct invasion of the nervous system (anosmia/ageusia), or by hematogenous route or by the microbiota-gut-brain axis dysbiosis or all together plus increase B cells levels. As before-cited, the main consequence of this aggression is increased IL-2R, IL-6, TNF-α, INF-β, among others (the cytokine release syndrome known as cytokine storm) and hyperinflammatory response to the virus with astrocytes, microglia, and monocyte-macrophage system activation and subsequence damage of the neurons and supporting cells, endothelial tissue and disruption of the blood-brain-barrier causing cerebral ischemia and haemorrhage and other complications. In addition, the increased concentration of CCR6+Th17 and CD8T cells also contributes to the over activation of T cells and those complications [104,105].

COVID-19 is associated with many neuro-ophthalmologic conditions, including inflammatory/demyelinating optic neuritis, cranial nerve disorders, intracranial hypertension (papilledema), Miller Fisher (ophthalmoplegia), acute inflammatory demyelinating neuropathy (facial palsy), Bell's palsy and ischemic optic neuropathy due to prolonged prone positioning [106]. In addition, four COVID-19 patients have been reported presenting inflammatory optic neuritis in the setting of pan uveitis [106-108].

Reports on demyelinating optic neuritis have been published regarding cases complaining of pain during extraocular movements and diminished visual acuity without focal neurological signs. One of these patients had 26-year-old and presented bilateral optic neuritis preceded by dry cough only, but PCR for SARS-CoV-2 and myelin oligodendrocyte glycoprotein (MOG) antibody were positive [109]. Almost at the same time, Sawalha et al. reported the second case report presented MOG-optic neuritis preceded by respiratory manifestations and COVID-19 PCR test positive [110]. The third report was well documented and presented a combination of COVID-19, optic neuritis, and symptoms of multiple sclerosis [111].

In a group of patients with MOG-associated and MS-associated optic neuritis, and acute disseminated encephalomyelitis, the relationship between postinfectious demyelinating syndromes para infectious diseases and viral prodrome has been well documented in the literature [112-114], and molecular mimicry is the unanimous accepted mechanism by other authors which explain how viral antigens stimulate a remarkable immune response against endogenous CNS proteins including myelin and MOG [114]. Last year, Zhou et al. reported a case infected by SARS-CoV-2 who developed MOG-IgG-related myelitis and optic neuritis, highlighting the potential of this virus on autoantibody production [115]

As confirmed, Covid-19 patients requiring prone positioning to improve their oxygenation receive its benefits, but patients in extended periods of prone positioning developing multisystem side effects have been reported. Among those complications is orbital compartment syndrome due to direct pressure on the globe and orbit because of lack of cushion eye protection [116,117] aggravating the inflammation of the optic nerves. One of these investigators reported two patients presenting orbital compartment syndrome after 18 hours of prone positioning in ICU. Both cases developed severe intraocular pressure, swelling of the optic disk and retinal haemorrhages secondary to COVID-19 coagulopathy [116]. Although there is no report of COVID-19 ischemic optic neuropathy (ION) due to prone positioning, it is having been well documented that prone positioning combined with systemic hypotension from iatrogenic aetiology of sepsis leads to ION. Therefore, this knowledge must be keeping in mind to avoid this complication [117] (Figure 5).
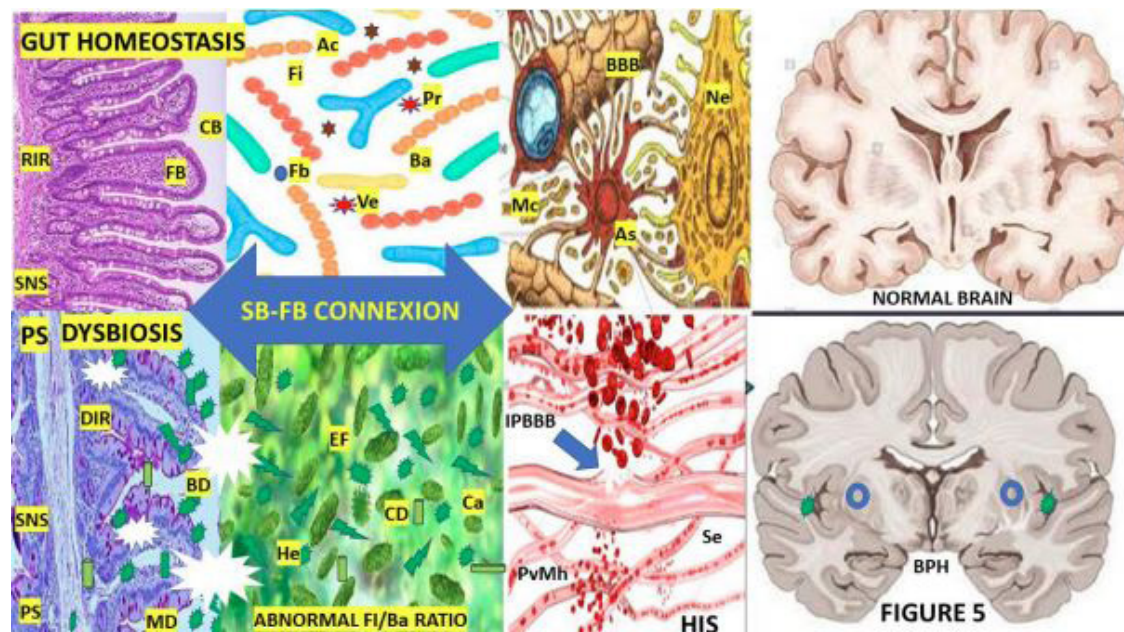
Figure 5. Graphical illustration of normal relationship between good microbiotas and normal brain (superior part) and ICH (BPH) secondary to dysbiosis in the inferior part of the figure. CO-commensal bacteria, RIR-regulated immune system, FB-functional barrier, GH- gut homeostasis, MD-microbial dysbiosis, BBB-blood-brain-barrier, BD-barrier defect, D-dysbiosis, PS-prolonged stress, DIR-dysregulated immune response, Fi-Firmicutes, Ba-Bacteroidetes, Ac-Actinobacteria, Pr-Proteobacteria, Fb-Fusobacteria, Ve-Verrucomicrobia, EF-Enterococcus faecalis, Ca-Campylobacter, He-Helicobacter, CD-Clostridium difficile, Se-serotonin; Do-dopamine, Ne-neurons, As-astrocytes, Mc-microglia, PvMh-perivascular microhaemorrhage, FB-first brain CNS), SB-second brain (enteric nervous system), BPH-bilateral putaminal haemorrhage, IPBBB-increased permeability of BBB, HIS-hyperinflammatory state.

Another group of COVID-19 cases presenting severe bilateral blindness, transient cortical blindness, papillophlebitis, and other ophthalmic manifestations of COVID-19 have been published [118-120] While; other authors did not find an association between ocular symptoms and COVID-19 in their outpatient population [121, 122]. Nonetheless, most of the publications confirmed the association of optic neuritis associated and COVID-19. In the process of molecular mimicry, most viral antigens induce an immune response against self-proteins causing tissue injury [123].

The presence of SARS-CoV-2 RNA in tear, conjunctival secretions, and conjunctival swabs confirms the SARS-CoV-2 entry to the globe through ocular's receptors [124,125], which vigorously promote the use of eye protection for health workers and everybody at risk of infection.

Finally, to comment that COVID blindness has been reported because of unjustified confirmation delay of aseptic meningitis and its therapy similar to anchoring bias [126]. The role of ACE2 receptor in the mechanism of cellular invasion by SARS-CoV-2 has been described before [104]. Therefore, now we will highlight the great importance of CD147 on the mechanism of cell entry. CD147, a plasma membrane protein known as Basigin or extracellular matrix metalloproteinase inducer (EMMPRIN), has two subtypes (1-2). The type 1 is commonly expressed in the surface of cone and rod visual receptors apart from its expression in the endothelium and epithelium of the conjunctiva and cornea, which also serve to understand why conjunctivitis as a complication of COVID-19 remains in 0.8% to 31.6% of COVID-19 patients plus other ocular complications including retinopathies [127,128].

Our literature review findings and other colleagues confirm the relationship between neuro-ophthalmological disorders and SARS-CoV-2, and we hope it will serve to encourage our colleagues for keeping a higher index of suspicion to investigate for concomitant SARS-CoV-19 infection in all probable cases, at least during the current pandemic considering that when they develop these neuro-ophthalmological manifestations most of them have little or no respiratory manifestations, like our case. In figure 4, we illustrate our proposed mechanism for SARS-CoV-2 neuro-ophthalmological manifestations [129,130].

Cerebrovascular diseases and dysbiosis: Even in patients without risk factors of arterial hypertension or anticoagulation treatment, ICH can be seen with or without SARS-CoV-2 infection as it's commonly seen in daily medical practice. Also, in patients presenting IS with or without COVID-19 secondary sinus venous thrombosis, revascularization therapy or to hemorrhagic transformation of embolic stroke among other causes. The takeaway knowledge here is the relationship between modified microbiome and ICH. First, it is important to highlight that prolonged stress is the most common cause of dysbiosis as we discussed recently [104].

Eight phyla of bacteria such as Proteobacteria, Actinobacteria, Firmicutes, Bacteroidetes, Spirochaetes, Tenericutes Deferribacteraceae, and Verrucomicrobia are the components grouped in phyla of bacteria [131] among one hundred trillion of microorganisms are living in our body. Some of these bacteria are shown in Figure 4.

Unfortunately, the medical research community ignored the role of microbiome for so many years, and microbiotas did not take the scientific attention they deserved. More than fifteen peer-reviewed medical journals have recently established two predominant groups in the microbial composition: Firmicutes and Bacteroidetes in humans/mice. The balance between these two groups is relevant in modulating the immune system, among other functions [132]. It has been proved that the abundance of phylum Firmicutes is an independent predictor for stroke risk [133,134], and a high Firmicutes/Bacteroidetes ratio/brainstem damage are firmly related, leading to most flawed neurological recovery and a higher fatal outcome. Firmicutes is the most significant component phylum present in stroke patients [135,136]. We found publications searching the medical literature suggesting stroke-induced altered microbial composition, gut dysbiosis worsens post-stroke outcome [137], and this mechanism in haemorrhagic stroke patients will be explained later.

Gut dysbiosis affects the lungs, brainstem and vice versa through the gut-microbiota-lung-brain axis [132], and other researchers have proved that ischemic stroke (IS) and intracerebral haemorrhage (ICH) stroke raise gut permeability, inducing bacterial translocation from the microbiome to mesenteric lymph nodes, lungs, livers, and spleens, leading to a high risk of infection secondary to gut dysbiosis (see Figure 4). On the other hand, a remarkable depletion of gut microbiota is seen in the gastrointestinal tract after stroke, while a relevant increased concentration of gut microbiota is

seen in the ling parenchymal of post-stroke mice. The same authors found that dysbiosis was caused by a stroke following by subsequence injury of the barrier defence/immune system and selectively leads to an elevated vascular permeability in the jejunum and ileum, increasing gut permeability in post-stroke mice [138]. Singh et al. [139] proved that Actinobacteria modulate post-stroke gut dysbiosis, while Bacteroidetes and Firmicutes, play an essential role in the pathogenesis of some neurological conditions. Haak et al. [140] concluded that increased abundance of Proteobacteria is present in stroke patients while levels of Firmicutes and Bacteroidetes (more than 90% of the microbial composition) were diminished.

Notwithstanding, the elevation of proinflammatory cytokine, chemokine, TNFα, macrophage inflammatory protein 1, interferon γ and other components from leukocytes infiltration, activated astrocytes, activated microglial other proinflammatory elements have been included in the pathogenesis of the cytokine realise inflammatory syndrome process causing damage on the cells and blood vessels, apart from the direct endothelial damage caused by dysbiosis leading to increase permeability of blood brain barrier (See figure 4) It has been confirmed that increased TNF-α, IL-6, CCL5 and Eotaxin are also present in mice with aged microbiota after stroke. Other investigators demonstrated an elevated IL-6 level in both young and aged mice after stroke. However, that level was highest in aged mice with a negative correlation between serum lipopolysaccharide-binding protein levels and the effects of ageing, leading to the enormous frequency of associated sepsis due to decreased level of immunity [141]. Three years back, Xia et al. discovered that leucocytosis is an independent predictor of severe stroke with a fatal prognosis after stroke [142]. In addition, the association between microbiota-derived metabolites, such as short-chain fatty acids, trimethylamine-N-oxide, and stroke, have been reported [143].

Augmented Firmicutes/Bacteroidetes ratio is crucial for ageing and dysbiosis. Furthermore, it worsened the neurological condition after IS, increasing the mortality rate in mice, and it has been associated with the risk factors of IS, such as hypertension, obesity, diabetes mellitus, and elevated D-diarmer. On the other hand, stroke reduces gut barrier permeability, allowing microbial travel through the gut-brain axis to the lateral wall of the medulla oblongata. As mentioned before, modifications in the gut-microbiota composition alter the equilibrium between gut-immune-homeostasis, and consequently lymphocytes move from the intestine to the brain [132].

These authors studied the relationship between microbiota alteration, ICH, and immune responses after hematoma-induced acute brain injury in a mouse model of ICH. They confirmed that ICH causes gut microbiota dysbiosis, aggravating the ICH outcome through the immune-mediated process. Furthermore, they found a prominently reduced species variability and microbiota overgrowth in the dysbiosis induced by ICH, reducing intestinal motility and increased gut permeability. In conclusion, gut microbiota imbalance leads to proinflammatory response induction, changes in T cell homeostasis, and poor outcome. On the other hand, recolonising ICH in animals with healthy microbiotas improved almost all functional deficits, neurobehavioral functions, and neuroinflammation post-ICH [144]. Because gut microbiota dysbiosis after ICH contributes to neuroinflammation by affecting T cell homeostasis, it is crucial to keep it in mind before selecting the best therapy including microbiota transplantation to ameliorate ICH-induced brain damage.

Conclusion

After a wide searching of available medical literature and detailed discussion, we concluded that our reported case is an atypical presentation of BPH, and blindness of unknown cause probably related with COVID-19 until proven otherwise.

Our review of the medical literature concluded that MRI is the best investigation to assess basal ganglia pathologies due to its superior contrast resolution. Nonetheless, CT has a relevant role in detecting calcification

while SW-MRI has poor accuracy [74], but when only one study is possible, SW-MRI is the best choice [75].

We have hypothesized that in our patient SARS-CoV-2 invade the CNS through afferent glossopharyngeal sensory cells by binding to ACE-2/Znl receptors and from here the virus moved to the lateral wall of medulla oblongata and posterior dissemination across the brain and consequent epithelial/endothelial damage/disruption of BBB/ICH.

We also concluded that in times of COVID-19 pandemic, all neuro-ophthalmological presentation (even with PCR negative) must be excluded from the extended list of clinical manifestations of SARS-CoV-2 infection-related and keeping in mind that most patients do not have respiratory symptoms.

Based on revised articles, we have hypothesised that in times of coronavirus pandemic, peoples under severe and prolonged stress are more prompt to develop abnormal microbiome composition and dysfunctional immune system facilitating the acquisition of SARS-CoV-2 infection and an associated vascular damage-causing cerebrovascular diseases which aggravate neuroinflammation in one way. On the other hand, in a reverse way, COVID-19 cerebrovascular disease causes dysbiosis, worsening neuroinflammation. On top of that, our review also supports that blindness secondary to SARS-CoV-2 optic neuritis by ischemia or demyelination is certain.

Further research is warranted to confirm a potential association between ICH/blindness/SARS-CoV-2 infection and the role played by microbiomes. Therefore, new studies must be done to support or reject this hypothesis or another one that best manages the ongoing COVID-19 pandemic and its SARS-CoV-2 mutations.

This is the first case of bilateral putaminal haemorrhage and reversible prequiasmatic blindness reported in the medical literature in times of coronavirus pandemic and dysbiosis, as far as we know.

Ethical Approval and Consent to Participate

Competing Interest

Funding

Declaration of Anonymity

The author certifies that he did not reveal the names, surnames, initials, or other identity issues of this case in this publication, and complete anonymity is guaranteed.

Availability of Data and Material

The data that support the findings of this study are available on reasonable request from the corresponding author.

Competing Interests

The author declares that he has no identifiable competing interests.

Data Availability

Acknowledgement

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