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A Study of Ocular Manifestations in Neurocutaneous Syndromes

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INTRODUCTION

Phakomatosis (from the Greek 'Phakos' meaning mother spot or mole or freckle) is a group of hereditary disorders characterized by the presence of hamartias and hamartomas involving different organ systems derived from all the three embryonic layers.

The term phakomatosis was coined in 1920 by Van der Hoeve.

Four classical syndromes included in phakomatosis are

1) Neurofibromatosis - I (Von Recklinghausen disease) & Neurofibromatosis - II
2) Tuberous sclerosis (Bourneville disease)
3) Angiomatosis retinae (Von Hippel-Lindau disease)
4) Encephalofacial angiomatosis (Sturge Weber syndrome)

Other phakomatoses or neurocutaneous syndromes include

1) Ataxia telangiectasia (Louis – Bar Syndrome)
2) Hypomelanosis of Ito (Incontinentia pigmenti)
3) Xeroderma pigmentosum
4) Cockayne syndrome
5) Gorlin syndrome
6) Sjogren –Larsson syndrome
7) Proteus syndrome
8) Menke's syndrome
9) Wyburn Mason syndrome
10) Klippel – Trenaunay – weber syndrome

LITERATURE REVIEW

GENETICS AND PREVALENCE

Neuro fibromatosis I - Autosomal Dominant (17q 11.2)
50% cases new mutations
1 in 3000 live births
Male: Female - 1:1

Neurofibromatosis II - Autosomal Dominant (22q 12)
1 in 40,000 live births

Male : Female - 1:1

Tuberous sclerosis - Autosomal dominant (9q 34; 16p 13.3) 1 in 10,000 prevalence

Sturge weber - Congenital and sporadic No chromosome abnormality

Von Hippel Lindau - Autosomal Dominant (3p 25-26)

Ataxia telangiectasia - Autosomal Recessive (11q 22q 23)

Hypomelanosis of Ito - Sporadic; 50% chromosomal problem (mosaicism, translocation)

Xeroderma pigmentosum- Autosomal recessive

Cockayne syndrome Autosomal recessive

Gorlin syndrome - Autosomal dominant

Menke's syndrome - X –linked recessive (Xq 13.3)

Sjogren Larsson syndrome - Autosomal recessive (17p)

PATHOLOGY

In general, pathology of phakomatosis include

a) Hamartias – Non tumourous growths on the skin or mucous membrane that arise from cells normally found in the tissue at the involved site. Eg. Congenital vascular malformations of ataxia telangiectasia.

b) Hamartomas - Localised tumours arising from cells normally found at the site of growth eg. Glial tumours of tuberous sclerosis & Lisch nodules (melanocytic hamartomas) of NF-I

c) True neoplasms – originate from undifferentiated embryonic cells or differentiated mature cells.

Phakomatosis may be differentiated embryologically depending on the germ layer affected. For eg. Neuro fibromatosis and tuberous sclerosis are neuro ectodermal dysplasias whereas sturge weber and Von Hippel Lindau are mesodermal disorders.

DIAGNOSTIC CRITERIA OF THE FOUR CLASSICAL SYNDROMES

NEUROFIBROMATOSIS - TYPE – I

Diagnostic criteria for Neuro fibromatosis type I (from national Institutes of Health Consensus Development Conference (1998). Neurofibromatosis conference statement. Arch. Neural., 45, 575-8)

Two or more of :

1. Six or more café-au-lait macules measuring – 5 mm in greatest diameter in prepubertal individuals and – 15 mm in greatest diameter in post-pubertal individuals
2. Axillary or inguinal freckling
3. Two or more dermal neurofibromas
4. A plexiform neurofibroma
5. A first – degree relative with NF1 (by the NIH consensus statement criteria)
6. Optic nerve glioma
7. Two or more Lisch nodules
8. A distinctive osseous lesion (eg. Sphenoid dysplasia or thinning of the long bone cortex)

a. with or without pseudoarthrosis

NEUROFIBROMATOSIS TYPE – II

Bilateral acoustic neuromas; or a first-degree relative with NF2 and either a unilateral acoustic neuroma, neurofibroma, glioma, meningioma, schwannoma, or early onset lens opacity. The severity of phenotypes can be defined by age of onset of symptoms (<20 years versus > 20 years), number of associated intracranial tumours (<2 tumours versus >2 tumours), and whether spinal tumours are present or absent (Evan et al. 1992a; Parry et al. 1994).

TUBEROUS SCLEROSIS

Diagnostic criteria for tuberous sclerosis (from Osbourne, J.P. and Fryer A.E.(1991). Tuberous sclerosis (epiloia, Bourneville's disease). In clinical neurology, (ed. M. Swash and J. Oxbury), p. 1256. Churchill Livingstone, Edinburgh)

One major or two minor criteria :

Major Criteria :

1. Definite shagreen patch
2. Subungual fibroma
3. Retinal hamartomas
4. Adenoma Sebaceum
5. Bilateral multiple renal angiomyolipomas
6. Subependymal glial nodules on CT/MRI

Minor criteria :

1. Atypical shagreen patch
2. Hypomelanocytic macules
3. Gingival fibromas
4. Bilateral polycystic kidneys
5. Single renal angiomyolipoma
6. Cardiac rhabdomyoma
7. Histological evidence of a cortical tuber
8. Honeycomb lung on x ray
9. Infantile spasms
10. Forehead fibrous plaques
11. Giant cell astrocytoma
12. A first degree relative with tuberous sclerosis

VON HIPPEL LINDAU DISEASE

Diagnostic criteria for VHL are :

i. evidence of more than one haemangioblastoma in the central nervous system or retina.

ii. Two types of tumours commonly found in VHL in the same patient (e.g. cerebellar haemangioblastoma and renal carcinoma) ; or

iii. A typical tumour related to VHL and a family history of VHL

STURGE WEBER SYNDROME

Characteristic 'port-wine' facial naevus or angioma and underlying leptomeningeal angioma / choroidal haemangioma +

Congenital glaucoma + Cutaneous vascularity with over growth of underlying connective tissue and bone.

Face + leptomeniges + eyes involved – trisystem

Face + leptomeniges or eye - bi system

CLINICAL FEATURES

NEUROFIBROMATOSIS – I

OCULAR FEATURES

I - Disorders of Motility

1. Strabismus (New man & cogen 1997)

a) Infiltration of extra ocular muscle (EOM) by tumour

b) compression of EOM by tumour

c) congenital absence of EOM

2. Ocular Motor Apraxia (Glower and Powe 1985 – 1 child)

II Orbit

1. Orbital neurofibroma

Orbital neurofibromas are rare accounting for 0.5 – 2.4% of all orbital tumours. Berney and spahn report a case of multiple intraorbital neurofibromas in a 82 year old woman without type –I NF. But orbital neuro fibromas are also seen in association withNF-I

2. Orbital bone defect :

a. Acquired erosion – due to growing NF tumour

b. congenital defect (Gurland 1936) posterior and superior wall (Savino 1977, Freeman 1987)

Cause proptosis with pulsation Sphenoid bone (Macfarlane 1995)

Enophthalmos

III Optic Nerve and Chiasma

1. optic Nerve glioma (Lewis 1985) – 15-20 % of NF-I cases

Usually Bilateral
Non progressive
Usually asymptomatic
Proptosis
Strabismus
Papilloedema
Optic atrophy
Subluxation of globe

Chiasmal Gliomas (Kohira and Yoshimura)

Endocrine abnormality due to tumour extension

Optic nerve sheath meningioma

Opticociliary shunt vessels

IV Eye lid

1. Plexiform neurofibroma (Farris and Grove 1996) commonly involve upper eyelid and temple

can cause proptosis and ptosis.
50% chance of developing glaucoma in ipsilateral eye
(Anderson sign)

2. Nodular neurofibroma
3. Congenital ptosis

V - Conjunctiva

Hamartomas (Font and Ferry 1972)
Mostly limbal and perilimbal
Firm
non tender
fixed in positions
covered by normal epithelium

VI Cornea

a. Neurofibroma (Kobrin 1979)

Central and peripheral

b. Enlarged / thickened corneal nerves –

Lignes grises (Braley 1954)
Should rule out multiple endocrine neoplasias

VII Uvea

a) Lisch Nodules (after karl Lisch 1907-1999) – Australian ophthalmologist
Term coined by Freidrich.C. Blodi
Projects from iris surface (Lisch 1937)
Pigmented (brown / yellow / white) – (Lubset 1998)
Initially unilateral then bilateral (Lewis 1981)
Multiple (Riccardi 1981)
In 10% < 6 years; 50% by 3rd decade (Lewis, Riccardi, 1981)
Seen even without slit lamp in 88-100% by 40 years – (Lubus 1981, Riccardi 1981).
Histologically composed of melanocytic hamartomas. Richetta and Giustini (2004) hypothesized that Lisch nodules are compatible with neurofibroma, histologically composed of 3 cell types – pigmented cells, fibroblast like cells and mast cells.

b) Iris mammillations :
Tiny, regularly spaced villiform lesions, May also be a sign of ocular hypertension or intraocular malignancy
c) Congenital ectropion uveae
d) NF of ciliary body and choroid (callander, Freeman 1934) can cause glaucoma
e) Thickening of entire uvea
f) Choroidal naevi
g) choroidal folds

VII - Glaucoma

(Grant and Watson 1968)
Congenital glaucoma in 50% cases of upper lid plexiform neuro fibromatosis (Anderson 1939)

Causes of Glaucoma :

1. Anterior insertion of iris
2. Trabecular meshwork covered by a membrane
3. Neurofibromatosis tissue replacing trab. (Eagle 1979)
4. Neurofibroma involving ciliary body causing thickening, forward rotation.

Study of 42 eyes by Quaranta and Turan showed mild anteriorization of iris in 29 (69%). The ciliary body was invisible in 54.84% or very narrow in 21.4%. 3 had bilateral juvenile congenital glaucoma. Abundant iris processes were also noted.

IX - Fundus

1) Papilloedema
   Intracranial tumour
   Aqueductal stenosis
2) Sectoral pigmentary disturbance (Lapinna 1977)
3) Hamartomas of RPE and retina (Destro 1991)
4) Cafe-au lait spot like areas (Cotlier 1977)
5) Capillary haemangiomas (Destro 1991)
6) Myelinated nerve fibre (Moore 1931)

7) U/L Diffuse retinal vascular occlusive disease (Moadet 1994)

SYSTEMIC FEATURES

It has been suggested that in NF- I, there is a fourfold increase in relative risk of cerebral tumours (Sorensen et al, 1986). Intra cerebral tumours occur in 1.5 – 8 percent of cases of NF1 (Brasfield and Das Gupta 1972; Huson et al. 1989). These are commonly optic nerve or brainstem gliomas or gliosarcomas.

Optic nerve glioma associated with neurofibro-matosis accounts for almost 10 percent of all patients with optic nerve gliomas, and approximately 1.5 percent of patients with NF1 will develop an optic nerve glioma. These tumours are commonly bilateral or involve the optic chiasm (Font and Ferry 1972; Listernick et al. 1989). Occasionally, optic nerve gliomas extend into the hypothalamus and cause precocious puberty. Optic nerve gliomas are commonly low grade and may not progress for many years. (Listernick et al 1994). There appears to be an association between plexiform eyelid neurofibromas and optic nerve glioma. There is also a high frequency of second malignancies (40 percent of patients)

The frequency of aqueduct stenosis is increased in NF1(Senveli et al 1989). Ventriculo-peritoneal shunting or ventriculo atrial shunting should only be contemplated in symptomatic patients (Spadero 1986). Upto 40 percent of patients with NF1 have mild learning difficulties and 6-10 percent have epilepsy, which may be associated with minor abnormalities such as gliosis, neuronal heterot-opia, and ependymal over growth (Carey et al. 1979; Riccardi 1981). Neurocognitive deficits may be subtle (Eldridege et al. 1989).

Bony anomalies, such as scoliosis, bone cysts, bone hypertrophy or skull and facial deformities, occur in 40-60 percent of patients with NF1. Gastro intestinal neurofibromas are usually asymptomatic but can cause abdominal pain. Renal hypertension occurs in 1.5 percent of affected individuals, sometimes as a result of renal artery stenosis. Phaeochromocytoma affects less than 1 percent of all cases. (Huson 1994).

MRI with gadolinium enhancement is the investigation of choice because it provides better soft tissue contrast. In NF1, optic nerve gliomas, astrocytomas, plexiform neurofibromas, and 'unidentified bright objects' may only be identified by MRI.

NEUROFIBROMATOSIS –II

OCULAR FEATURES

I Iris -Lisch nodules are rare

II Lens Juvenile posterior sub capsular cataract (85% Keiser 1989)

Central posterior cataract (5/9 kaye 1992)

Peripheral wedge cataract (5/9 kaye 1992)

III Retina

Epiretinal membrane (7/9 Kaye 1992; 6/12 Ragge 1993)

In posterior pole

In macula

Combined RPE and retinal hamartomas (22% Ragge 1995) may be Bilateral

IV Optic nerve sheath meningioma

Hardly and Moore reported a case of Bilateral optic nerve sheath meningioma.

SYSTEMIC FEATURES

In NF2 typical tumours are benign schwannomas of the vestibular portion of the acoustic nerves, although meningiomas frequently coexist. Ninety-five per cent of patients with an acoustic neuroma do not have NF2. Most commonly, patients with NF2 have few or no cutaneous manifestations of neuro fibromatosis; however, café-au-lait spots, axillary freckling, and subcutaneous neurofibromas do rarely occur. Multiple cutaneous plexiform schwannomas can also occur occasionally in NF2. There may be a family history of acoustic neuroma.

Morethan 95 percent of people with the NF2 gene develop bilateral vestibular nerve tumours. Presentation is generally with deafness or tinnitus although headache, vertigo, or unsteadiness related to cerebellar involvement can occur. The

characteristic hearing-loss pattern is sensorineural hearing loss with impairment of speech discrimination more so than pure tone loss. Bilateral acoustic neuromas of NF2 are likely to be identified earlier by MRI than by CT. Most tumours are hypointense (66 percent) or isointense (33 percent) with brain on T1- weighted images. All enhance with gadolinium, either homogeneously (66 percent) or patchily (33 percent). The coexistence of NF and tuberous sclerosis or von Hippel-Lindau disease is well recognized.

TUBEROUS SCLEROSIS
OCULAR FEATURES

a. Retinal astrocytomas in 50%. Appear as
b. Semi translucent nodule or
c. White relatively flat well circumscribed plaque
d. Calcified mulberry like tumour

Hypopigmented Spots on iris, retina.
Papilloedema and VI CN palsy due to raised ICT

SYSTEMIC FEATURES:
Adenoma sebaceum (facial angiofibromas) is the most common outward manifestation of this disorder. Other skin changes include hypopigmented macules, café-au-lait spots and 'shagreen patches'. Facial angiofibromas are most commonly seen over the cheeks and nasolabial folds. Hypopigmented macules are frequently shaped like an ash leaf, are 1-3 cm in diameter, and are most easily identified by shining ultraviolet light over the skin. Subungal fibromas are found in approximately 50 percent of cases. Seizures are common and can be partial (focal) multifocal, or generalized. Tuberous sclerosis can also be associated with gangliogliomas and pleomorphic Xanthoastrocytomas.
Patients with tuberous sclerosis are at a higher risk of renal disease associated with angiomyolipomas of the kidneys and renal cysts. Hepatic angiomyolipomas are commonly asymptomaic but can occur and present with abdominal pain followed by malaise and possibly hepatomegaly.

STURGE WEBER SYNDROME
OCULAR FEATURES
Glaucoma
Isolated trabeculodysgenesis
Raised episceral venous pressure associated with arteriovenous
communication is an episcleral angioma.
Diffuse choroidal haemangioma

SYSTEMIC FEATURES
Sturge-weber syndrome usually presents with a characteristic 'port-wine' facial naevus or angioma associated with an underlying leptomeningeal angioma or other vascular anomaly. There can be seizures, low IQ and underlying cerebral hemisphere atrophy. Ninety eight percent of people with Sturge-Weber syndrome have a cranial port wine naevus, and 52 percent have extracranial involvement. Atleast 60 percent of patients will develop glaucoma; 83 percent, seizures; and 65 percent have neurological difficulties. MRI with gadolinium enhancement is more sensitive than CT, and the characteristic features are leptomeningeal angiomatosis, hemiatrophy, cortical calcification and patchy parenchymal gliosis, and demyelination (Adamsbaum et al 1996).

VON HIPPEL – LINDAU SYNDROME
OCULAR FEATURES
Capillary haemangiomas of retina or optic nerve head
SYSTEMIC FEATURES
Tumours - Haemangioblastoma of cerebellum, spinal cord,
medulla or pons
Renal carcinoma
Pheochromocytoma
Cysts - Renal
Pancreatic
Hepatic
Epididymal
Ovarian
Pulmonary
Polycythemia

ATAXIA TELANGIECTASIA

Ataxia telangiectasia is an autosomal recessive trait in which affected individuals have a progressive cerebellar ataxia, oculocutaneous telangiectasia, radiosensitivity, predisposition to lymphoid malignancies, and immunodeficiency (Shiloh and Rotman 1996)

Other skin changes such as hypopigmentation or hyper pigmentation and premature greying of hair are commonly found. There is commonly an ocular dyspraxia with nystagmus and frequent blinking. There is an increased incidence of sinus infections and respiratory infections, with bronchiectasis and lung abscesses related to deficiencies in serum immunoglobulins (especially IgA). Hypogonadism, growth failure with normal growth hormone levels, and diabetes mellitus which may be insulin resistant, also occur.

INCONTINENTIA PIGMENTI

Cicatricial retinal detachment in 1/3rd children
Peg shaped teeth
Cicatricial Alopecia
Grey white hair
Hypopigmentation of face
Tumours – choroid plexus papilloma, medulloblastoma
Mental retardation, seizures.

COCKAYNE SYNDROME

Impaired DNA repair
Photosensitivity seen in 80%
Premature aging
Bird beak facies
Short stature
Cardio vascular disease
Neuropathy
Retinitis pigmentosa like picture

MENKE'S SYNDROME

Colourless, friable, kinked, curly hair with split shafts
Psychomotor retardation, seizures
Microcysts of iris pigment epithelium, optic atrophy

XERODERMA PIGMENTOSUM

Abnormality of DNA repair
Skin - Freckles on Skin, lids
Photo sensitivity
1000 fold increase in risk of developing skin cancers like Basal cell carcinoma, squamous cell carcinoma and melanoma
Eye - Chronic blepharitis, lower lid atrophy
Basal cell carcinoma lid
Dry eye
Anterior uveitis
Neurological - Dementia
Cerebellar ataxia
Seizures
Dystonia

GORLIN SYNDROME

Multiple naevoid basal cell carcinomas
Anomalies of eye – congenital cataract, strabismus, coloboma of choroid and optic disc
Odontogenic keratocysts of mandible
Anomalies of skeleton
Reproductive system anomalies
Medulloblastomas

SJOGREN – LARSSON SYNDROME :

Congenital icthyosis
Mental retardation, speech abnormality, spasticity
Pigmentary retinopathy

PROTEUS SYNDROME

Partial enlargement of hands or feet
Hemiatrophy of one side
Pigmented naevi, tumours (lipomas, lymphangiomas)
Skeletal, nasal, pulmonary and neurologic abnormalities

WYBURN MASON SYNDROME

Racemose haemagioma of retina, optic nerve head.
Congenital AV communication involving mid brain, naso frontal region, posterior fossa

KLIPPEL –TRENAUNAY WEBER SYNDROME

Hemihypertrophy of the connective tissue and long bones, cutaneous haemangiomas and varicose veins

Enophthalmos, Iris heterochromia & coloboma, retinal vascularity, choroidal angioma

MANAGEMENT

Multi disciplinary approach

1. Ophthalmologist

Glaucoma - Try medical therapy

Early surgical intervention preferred.

Goniotomy may be successful in eyes with angle anomalies.

Combined trabeculotomy – trabeculectomy gives good results in early cases.

Retinal tumours

Usually benign like retinal astrocytoma

May result in rubeotic glaucoma, vitreous haemorrhage and RD

Surgical therapy includes retinal cryopexy, xenon and argon photocoagulation, scleral buckling, and pars plana vitrectomy with excisional retinal biopsy.

Orbital tumours- may require decompression and biopsy

Cataract - Extraction and IOL implantation

2. Neuro Surgeon

Seizures- treatment by anticonvulsant therapy

Asymptomatic CNS tumours - follow up

Symptomatic tumours - Biopsy and surgical or radiation treatement depending on type and grade of tumour

Ventriculoperitoneal shunt for aqueductal stenosis

3. Dermatologist for management of icthyosis, photosensitivity, benign and malignant skin lesion.

4. Endocrinologist and oncologist for management of other tumours and associated endocrine dysfunction like pituitary abnormality caused by chiasmal gliomas

5. Paediatrician for early detection and referral of phakomatosis cases and management of intercurrent infections as in Ataxia telangiectasia.

6. orthopaedician for management of musculo skeletal abnormalities

AIM OF THE STUDY

- To study the prevalence of ocular manifestations in neurocutaneous syndromes with emphasis on neurofibromatosis.
- To assess the prevalence of other systemic associations and disabilities in these patients

MATERIALS AND METHODS

Type of study - Prospective

Centre of study - Government Rajaji Hospital, Madurai

Time period - February 2003 - February 2005

Number of patients - 28

Neuro fibromatosis I	-	17
Neurofibromatosis II	-	2
Sturge weber syndrome	-	2
Tuberous sclerosis	-	4
Incontinentia pigmenti	-	1
Cockayne syndrome	-	1
Ataxia telangiectasia	-	1

Inclusion Criteria

1. All phakomatoses referred from other speciality departments for ophthalmological evaluation.
2. Cases diagnosed in ophthalmology department during routine evaluation of unrelated ocular symptoms or presenting with clinical features like headache, proptosis or glaucoma related to phakomatosis.

Method of Study

- A thorough history with reference to complaints specific for neurocutaneous syndromes, past treatment history, past history of trauma, systemic and eye illness and detailed family history was taken.

- A general examination and systemic examination of CNS, skin, skeletal, endocrine, GIT, CVS and respiratory system was done.

- Ocular examination included slit lamp examination, detailed fundus examination including I/O if necessary and recording of vision, colour vision, fields, tension and refraction. A gonioscopy was done to rule out angle anomalies.
- Radiological investigations included plain x ray skull, CT brain whenever possible and MRI if needed. Ultrasonography was also done in some cases.

Limitations of the Study

1. As majority of patients belonged to a low socio-economic group, costly investigations like CT and MRI was not possible in every patient.
2. Few patients did not come for follow up after treatment.

OBSERVATION AND DISCUSSION

Distribution of Cases

A total of 28 cases of phakomatoses were studied of which majority (60.7%) were NF-I followed by tuberous sclerosis (14.28%)

Condition	Number	%
NF – I	17	60.71
NF –II	2	7.14
Tub.Sclerosis	4	14.28
Sturge Weber	2	7.14
Incont. Pigmenti	1	3.57
Atax. Telangiectasia	1	3.57
Cockayne	1	3.57

In other studies also NF-I is the most common neurocutaneous syndrome followed by tuberous sclerosis and incontinentia pigmenti. In this study incontinentia pigmenti comes fourth in frequency.

Age wise Distribution

Age	NF-1	NF-II	Tuberous sclerosis	Sturge weber	Ataxia telengect	Incont. Pigmenti	Cocka yne
0-15	2(11.7%)	-	2(50%)	2(100%)	1(100%)	1(100%)	-
16-30	8(47%)	2(100%)	1(25%)	-	-	-	1(100%)
31-45	2(11.7%)	-	1(25%)	-	-	-	-
46-60	5(29.4%)	-	-	-	-	-	-

Majority of NF-I were in the age group 16-30 (47%). Both cases of NF-II were also in the same age group. All cases of cockayne, Incontinentia pigmenti, ataxia telangiectasia and Sturge weber syndrome were in below 30 age group. 50% cases of tuberous sclerosis were below 15 years. The lesions of phakomatosis evolve during childhood and adolescence which may be the reason for increased frequency of presenting patients encountered in under 30 age group.

Sex Distribution

Sex	NF-1	NF-II	Tuberous sclerosis	Sturge weber	Ataxia telangiect	Incont. Pigmenti	Cocka yne
Male	6(35.2%)	2(100%)	1(25%)	2(100%)	-	-	1(100%)
Female	11(64.7%)	-	3(75%)	-	1(100%)	1(100%)	-

Majority of NF-I patients were females. Other studies show equal male: female ratio. Both NF-II patients were males.

Family history:

2 out of 17 NF-I patients (11.7%) gave history of NF in siblings / parents

2 out of 4 (50%) tuberous sclerosis patients also gave positive family history.

NEUROFIBROMATOSIS - I

LISCH NODULE

a) Presence :

Condition	Number of patients and percentage	
	No Lisch Nodule	With Lisch Nodule
NF- I	6 (35.21%)	11 (64.0%)
NF – II	2(100%)	-

b) Distribution by number

NF- I	Number of eyes with		
	Multiple L.N.	Single L.N.	No L.N.
33 eyes of 17 patients (1 proptosis)	14 (42.4%)	5(15.15%)	14 (42.4%)

C) Laterality

NF- I	Unilateral	Bi lateral
11 patients	3 (27.27%)	8 (72.72%)

d) Location

NF – I	Superior Half	Inferior half	Uniform
14 eyes of 11 patients	1(5.26%)	9 (47.36%)	9 (47.36%)

e) Age wise distribution

NF – I	0-15 years	16-30 years	31-45 years	45-60 years
With L.N.	2 (100%)	6 (75%)	0	3 (60%)
Without L.N	0	2(25%)	2(100%)	2 (40%)

f) Sex Distribution

NF 1	Number and percentage
No.of males with NF – 1	6
No.of NF-1 males with LN	6 (100%)

NF 1	Number and percentage
No.of females with NF – 1	11
No.of NF-1 females with LN	5 (45.45%)

In this study, Lisch nodules were present in 64% of NF-I patients. In all age group it is present in more than 60%. Of 2 patients in 31-45 year age group, one was a case of plexiform neurofibro-matosis. Of 5 patients in 45-60 year age group, 2 patients had only segmental NF findings.

This could be the reason for relatively lower percentage of prevalence of Lisch nodule in these age groups. Study by Lewis 1981, Riccardi 1981 have shown presence of Lisch nodule in 50% by 3rd decade. They also found that initially they are unilateral and then become bilateral and multiple. In our study 27.27% cases had unilateral Lisch nodule and all these belong to < 30 age group. All patients above 30 years (72.2% of total cases) had bilateral involvement. Single Lisch nodule was noted in 5% of total eyes and multiple Lisch nodules in 42.4%.

47.36% eyes had uniform distribution of Lisch nodules. In those eyes with fewer Lisch nodules they were predominantly inferior in location (47.36%). Only 5.26% eyes had superior Lisch nodules. Nichols and Amato et al study showed 80% inferior distribution.

Another interesting finding is that all the male patients with NF1 had Lisch Nodules while only 45.45% of female patients with NF1 had Lisch nodules.

Otsuka et al. (2001) performed serial ophthalmologic examination on 70 patients of various ages with NF1. Lisch nodules were more frequent in familial cases than in sporadic cases, which is likely to be significant as the average age of the first examination was younger for familial cases in this study.

In my study, 2 cases of NF-I who gave positive family history showed presence of Lisch nodules while 6 cases of NF-I without Lisch nodule gave negative family history.

PAPILLOEDEMA :

5 NF cases with intracranial CT findings	
With papilloedema	3 (60%)
Normal Fundus	2 (40%)

NF-I	< 15 years	16-30 years	> 30 years	Total (all age)
With papill	-	4 (50%)	-	4 (23.5%)
Normal F	2 (100%)	4 (50%)	7 (100%)	13(76.47%)

Nearly one fourth (23.5%) of all NF-1 patients had papilloedema and all were in 16-30 age group. And this accounted for 50% of all patients in this age group. Evolution of lesions of phakomatoses occur during childhood and adolescence, which may be the reason for increased frequency of intracranial neoplasms in this age group. Interestingly 40% of NF cases with CT findings had normal fundus. This shows the importance of brain radiology in all cases of phakomatosis.

RADIOLOGY

MRI / CT finding in NF	No. of patients	Percentage
Obstructive hydrocephalus	3	15.80
Optic N- sheath meningioma	1	5.26
Olfactory groove meningioma	1	5.26
Calcified intraventricular meningioma	1	5.26
Intra cerebral calcification	1	5.26
Pilocytic astrocytoma	1	5.26
Acoustic neuroma	1	5.26
Focal gliosis	1	5.26
Multiple UBO	1	5.26
Arachnoid cyst	1	5.26
Epidermoid cyst	1	5.26

Intra cerebral tumours occur in 1.5 – 8% cases of NF-I (Brasfield and Das Gupta 1972). In this study 2 cases of NF-I had intracerebral tumours (11.7%).

Pilocytic astrocytomas and multiple UBO (unidentified bright objects) were seen in MRI in one patient each in this study. These lesions are usually detectable only by MRI (Riccardi 1981). Riccardi also reported minor abnormalities such as gliosis, neuronal heterotopia and ependymal over growth. Focal gliosis and areas of intraventricular and intracerebral calcification were noted in this study also. 15% cases of NF-I are associated with optic nerve gliomas (Lewis 1985). In this study, though optic nerve gliomas were not encountered, there were patients with optic nerve sheath meningiomas, olfactory groove meningioma and calcified intraventicular meningiomas.

Obstructive hydrocephalus was found in 3 patients. Frequency of aqueductal stenosis is increased in NF-1, (senveli et al. 1989) which can lead to obstructive hydrocephalus. Ventriculo peritoneal shunt was done for all 3 patients for symptomatic relief.

Other Ocular Findings in NF-I

Defects	No.of patients with defects / Total no.of NF-I patients
Ocular motility defects	3/17
Nystagmus	1/17
Proptosis	1/17
Lid nodule	1/17
Plex. Fibro lid	2/17
Ptosis	2/17
Nodular episcleritis	1/17
Dry eye	1/17
Anterior staphyloma	1/17
Enlarged corneal nerves	3/17
Corneal infiltration	1/17
Secondary glaucoma	1/17
Anterior insertion of iris	1/17
Abundant iris processes	1/17
Iris mammillations	1/17

Other finding in NF- II

Nystagmus - 1 / 2
Proptosis - 1 / 2
Persistant pupillary membrane - 1 / 2
Posterior sub capsular cataract - 2 / 2

Positive systemic findings NF -I

N F – I	No.of patients
Skin (Dermal neurofibroma / cafe au lait spot)	15 / 17
Bone (1 short stature, 1 pectus carinatum)	2 / 17
GIT (1 oral Gingival papilloma, 1 anorexia)	1 /17
CNS (1 seizure)	1 /17
CVS (1 Hypertension)	1 /17
Endocrine (1 hyperthyroidism)	1/17

N F - II

CNS (Generalised tonic clonic seizure) - 1 /2
Bilateral V Cranial nerve paresis - 1 /2
VII LMN (Lt)
- 1 / 2
VIII Lt
- 1 /2

STURGE WEBER SYDROME

Megalocornea - 2 /2
Glaucoma - 2 /2
Port wine stain - 2 /2
Seizures - 2 / 2
Dilated episcleral vein- 1 /2

Studies have shown that 92% of people with sturge weber have port wine staining, 60% develop glaucoma and 83% develop seizures.

Of the 2 patients in my study, one was a child with congenital glaucoma detected in first few months of life. It had 40% cupping with IOP in the range of thirties. Now the IOP was under control with medical treatment with 0.5% Timolol BD both eyes.

Other patient's IOP was in twenties and he had very poor vision < 2 /60 in one eye due to glaucomatous optic atrophy. Other eye had 6/6 vision, normal tension and 30% cup.

TUBEROUS SCLEROSIS

Findings	No.of patients (four)
Positive family history	2 /4
LMN facial palsy	1 /4
Hypopigmented iris	2 /4
Retinal astrocytoma	1 / 4
Low intelligence	1 / 4
Seizures	1 / 4
Hepatic angiolipomas	1 / 4
Renal angiolipomas	1 / 4
Multiple subependymal cerebral calcification	1 / 4
Hyperostosis of cranial vault	1 / 4

Retinal finding was seen only in one patient in the form of bilateral retinal astrocytomas. It was seen as a semitranslucent, white, relatively flat well circumscribed lesion in the superotemporal quadrant. Retinal astrocytomas are usually benign and do not require treatment.

Hypopigmented spots on iris which is another feature of the condition were seen in 2 patients. LMN type of facial palsy was seen in one patient.

INCONTINENTIA PIGMENTI

1 case - Right divergent squint
Posterior cortical cataract BE
Retinal detachment BE
Cicatricial alopecia
Peg teeth
Peculiar facial pigmentation

Child had presented with leukocoria both eyes. She had retinal detachment both eyes. USG BE revealed retinal fibrosis also. About one third of children with this condition develop cicatricial RD in the first year of life (Kanski).

COCKAYNE SYNDROME

1 case -constricted visual fields (only central 15o)
posterior subcapsular cataract BE
Retinitis pigmentosa BE
Short stature
Premature aging
Bird beak facies
Coronary heart disease (anterior wall MI)

Ozdirim et al 1996 study showed skin manifestations in the form of photo sensitivity (84%), neurological problems related to learning difficulties, progeroid appearance, salt and pepper retinopathy, ataxia, short stature, and neuropathy.

ATAXIA TELANGIECTASIA

1 case - Ocular motor apraxia
conjunctival telangiectasia BE
Ataxia
Chorioathetosis
Bronchiectasis
Cerebral atrophy

Affected individuals of this condition develop progressive cerebellar ataxia, oculocutaneous telangiectasia, radiosensitivity, predisposition to lymphoid malignancy and immuno deficiency. (Shiloh and Rotman 1996)

Table Showing Important Comparision Studies

	Study Factor	Result of Present study	Result of other studies	Study by
I	Most common Phakomatosis	NF – I (64%)	NF-I	Riccardi VM 1997 Gutnam et al 1997
II A	Neuro Fibromatosis – I Lisch Nodule (Most common ocular finding) Over all frequency Above 45 years age Location Bilaterality Intracerebral tumours	 64% 60% 47.36 % Inferior 47.36% Uniform 05.20 % superior 72.72 % 11.7%	 63.2% 80 % 80% Inf. 3rd decade 50% 1.5 – 8% 9.9%	 Nichols JC 2003 Amato JE Riccardi 1981 Mustonel et al 1997 Nichols JC Amato JE2003 Lewis Riccardi 1981 Lubs et al 1981 Brasfield & Das Gupta 1972 Sorensen SA, NielsenA 1986
III	Neurofibromatosis II (only 2 patients) Posterior subcapsular cataract (Most common ocular finding)	 100%	 85% 63% 81%	 Kaiser kupfer et al 1989 Mautner et al 1996 Parry et al 1996
IV	Tuberous sclerosis Retinal Astrocytoma (Most common ocular finding)	25%	50% 50% 50%	Lagos & Gomez 1967 Robertson 1979 Nyboer JH 1976
V	Sturge Weber Syndrome (Only 2 patients) Glaucoma (most common ocular finding)	100 %	71%	Sulliven et al 1992

SUMMARY

Ocular manifestations of 28 cases of phakomatoses were studied. To summarize -

1. NF-1 accounted for most of (60.71%) the cases of phakomatosis followed by tuberous sclerosis (14.28%)
2. Majority (47%) of NF-I and all 2 cases of NF-II were in 15-30 age group
3. 64.7% of NF-I cases were females
4. 11.7% of NF-I patients gave positive family history
5. Lisch nodules, the most common ocular finding in NF-I, were present in 64% of patients. Of these 72.2% were bilateral and 47.3% were uniformly distributed on iris followed by a preponderant inferior location (47.36%) in the rest.
6. Papilloedema was present in nearly 1/4th of patients and were in 16-30 age group. 40% of NF patient with CT brain abnormality had no papilloedema.
7. Obstructive hydrocephalus was present in 15.8% NF patients
8. Plexiform neurofibromatosis was seen in 2 patients
9. Enlarged corneal nerves were seen in 17.6% patients
10. Ocular motility defect and anterior iris insertion were observed in few patients.
11. Posterior subcapsular cataract was present in both NF-2 patients.
12. Megalocornea and Glaucoma were seen in both sturge weber patients
13. Retinal astrocytoma, the most common finding in tuberous sclerosis was seen in 25% cases. Hypopigmented spots on iris were also seen in 2 cases.
14. A case of incontinentia pigmenti had posterior cortical cataract and retinal detachment

15. A case of cockayne syndrome had retinitis pigmentosa and posterior subcapsular cataract
16. A case of Ataxia telangiectasia had ocular motor apraxia and conjunctival telangiectasia

CONCLUSION

Phakomatoses in general, are characterized by hereditary transmission, multisystem involvement, slow evolution of lesions in childhood and adolescence, tendency to form hamartomas and a disposition to malignant transformation.

So the management of condition involves a multi disciplinary approach.

Since these conditions are hereditary, a pedigree analysis of the family and karyotyping (if facilities are available) should be done and genetic counseling offered to the parent or proband. Prenatal diagnosis also has a role in certain disorders.

Ophthalmologist has a role in early recognition of the neurocutaneous syndrome from specific ocular features (like Lisch nodule in NF-I), reduce ocular morbidity by timely treatment (of conditions like glaucoma) and prompt referral to appropriate specialists for management of disabilities involving other systems. These measures can at times be life saving as phakomatoses are often associated with intracranial neoplasms and other malignancies.

Considering the slow evolution of lesions in phakomatosis and latency before the onset of symptoms, radiological investigations like USG, CT and MRI done even in an asymptomatic patient will be useful in early detection of the pathology.

It is also necessary to follow up these patients as many lesions can undergo malignant transformation in course of time.

To conclude - by co-ordinated effort between the ophthalmologist and other specialists, the morbidity and mortality of individuals affected by phakomatosis can be reduced and quality of life can be improved by proper rehabilitative measures.

PROFORMA

OCULAR MANIFESTATIONS IN NEUROCUTANEOUS SYNDROMES

Name Age Sex
IP/OP No.:
Address : Marital Status :

Complaints
Ocular
Specific for NF : Lid Swelling (Neurofibroma)
Lid drooping (Congenital/mechanical ptosis
Diplopia(Muscle involvement / raised ICT)
Eye protrusion (bony defect/orbital tumour)
Diminished vision(Optic atrophy ; papilloedema – blurring ; field defects – chiasmal glioma)
Non specific : Redness / watering / discharge / itching
FB Sensation / photophobia / photopsia /floaters
Non ocular: Headache/vomiting / seizures / deafness/others

Past History :
Intervention (surgery)
Trauma
Drug allergy
Eye disease
Systemic disease (HTN/DM/TB/Hansen/Syphilis/Asthma/CHD/Others)
Others
Family History :
In parents /siblings / offsprings
General Examination :
Pulse : BP :
Pallor : Lymphadenopathy:
Others :
Systemic Examinations :

Skin - Neurofibroma / café au lait spots/Axillary freckling/portwine
Bone - Skull & facial / Scoliosis / short stature
CNS - Mental retardation / Focal neurological deficit /CN palsy
Endocrine- preco, puberty / Hyperparathyroidism / Myxoedema/ Addisons / MEN
GIT - NF of GIT / Carcinoid of small bowel / Hepatic cysts
CVS - CAHD
RS - Bronchiectasis
Renal - Renal cysts

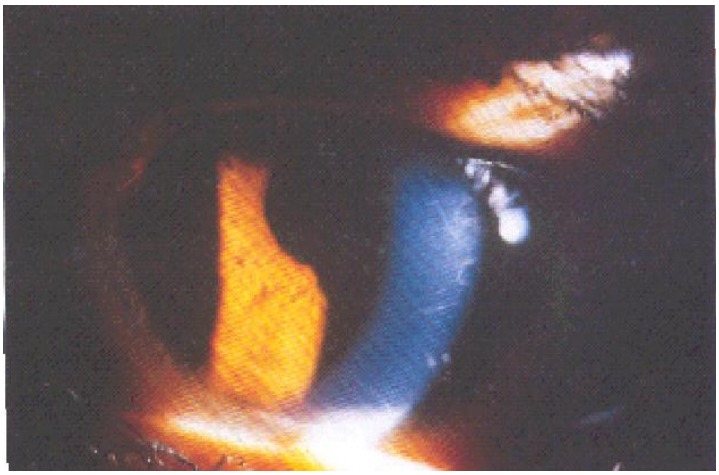
Ocular Examination :

Head posture (Head tilt/ face turn/ Chin elevation or depression)
Ocular movements (Full / Restricted)
Visual axis (Orthophoric / Strabismus)
Ocular size and position(Proptosis+/- pulsations/Enophthalmos)
Forehead wrinkling and Facial asymmetry
Slit Lamp :
Lids & adnexae
OD OS
Swelling
Ptosis
Conjunctiva :
NF Nodule
Pigmentation
Cornea :
Neurofibroma
Enlarged corneal nerves
Megalocornea
Anterior chamber :
Depth & Clarity
Pupil :
Size & shape
Reaction
Persistent papillary membrane
Pseudoexfoliation
Iris :
Colour
Pattern
Lisch Nodule
Number
Location
Size
Shape
Flat / Elevated
Margins
Others
Lens :
Posterior subcapsular cataract
Central posterior cataract
Peripheral wedge shaped cataract
Fundus :
Retinal / RPE hamartomas
Sectorial pigmentary disturbance
Café au lait spot like lesion
Capillary haemangiomas
Diffuse Ret. Vasc. Occl. Disease
Myelinated nerve fibre
Epiretinal membrane
Choroidal folds
Astrocytomas
Choroidal haemangioma
Racemose haemangioma
Telangiectasia
Retinal detachment
Visual Acuity :
Colour vision :
Field :
Refraction :
Diplopia chart :
Muscle Balance :
Tension :
Gonioscopy :
NF tissue replacing trab.
Iris insertion ant. to SS
Membrane at the angle
Investigations :
X ray skull
Integrity of optic foramen
Signs of raised ICT
Silver beaten appearance
Separation of sutures
Erosion of Post. Clinoid Process
Ballooning of sella

Shift of Pineal calcification
CT Scan
MRI
USG

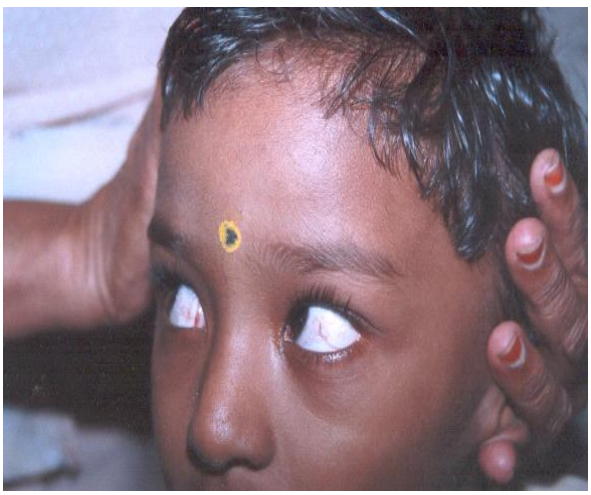
FFA
Others

PROMINENT CORNEAL NERVES



LISCH NODULE

CONJUNCTIVAL TELANGIECTASIA



PLEXIFORM NEUROFIBROMA

Condition	Number	%
NF – I	17	60.71
NF –II	2	7.14
Tub.Sclerosis	4	14.28
Sturge Weber	2	7.14
Incont. Pigmenti	1	3.57
Atax. Telangiectasia	1	3.57
Cockayne	1	3.57

Sex	NF-1	NF-II	Tuberous sclerosis	Sturge weber	Ataxia telangiect	Incont. Pigmenti	Cocka yne
Male	6(35.2%)	2(100%)	1(25%)	2(100%)	-	-	1(100%)
Female	11(64.7%)	-	3(75%)	-	1(100%)	1(100%)	-

Sex	NF-1	NF-II	Tuberous sclerosis	Sturge weber	Ataxia telangiect	Incont. Pigmenti	Cocka yne
Male	35.2	100	25	100	0	0	100
Female	64.7	0	75	0	100	100	0

Condition	Number of patients and percentage	
	No Lisch Nodule	With Lisch Nodule
NF- I	6 (35.21%)	11 (64.0%)
NF – II	2(100%)	-

	No Lisch Nodule	With Lisch Nodule
NF- I	35.21	64
NF – II	100	0

	Number of eyes with		
NF- I	Multiple L.N.	Single L.N.	No L.N.
33 eyes of 17 patients (1 proptosis)	14 (42.4%)	5(15.15%)	14 (42.4%)

Multiple L.N.	42.40%
Single L.N.	15.20%
No L.N.	42.40%

NF- I	Unilateral	Bi lateral	Bilateral	72.72
11 patients	3 (27.27%)	8 (72.72%)	Unilateral	27.27

d)Location :

NF – I	Superior Half	Inferior half	Uniform	Superior Half	
					5.26
14 eyes of 11 patients	1(5.26%)	9 (47.36%)	9 (47.36%)	Inferior half	47.36
				Uniform	47.36

e) Age wise distribution

NF – I	0-15 years	16-30 years	31-45 years	45-60 years
With L.N.	2 (100%)	6 (75%)	0	3 (60%)
Without L.N	0	2(25%)	2(100%)	2 (40%)

NF – I	0-15 years	16-30 years	31-45 years	45-60 years
With L.N.	100	75	0	60
Without L.N	0	25	100	40

NF 1	Number and percentage		
No.of males with NF – 1	6	No.of males with NF – 1	6 11
No.of NF-1 males with LN	6 (100%)	No.of NF-1 males with LN	6 5

NF 1	Number and percentage	NF-1 males with LN	100
No.of females with NF – 1	11	NF-1 females with LN	45.5
No.of NF-1 females with LN	5 (45.45%)		

With papilloedema	3 (60%)	With papilloedema	60
Normal Fundus	2 (40%)	Normal Fundus	40

NF-I	< 15 years	16-30 years	> 30 years	Total (all age)
With papill	-	4 (50%)	-	4 (23.5%)
Normal F	2 (100%)	4 (50%)	7 (100%)	13(76.47%)

NF-I	< 15 years	16-30 years	> 30 years	Total (all age)
With papill	0	50	0	23.5
Normal F	100	50	100	76.47

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MASTER CHART

S. No.	Name	Age	Sex	Diag	Fam.H	Ocula rmaturity Position		Lids adimaxa		Conj sclera		Cornea		Ac Angle		Pupil		Iris	
						R	L	R	L	R	L	R	L	R	L	R	L	R	L
1.	Alagumadathi	45	F	NF-1	-	N	N	N	N	N	N	N	N	N	N	N	N	N	N
2.	Seethalakshmi	10	F	NF-1	-	Ny	P	N	P	N	P	C	P	N	P	N	P	MLI	P
3.	Kamatchi	60	M	NF-1	-	N	N	NO	NO	N	N	N	N	N	N	SL	SL	LI	MLI
4.	Rajendran	23	M	NF-II	+	NyR	NyR	N	N	N	N	L5	L5	N	N	SLPM	SLPM	N	N
5.	Jeyalakshmi	18	F	NF-1	-	N	PR	N	PTML	N	MC	N	N	N	N	N	N	N	N
6.	Ponnupappa	50	F	NF-1	-	N	N	N	N	N	N	N	N	N	N	N	N	MLU	MLU
7.	Kamatchi	40	F	NF-1	-	N	N	PXPT	NE	N	N	N	N	N	A	N	N	N	N
8.	Durai singh	25	M	NF-1	-	N	N	N	N	N	N	N	N	N	N	N	N	MLU	MLU
9.	Muthu	29	M	NF-1	MSI	R	R	N	N	N	N	N	N	N	N	N	N	LI	N
10	Naina Mohamed	22	M	NF-1	-	N	N	N	N	N	N	C	C	N	N	N	N	MLS	MLU
11	Sakthivel	26	M	NF-1	M	N	N	N	N	N	N	N	N	N	N	N	N	LI	MLI
12	Antony samy	63	M	NF-1	-	N	N	NO	N	N	N	DE	N	IP	IP	N	N	MLI	LI
13	Rama Sakthi	25	F	NF-1	-	PR	N	PRPTPX	N	CS	N	CI	N	N	N	N	N	N	N
14	Saravanan	29	M	NF-II	-	PR	N	N	N	N	N	N	N	N	N	N	N	N	N
15	Deivana	55	F	NF-1	-	N	N	N	N	N	N	N	N	N	N	N	N	PX	PX

S. No.	Name	Age	Sex	Diag	Fam.H	Ocula rmaturity Position		Lids adimaxa		Conj sclera		Cornea		Ac Angle		Pupil		Iris	
						R	L	R	L	R	L	R	L	R	L	R	L	R	L
16	Karuppayee	50	F	NF-1	-	N	N	N	N	N	N	N	N	N	N	N	N	N	N
17	SheelaDevi	25	F	NF-1	-	N	N	N	N	N	N	N	N	N	N	N	N	MLU	MLU
18	Karthik	15	F	NF-1	-	N	N	N	N	N	N	C	C	N	N	N	N	LI	N
19	Umayal	25	F	NF-1	-	N	N	N	N	N	N	N	N	N	N	N	N	MLU	MLU
20	Lalith	1	M	SWS	-	N	N	N	N	N	N	CD	CD	N	N	N	N	N	N
21	Ramesan	14	M	SWS	-	N	N	N	N	N	DE	N	CD	N	M	N	S	N	N
22	Marathavalli	29	F	TS	SI	N	N	N	N	N	N	N	N	N	N	N	N	N	N
23	Chellapandi	11	M	TS	-	N	N	N	N	N	N	N	N	N	N	N	N	HS	N
24	Kannathil	42	F	TS	-	N	N	LG	N	N	N	N	N	N	N	N	N	N	N
25	Vani	3	F	TS	M	N	N	N	N	N	N	N	N	N	N	N	N	HS	N
26	Kasthuri	6	F	INP	-	RS	N	N	N	N	N	N	N	N	N	N	N	N	N
27	Balakrishnan	25	M	CO	-	N	N	N	N	N	N	N	N	N	N	SL	SL	N	N
28	Pandimeena	4 ½	F	ATG	-	OA	N	N	CT	CT	N	N	N	N	N	N	N	N	N

S. No.	Name	Age	Sex	Diag	Lens		Fundus		BCUA Vitreous		Field		C.V		Tension	
					R	L	R	L	R	L	R	L	R	L	R	L
1.	Alagumadathi	45	F	NF-1	N	N	N	RA	6/6	6/9	N	N	N	N	N	N
2.	Seethalakshmi	10	F	NF-1	N	P	N	P	6/6	-	N	-	N	-	17.3	In
3.	Kamatchi	60	M	NF-1	IMC	IMC	N	N	6/36	6/60	N	N	N	N	N	N
4.	Rajendran	23	M	NF-1	PSC	PSC	N	N	1/60	1/60	-	-	-	-	N	N
5.	Jeyalakshmi	18	F	NF-1	N	N	N	N	6/6	6/18	N	N	N	N	N	-
6.	Ponnupappa	50	F	NF-1	N	N	N	N	6/12	6/6	N	N	N	N	N	N
7.	Kamatchi	40	F	NF-1	N	N	N	N	6/9	6/9	N	N	N	N	N	N
8.	Durai singh	25	M	NF-1	N	N	PE	PE	6/9	6/9	E	E	N	N	N	N
9.	Muthu	29	M	NF-1	PSC	PSC	PE	PE	6/12	6/12	E	E	N	N	N	N
10	Naina Mohamed	22	M	NF-1	N	N	PE	PE	6/12	6/12	E	E	N	N	N	N
11	Sakthivel	26	M	NF-1	-	-	P	P	6/9	6/12	N	N	N	N	N	N
12	Antony samy	63	M	NF-1	IMC	IMC	N	N	1/60	6/64	-	N	-	N	N	N
13	Rama Sakthi	25	F	NF-1	N	N	-	N	1/60	6/36	-	N	-	N	N	N
14	Saravanan	29	M	NF-II	PSC	PSC	N	N	6/9	6/9	N	N	N	N	N	N
15	Deivana	55	F	NF-1	N	N	N	N	6/6	6/6	N	N	N	N	N	N

S. No.	Name	Age	Sex	Diag	Lens		Fundus		BCUA Vitreous		Field		C.V		Tension	
					R	L	R	L	R	L	R	L	R	L	R	L
16	Karuppayee	50	F	NF-1	L	L	N	N	6/12	6/12	N	N	N	N	N	N
17	SheelaDevi	25	F	NF-1	N	N	N	N	6/12	6/12	N	N	N	N	N	N
18	Karthik	15	F	NF-1	N	N	N	N	6/6	6/6	N	N	N	N	N	N
19	Umayal	25	F	NF-1	N	N	N	N	6/6	6/6	N	N	N	N	N	N
20	Lalith	1	M	SWS	N	N	40%	40%	N	N	-	-	-	-	In	In
21	Ramesan	14	M	SWS	N	N	30%	100%	6/6	1/2/60	N	-	N	-	N	In
22	Marathavalli	29	F	TS	N	N	T	N	6/6	6/6	N	N	N	N	N	N
23	Chellapandi	11	M	TS	N	N	AR	AR	6/6	6/6	N	N	N	N	N	N
24	Kannathil	42	F	TS	N	N	N	N	6/18	6/24	N	N	N	N	N	N
25	Vani	3	F	TS	N	N	N	N	N	N	N	N	N	N	N	N
26	Kasthuri	6	F	INP	PCC	PCC	RD	RD	H	2/60	--	-	-	-	N	N
27	Balakrishnan	25	M	CO	PSC	PSC	RP	RP	2/60	3/60	10	10	-	-	N	N
28	Pandimeena	4 ½	F	ATG	N	N	N	N	6/6	6/6	-	--	-	-	N	N

S. No.	Name	Age	Sex	Diag	SKIN	BONE	CVS	INDS	GIT	CNS	RESP	
1.	Alagumadathi	45	F	NF-1	DNAF	N	N	N	N	N	N	-
2.	Seethalakshmi	10	F	NF-1	CF	SS	N	N	N	N	N	S
3.	Kamatchi	60	M	NF-1	DNCF	N	N	N	N	N	N	-
4.	Rajendran	23	M	NF-1	N	N	N	N	N	S,L7,8	N	C
5.	Jeyalakshmi	18	F	NF-1	N	N	N	N	N	N	N	S s
6.	Ponnupappa	50	F	NF-1	V	N	N	N	AX	N	N	-
7.	Kamatchi	40	F	NF-1	PX	N	N	N	N	N	N	-
8.	Durai singh	25	M	NF-1	DN	N	N	N	N	S	N	I
9.	Muthu	29	M	NF-1	DN CF	N	N	N	N	N	N	C
10	Naina Mohamed	22	M	NF-1	DN AF	N	N	N	N	N	N	C
11	Sakthivel	26	M	NF-1	DN CF	PC	N	N	N	N	N	I c
12	Antony samy	63	M	NF-1	DN	N	N	N	N	N	N	-
13	Rama Sakthi	25	F	NF-1	PX	N	N	N	N	N	N	-
14	Saravanan	29	M	NF-1	N	N	N	N	N	N	N	C c
15	Deivana	55	F	NF-1	DN CF	N	HTN	HY	N	N	N	-

S. No.	Name	Age	Sex	Diag	SKIN	BONE	CVS	INDS	GIT	CNS	RESP	Positive Findings in USG/ CT / MRI
												-
16	Karuppayee	50	F	NF-1	DNCF	N	N	N	OP	N	N	-
17	SheelaDevi	25	F	NF-1	DN	N	N	N	N	N	N	-
18	Karthik	15	F	NF-1	DN	N	N	N	N	N	N	-
19	Umayal	25	F	NF-1	DN	N	N	N	N	N	N	-
20	Lalith	1	M	SWS	PW	N	N	N	N	S	N	-
21	Ramesan	14	M	SWS	PW	N	N	N	N	S	N	-
22	Marathavalli	29	F	TS	AS FP SH	N	N	N	N	N	N	Mult. Hep. & renal angio liopoma, Multi.sub.epenty.calcifn. cerebrum, hyperostosis cranial vault
23	Chellapandi	11	M	TS	AS AM FP	N	N	N	N	LI	N	-
24	Kannathil	42	F	TS	AS	N	N	N	N	L7	N	-
25	Vani	3	F	TS	AL	N	N	N	N	S	N	-
26	Kasthuri	6	F	INP	A,PH,F	N	N	N	N	N	N	USG – RD with fibrosis
27	Balakrishnan	25	M	CO	PA	BF	CA	N	N	N	N	-
28	Pandimeena	4 ½	F	ATG	N	N	N	N	N	AT, CH	BR	Cerebral atrophy

ABBREVIATIONS

A	ALOPECIA	D	DRY EYE	LI	LISCH NODULE SINGLE INFERIOR
AF	AXILLARY FRECKLING	DE	DILATED EPISCLERAL VEINS	M	MOTHER AFFECTED
AM	ASH LEAF MACULE	DN	DERMAL NEUROFIBROMA	MC	MASS INVADING CONJUNCTIVA
AI	ANTERIOR IRIS INSERTION	E	ENLARGED BLIND SPOT	ML	MASS LID
AS	ADENOMA SEBACEUM	F	FACE PIGMENTATION	MLI	MULTIPLE LISCH NODULE INFERIOR
AR	ASTROCYTOMA	FP	FOREHEAD PAPULE	MLS	MULTIPLE LISCH NODULE SUPERIOR
AT	ATAXIA	HS	HYPOPIGMENTED SPOTS	MLU	MULTIPLE LISCH NODULE UNIFORM
AX	ANOREXIA	HT	HYPERTENSION	NE	NODULAR EPISCLERITIS
BF	BIRD BEAK FACIES	HY	HYPERTHYROIDISM	NO	NODULAR NEUROFIBROMA
BR	BRONCHIECTASIS	IM	IRIS MAMMILATIONS	NY	NYSTAGMUS
C	ENLARGED CORNEAL NERVES	IMC	IMMATURE CORTICAL CATARACT	OA	OCULAR MOTOR APRAXIA
CA	CAHD	IN	INCREASED IOP	OP	ORAL PAPILLOMA
CD	MEGALOCORNEA	IP	IRIS PROCESS ABUNDANT	PA	PREMATURE AGING
CF	CAFÉ AU LAIT SPOT	L	PCIOL	PC	PECTUS CARINATUM
CH	CHOREOATHETOSIS	L5	5 CN PALSY	PCC	POSTERIOR CORTICAL CATARACT
CI	CORNEAL INFILTRATION	L7	LMN 7 CN PALSY	PE	PAPILLOEDEMA
CS	CILIARY STAPHYLOMA	L8	8 CN PALSY	PF	PSEUDO EXFOLIATION
CT	CONJUNCTIVAL TELANGIECTASIA	LG	LAGOPHTHALMOS	PM	PERSISTENT PUPILLARY MEMBRANE
PR	PROPTOSIS	LI	LOW INTELLIGENCE	PH	PEG TEETH
PSC	POSTERIOR SUBCAPSULAR CATARACT	R	RESTRICTED MOVEMENT	S	SEIZURE
PT	PTOSIS	RA	RPE ATROPHY	SI	SIBLING AFFECTED
PW	PORT WINE HAEMANGIOMA	RD	RETINAL DETACHMENT	SH	SUBUNGUAL HAMARTOMA
PX	PLEXIFORM NEUROFIBROMA	RP	RETINTIS PIGMENTOSA	SL	SLUGGISH PUPIL
RS	RIGHT DIVERG. SQUINT	SS	SHORT STATURE	V	VARICOSE VEIN
SWS	STURGE WEBER SYNDROME	TS	TUBEROUS SCLEROSIS	INP	INCONTINENTIA PIGMENTI
CO	COCKAYNE SYNDROME	ATG	ATAXIA TELANGIECTASIA	NF	NEURO FIBROMATOSIS