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Case Report

Unusual and Rare Ocular Findings of Neurofibromatosis 1: A Case Study

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Abstract

Neurofibromatosis type 1 (NF1) also known as Von Recklinghausen disease, is an autosomal dominantly inherited multisystem neurocutaneous disorder, with approximate incidence of 1:3500 [1]. Recklinghausen's disease characterized by flat, light brown spots on the skin (café-au-lait spots), axillary freckling, neurofibromas, Lisch nodules of iris, skeletal dysplasias, gliomas and various systemic vascular ischemic manifestations mainly in the aorta, brain and kidney [2,3].

Keywords: *Neurofibromatosis Type 1 (NF1); Lisch Nodules*

Introduction

Clinical diagnosis based on presence of 2 or more major criteria: at least having 6 or more café au lait spots is a strong indication of NF1, inguinal and/or axillary freckling, 2 or more soft bumps on or under the skin (cutaneous neurofibromas), 1 plexiform neurofibroma, characteristic osseous lesions (such as thinning of long bone cortex or sphenoid wing hypoplasia, with or without pseudarthrosis), an optic glioma, 2 or more iris Lisch nodules (iris hamartomas) [4].

However, it is known from the literature that the phenotypic variability can pose a huge diagnostic difficulty. NF1 represents a major risk factor for development of peripheral (neurofibromas, malignant peripheral nerve sheath tumors) and central (optic pathway glioma, malignant glioma) nervous system tumors [4].

NF1 may present with a variety of ophthalmic manifestations. However, in most patients with NF1 retinal and choroidal lesions had been considered unusual. Rare ocular findings include multiple choroidal nevi, combined hamartoma, choroidal schwannoma, myelinated nerve fibers, choroidal melanoma, retinal vasoproliferative tumor, (RVPT) [5-7]. Early detection of RVPTs and prompt initiation of treatment may prevent severe vision loss and blindness. Few cases with retinal vascular occlusive disease have been described [8-11]. Cases with peripheral retinal ischemia and neovascular glaucoma have also been recently described [12,13].

We describe a case of young Belorussian men suffered from NF-1 manifested primarily with macula on recurrent rhegmatogenous unilateral retinal detachment accompanied with retinal dialysis of right eye, recently detected preretinal hemorrhage of right eye, chorioretinitis of left eye, proptosis and glaucoma of both eyes. Brain and spinal cord with multiple tumors, accompanied with tumors in oculomotor muscles-OU.

To our knowledge, this is the first report in literature of macula on recurrent unilateral retinal detachment with retinal dialysis in NF1 associated with exudative retinopathy, without vasoproliferative tumours of the retina (VPTR), optic nerve gliomas, or other retinal

tumors which may be accompanied by the development of tractional retinal detachment, vitreous hemorrhage and proliferative vitreoretinopathy in patients with NF [14-16].

He had never been expose to ocular trauma or detected to have any preexisting factors that could cause retinal detachment in the age of 19.

Since the coexistence of recurrent macula on rhegmatogenous retinal detachment associated with retinal dialysis and NF1 is rare, this case provided us unique chance to examine the relationship between recurrent macula on retinal detachment without characteristic causative factors of retinal detachment in NF1 patient.

The goal of this case is to review our personal experience of unusual ocular presentation of NF1 firstly manifested with ocular and dermatologic symptoms, and additionally recently detected MRT finding: involvement of brain, spinal cord and oculomotor muscles with numerous tumors.

Case Report

A 22 year old male with neurofibromatosis type 1 after his routine annual eye examinations due to systemic risk factors was referred to department of ophthalmology of city clinical hospital №10 Minsk, Belarus. He was diagnosed with NF-1 according to the criteria of National Institutes of Health in childhood [4]. Patient had no visual symptoms. On ophthalmological examination his VA: OD = 0,3 sph-1,5 = 1,0 OS = 1,0.

The results of the physical and ophthalmologic examination: Patient is 22 year old man accountant. Body weight 60 kg, height 189 cm. Body temperature 36.6°C. Arterial blood pressure 120/70 mm/Hg. heart rate 68.

Physical Examination revealed more than 25 different size café au lait spots throughout the body, especially on the face and back region, freckles in the axillary and inguinal region, large head size, scoliosis with kyphosis, mental status did not obtain any attention deficit, hyperactive disorder, social anxiety disorder or learning disabilities. Intelligence was normal, no history of headache, Seizures, or brain Tumors. Young male was systemically well, on no medications. Was born at full term with a birth weight of 2500g.

Figure 1 shows scattered flat patches on the skin that are darker than the surrounding area “cafe-au-lait” spots are visible on the back and upper limb region. The biggest skin tumor is approximately 3,9 cm in diameter at the back.

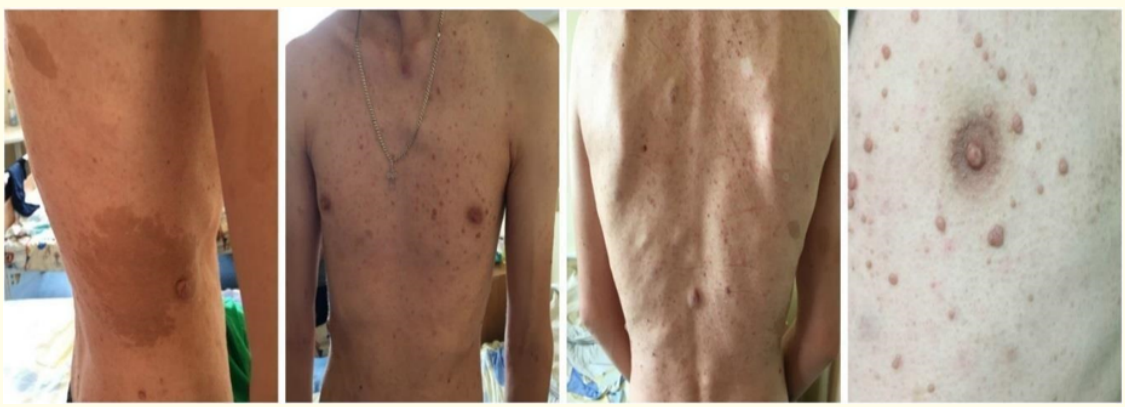

Figure 1

Laboratory investigations such as sedimentation rate, WBC count, red blood cell count, hemoglobin and hematocrit, platelet count and fasting blood glucose, coagulation profile, chest X-ray, Mantoux test, rheumatoid factor and anti-nuclear antibody within normal limits. Non-invasive Doppler flow study of carotid arteries did not show any stenosis.

Past medical history

The disease was diagnosed in childhood when hyperpigmented skin plaques in his back region became remarkable. At the age of 4 a lot of cutaneous tumors appeared and started growing bigger all over the body surface. After this, he was referred for routine ophthalmological assessment once a year. In 2013 on regular follow up at the age of 19, during his annual eye exam detailed fundus examination was performed, and rhegmatogenous retinal detachment was visualized. To confirm the diagnosis B-scan was performed which confirm retinal detachment of the right eye H-2, 06 mm.

Patient was hospitalized with visual acuity OD = 1,0, OS = 1,0. We explained the diagnosis in details to the patient. Informed consent was obtained for cerclage + scleral buckling surgery on the right eye.

Scleral buckling surgery was performed successfully. Two-month postoperatively, full anatomical and functional success was reached with visual acuity was OD = 0,4 sph-3,5 = 1,0 OS = 1,0. The patient was followed for a year with no further progression or worsening of his ocular findings.

In 2014 during next annual eye exam visual acuity was OD = 0,4 sph-3,5 = 1,0 OS = 1,0. In dilated fundus examination recurrent macula on rhegmatogenous retinal detachment without new breaks was detected. B-scan confirmed retinal detachment with H-1.62 mm. We achieve clinical course of the patient with corticosteroid therapy and after week laser coagulation was performed. Four weeks after laser coagulation and corticosteroid therapy full anatomical and functional success was reached.

In 2016 during next ophthalmological examination patients visual acuity was OD = 0,3 sph-1,5 = 1,0 OS = 1,0. Intraocular pressure OD = 30 mmHg, OS = 20 mmHg.

Slit-lamp examination

Lacrimal system: Normal anatomy and contours. Conjunctiva/sclera: White and quiet. Cornea: Clear.

Anterior chamber: normal. Iris: dome-shaped brown elevations projecting from the surface of the iris (Multiple Lisch nodules) bilaterally. Pupillary reactions: normal. Color vision: normal; The anterior chamber was within normal limits in both eyes, without neovascularization.

Both eyes with Lisch nodules (Figure 2). The left eye otherwise within normal limits. Colour vision was normal in both eyes and confrontation fields showed mid peripheral constriction of right eye.

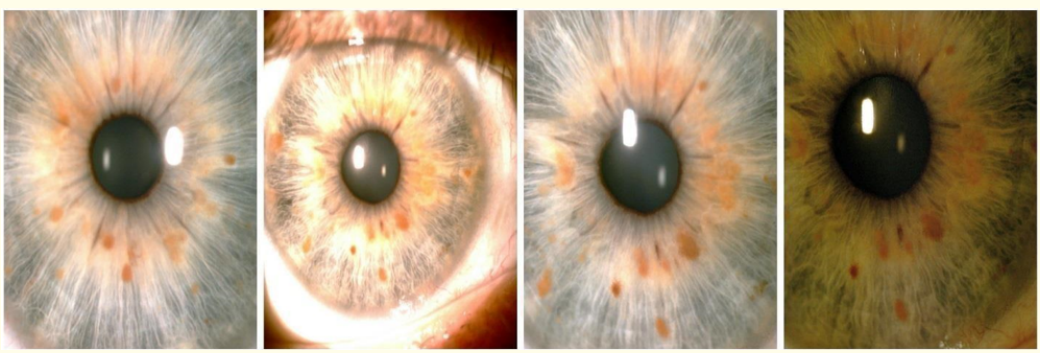

Figure 2

Normal papillary light reflexes, symmetrical pupils, no relative afferent pupillary defect, extrinsic muscles without alterations.

B-scan ultrasound of right eye showed subtotal retinal detachment h-3,31 mm.

Fundus examination showed a superior retinal detachment of upper nasal segment and extensive retinal pigment epithelial (RPE) dystrophy of right eye (Figure 3). Fundus examination revealed no retinal breaks. The detached area was within the area where the visual field was lost, and we observed a clinical course of this eye without any surgical intervention. Retinal detachment was kept localized and not extended.

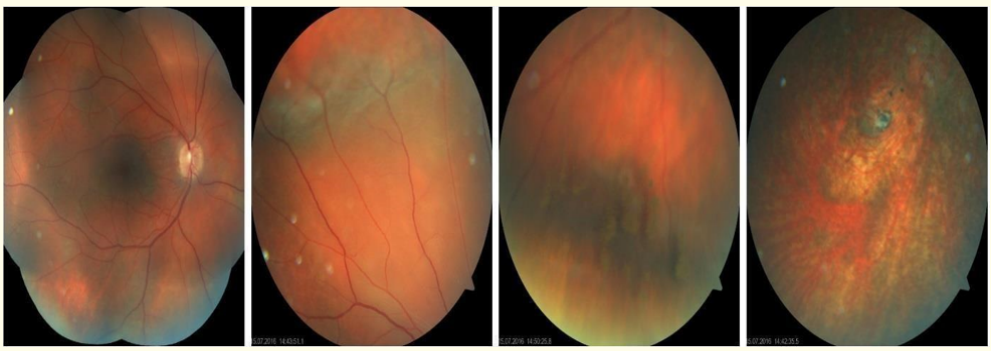

Figure 3

To confirm the macula status, an optical coherence tomography (OCT) was performed that revealed a macula-on retinal detachment of the right eye. Changes seen in the OCT scan were characteristic of an local retinal detachment of retinal neuroepithelium in upper nasal segment segments OD.

Fundus autofluorescence imaging and 3D OCT -confirmed retinal detachment of retinal neuro epithelium in upper nasal segment of the right eye (Figure 4). The fundus fluorescein angiography of both eyes showed a normal arm-retina time with normal filling of all vessels. The left eye was within normal ranges except for neurochorioretinitis in remission.

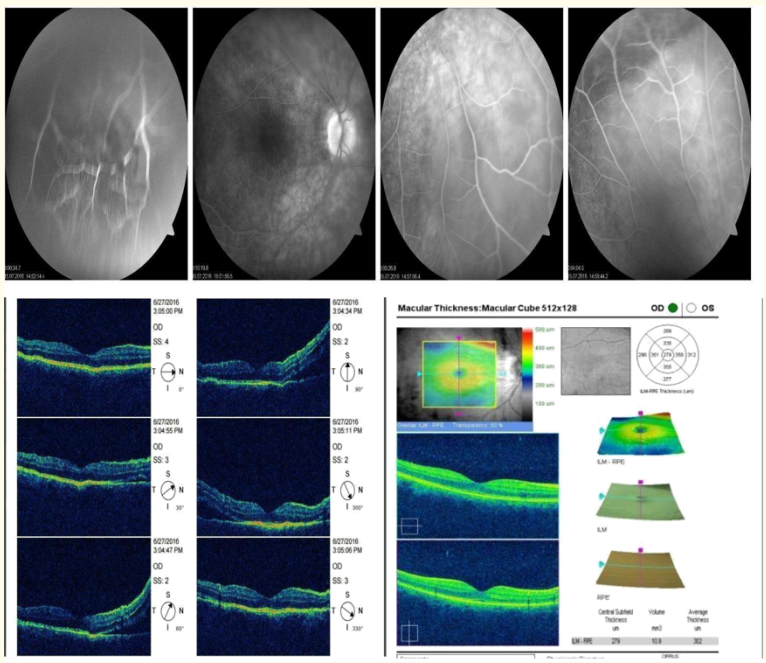

Figure 4

Magnetic resonance imaging (MRI) of brain/orbits of our patient has revealed focal areas of high signal intensity on T2-weighted images of brain and cervical region (Figure 5). An MRI scan of his head and cervical regions revealed several extra medullar tumors in C1-C2 level and several brain tumors, which suggested neurofibromatosis [17]. Rare finding what we determined on his cranial MRI scan was tumors on his oculomotor muscles-OU (Figure 5).

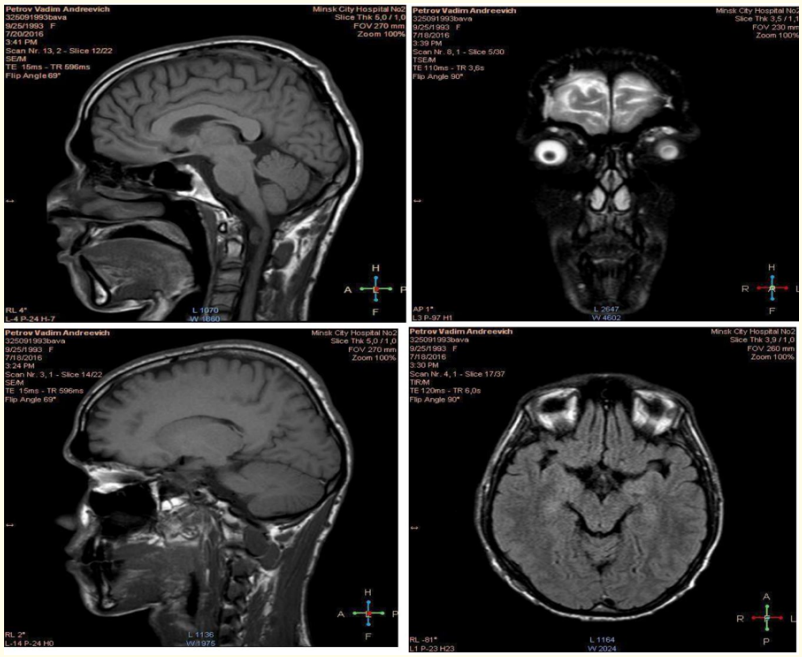

Figure 5

Discussion

Ocular manifestations of NF1, caused by genetic abnormalities on chromosome 17, include iris (Lisch) nodules, congenital glaucoma, optic nerve gliomas, plexiform neurofibromas of the eyelids, uveal hamartomas, and, rarely, retinal lesions [18-21]. NF1 is a variable condition, with different manifestations between patients, some of them have only very mild manifestations, whereas others are severely affected [22-24]. There is no consistency in manifestations within a pedigree. Family history of our patient did not reveal any members with NF1.

According medical history of our patient, Café-au-lait spots and externally visible plexiform neurofibromas was apparent within the first year of life. Dermatologic manifestations of our patient became apparent at the age of fourth. Freckling, scoliosis with kyphosis occurred by 7 years of age, head size larger than normal was noticed during this period of life. Usually, spinal deformities is seen in more than 50% of patients with NF1. Scoliosis is the most common skeletal complication, affecting 21% of patients with NF1 [25].

Most frequent ophthalmic manifestation of NF1 include Lisch nodules of the iris, plexiform neurofibromas of the eyelids, congenital glaucoma, optic glioma, retinal astrocytic hamartomas, retinal capillary hemangiomas and microvascular retinal abnormalities [26]. Findings in the fundus include retinal astrocytic hamartomas, choroidal hamartomas, combined retinal and retinal pigment epithelial hamartomas, retinal capillary hemangiomas [19]. Retinal hamartomas occur in a small percent of patients, sometimes causing retinal dialysis and traction retinal detachment [27]. Cutaneous neurofibromas and iris Lisch nodules are unusual before 2 years of age. We detected Lisch nodules of our patient when he was 20. Malignancies are mostly problems of adults [28-33].

During recent MRT (2016) we detected multiple tumors of brain, spinal cord and oculomotor muscles. In patients with NF1 glaucoma is not common diagnosis but may be present at birth or in early childhood. The most common cause is obstruction of the aqueous drai-

nage pathway and neurofibromatous infiltration [34-38]. Neurofibromatous infiltration of the ciliary body may cause secondary angle closure glaucoma. Diagnosis of glaucoma of our patient was confirmed in 2016. The remarkable feature of our case is the rare and unusual ocular manifestations, presented mainly with unilateral recurrent macula on retinal detachment with retinal dialysis and without preexisting factors that could cause retinal detachment in our patients with NF1. Preretinal hemorrhage of the right eye which was detected in 2016 by fundus examination, was confirmed on last MRT scan. We think that it is possible this preretinal hemorrhage may be the manifestation of exudative retinopathy.

The differentiation between recurrent macula on rhegmatogenous retinal detachment due to retinal dialysis or recurrent macula on rhegmatogenous retinal detachment due to exudative retinopathy in this case is very difficult. We favour the diagnosis of recurrent macula on rhegmatogenous retinal detachment due to exudative retinopathy according the following ocular expression of our patient: 1. Full anatomical and functional success was managed by scleral buckling surgery in 2013. 2. Full anatomical and functional success was reached in 2014 after corticosteroid treatment and laser coagulation and in 2016 after only corticosteroid treatment. 3. Not in 2014 nor in 2016 we can‘t determine any other new retinal breaks or proliferative vitreoretinopathy.

Recurrent macula on rhegmatogenous retinal detachment due to exudative retinopathy was the very unusual presentation of NF1 because of the lack this manifestation in literature we can’t surely said this is recurrent retinal detachment with exudative retinopathy or this is manifestation of retina with retinal dialysis in patient with NF type 1.

We observed a clinical course of the patient without any additional surgical treatment. Corticosteroid therapy was then applied to the detachment. By four weeks after corticosteroid therapy, reabsorption of subretinal fluid and visual acuity improvement were noted. With the increasing knowledge of neurofibromatosis, more attention is paid to the ocular manifestations of this disease. Through literature review, we summarized the ocular findings in type 1 neurofibromatosis. Unfortunately, some of the signs are limited to case reports, with a lack of occurrence data based on population studies.

Early and regular ophthalmological assessment of all NF1 suspect/confirmed cases is of paramount importance in order to detect related and unrelated ocular manifestation in patients with NF1, resulting in timely intervention and salvage of vision. Different complications occur at specific times and some complications worsen over time. It is important to pay attention to ocular signs at an early age in neurofibromatosis patients in order to preserve good visual quality by administering the proper treatment. According most authors annual eye examinations by a pediatric ophthalmologist are essential until 10 years of age. But we think our case clearly demonstrate that it is very important to continue annual dilated fundus eye examination of all patients with NF-1 even if patient is asymptomatic with 20/20 vision to rule out such retinal manifestations as we meet in our patient throughout their entire life Because eye manifestation in NF1 can be detected at any age. This case serves as a reminder of phenotypic variability and expands the potential presenting profile for neurofibromatosis type 1 (NF1).

Conclusion

To the best of our knowledge, this is the first report to ever be published in the literature of a patient with NF 1 presented with macula on recurrent rhegmatogenous retinal detachment due to retinal dialysis, and associated exudative retinopathy without preexisting or existing factors such as vasoproliferative tumours of the retina (VPTR), optic nerve gliomas, or other retinal tumors which may be accompanied by the development of a vitreous hemorrhage, tractional retinal detachment, and proliferative vitreoretinopathy in patients with NF.

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None of the authors has a financial or proprietary interest in any materials or methods mentioned.

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