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Case report

CASE REPORT OF VON RECKLINGHAUSEN'S DISEASE

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ABSTRACT

Neurofibromatosis type -1 is a familial tumour syndrome belonging to genodermatosis group of disorders. It is genetically transmitted by autosomal dominance with variable penetrance. The disorder is characterized by benign growths of the peripheral nerve sheaths, neurofibromas and café au lait macules. A 45 year old male came with complaint of multiple asymptomatic swelling all over his body since birth. They were continuously progressing in size, one of which on the back, weighed 2.5 kgs , causing dragging pain. No constitutional or systemic symptoms were present. Patient was completely evaluated. Neurofibroma was confirmed with a biopsy. The results being normal. The plexiform lesion was excised. The patient is on regular follow up.

Keywords: Neurofibroma, Lisch's nodules, Genodermatosis, Schwann cells, Neurofibrin.

INTRODUCTION

Neurofibromatosis type -1 was formerly referred to as von Reckling Hausens disease after Friedrich Daniel von Recklinghausen, who first described it. It is a distinct genetic disorder characterised by benign growths of peripheral nerve sheaths, neurofibroma, and Café au lait macules. Also is associated with a repertoire of other cutaneous and systemic manifestations. The disease is classified under familial tumour syndromes, a group of Genodermatosis.

CASE REPORT

Krishna murthy a 45 year old male, an astrologer by occupation came with complaints of multiple swellings all over the body since

childhood and dragging pain due to a solitary swelling on his back. The swellings began as small papules and nodules, gradually progressed to present size. A solitary swelling on the back progressed to present size of 10*20 cms weighing 2.5 kgs over 6 years. H/O headaches, dull aching, intermittent in occurrence. No H/O pain in other swellings , pruritis, secondary changes on the overlying skin, learning disabilities , visual impairment, seizures, hearing abnormalities, bleeding tendencies, burning micturation, constipation . Not a known case of TB, DM, HTN, not undergone any surgical procedure. He is the last born of 11 siblings, out

of nonconsanguinous marriage. None of the other siblings are affected. Chews beetle leaf and nut, non smoker, non alcoholic.



Fig.1: Multiple swellings

Physical Examination: A 45 yr old male poorly built & nourished . Conscious and oriente. Pallor, Icterus, Clubbing- absent, Cyanosis , Lymphadenitis, Pedal Edema- absent. No obvious skeletal abnormalities. Macroglossia present. Vitals are stable and normal.

Dermatological Examination:

Multiple swellings(fig-1&2) present all over the body ranging from 2cm to 5cm in diameter. Soft to firm in consistency , pedunculated and sessile in nature. No vascular prominence.



Fig.2: Button hole sign - positive.

Café-au-lait macules(fig-3) present, >6 in number. Two plexiform swellings present over the back. One of which is 5×10 cm, approx 2 kgs weight (insitu), bag of worms feel, overlying skin is normal. Another plexiform swelling on

the palm(left). Axillary freckling present(Crowe's sign). Patrick-Yesudian sign – positive . Hair changes: none. Nail changes: none. Mucosa: oral and genital : normal



Fig-3 Café-au-lait macule

Systemic examination: CVS: S1, S2 heard, no murmurs. RS: Normal vesicular breath sounds heard , no added sounds. CNS: Clinically sound. Abdomen: Soft, no organomegaly, bowel sounds heard.

Investigations: Haemoglobin: 15.4g, Neutrophils : 57%, Eosinophils: 6%, BT: 2 mins 3 secs. ESR1/2 hr, CT: 4 mins, Lymphocytes 37%, Platelets: 3.85 lakhs/cumm, X-ray(A-P): normal. ECG: Normal. USG: Normal study, MRI BRAIN: Few small ill defined lesions showing hyper intense signal in both cerebellar hemispheres & right cerebellar peduncle representing white matter lesions.

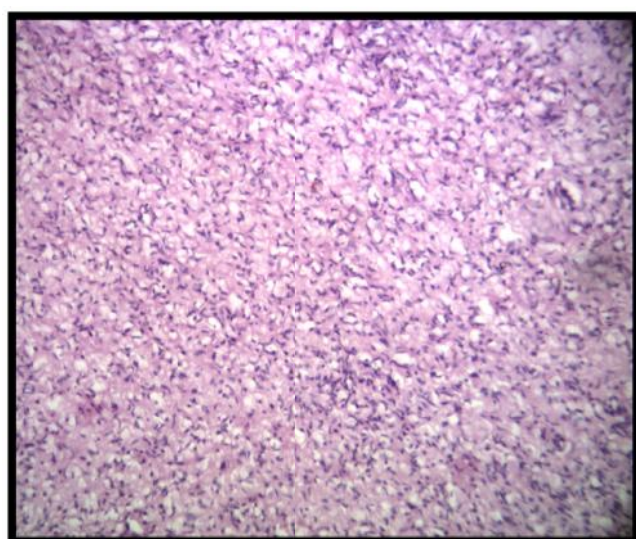


Fig.4: Biopsy: concomittant with neurofibroma(40X)

Slit lamp examination: Lisch's nodules present. ENT audiometry: normal. This patient underwent reduction surgery by plastic surgeon.



Fig:5 Plexiform neurofibroma (excised surgically)

DISCUSSION

Type 1 neurofibromatosis is also called Von Recklinghausen's disease. It is a multifactorial Autosomal Dominantly inherited disorder with variable penetrance. The incomplete or monosymptomatic form is common⁵. Random spontaneous de novo mutation of Neurofibrin gene on the chromosome² 17q11 occurs. Neurofibrin⁶ (GTPase activating enzyme) is a tumor suppressor gene which inhibits P21 RAS oncoprotein. RAS encodes membrane associated guanosine nucleotide binding protein involved in regulation of cell differentiation, proliferation & learning. Has variable expressivity. Affects cells of the neural crest (schwann cells, endoneural fibroblasts, melanocytes). 82% of affected children develop lesions by the age of one¹.

Pathology : Derived from peripheral nerves and supporting tissues. Arborising Schwann cells in collagenous interstitial tissue. Giant pigment cells in epidermal cells and melanocytes.

Types: Type 1-Von Recklinghausen's, Type 2-Acoustic, Type 3-Mixed, Type 4-Variant, Type 5-Segmental(non familial), Type 6-CALM, Type 7- Late onset(manifestations beyond 20 yrs), Type 8-Not otherwise specified

RICCARDI Diagnostic criteria^{3,6}:(any two)

1. Two or more neurofibroma cutaneous or subcutaneous on or under the Skin, one plexiform neurofibroma.
2. Intertrigous Freckling - axilla(Crowe's sign)
3. Six or more Café-Au-Lait⁷ spots >5mm in diameter in pre pubertal & >15mm in post pubertal individuals.
4. Skeletal abnormalities-Sphenoid wing dysplasia, kyphoscoliosis, thinning of long bones, with or without pseudoarthrosis.
5. On slit lamp examination-Lisch's nodules⁴ (vascular hamartomas of the iris).
6. Tumors of the optic pathway(gliomas).
7. A first degree relative with NF 1 by the above criteria.

Frequent associations aiding diagnosis:

1. Macrocephaly in 30% -50% of pediatric population(without hydrocephaly).
2. Epilepsy.
3. Juvenile posterior lenticular opacity.

Differential diagnosis: Café-au-lait⁷ macules may be present in normal individuals in 10%-20% of cases¹. Tuberous sclerosis, Bloom syndrome, Cowden's disease, Fanconi anaemia, Watson syndrome, Silver-Russel syndrome may also show café-au-lait macules. In children the presence of Plexiform lesions may stimulate congenital melanocytic naevus due to pigmentation and hypertrichosis.

Complications: Skeletal deformities-scoliosis may lead to nerve root compressions, spinal cord injury, osteomalacia, osteoporosis, short stature, Plexiform lesions may turn sarcomatous. Pheochromocytoma (most common). CML, Juvenile Xanthomatosis. Rhabdomyosarcoma, GIT stromal tumor, Somatostatinoma. Vasculopathy- renal stenosis with HTN, Cerebral infarct, bleeding aneurysms, intermittent claudication. Endocrine abnormalities: Acromegal, Addison's disease, precocious puberty, gynaecomastia, hyperparathyroidism. Subnormal Intelligence, Learning disabilities, attention deficits. Visual perceptual disabilities, UTI, constipation, pulmonary HTN. Speech impediments.

Neurological⁸ manifestations-intra cranial solitary tumors(optic nerve glioma, astrocytoma, schwannomas), Malignant peripheral nerve sheath tumors (MPNST). Wilms'tumor Malignant melanoma, Retinoblastoma.

Treatment modalities: Café-au-Lait spots causing cosmetic disfigurements can be treated with LASER(Carbondioxide¹, Ruby,YAG). Cutaneous Neurofibromas can be surgically excised(gamma knife surgeries are an option) Plexiform neurofibromas are excised Surgically, Pirfenidone¹⁴ (antifibrotic agent), PEG –interferon, INF- 2b methotrexate and vinblastine combination are being studied for use.

Prenatal diagnosis:Embryo-genetic testing/ counselling.Fetus -amniocopy , chorionic villous sampling, Fetoscopy can be done to plan the course of pregnancy.

CONCLUSION

This is a characteristic case of von Reckling Hausens disease with 4 out of the 7 diagnostic criterias fulfilled.the patient had no systemic manifestations.

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