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CLASSICAL CASE OF VON RECKLINGHAUSEN'S DISEASE MISTREATED AS NEUROTIC EXCORIATIONS

Neurology

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ABSTRACT

Von Recklinghausen's Disease, commonly known as Neurofibromatosis type 1 (NF1), is a multisystem disorder affecting approximately 1 in 3500 people. Most of the patients with NF1 are asymptomatic but neurological and bone abnormalities may be the present in some. Being autosomal dominant, family members are affected with great variability in expression of disease. These patients sometimes may have cognitive problems and learning disabilities and hence must be dealt with care. NF1 has a significant impact on quality of life through alteration of health and appearance. Adolescence is a particularly difficult time when neurofibromas may grow rapidly in response to hormonal changes. We hereby report a classical case of Von Recklinghausen's Disease which was missed at many instances and hence mistreated as Neurotic Excoriations thus leaving the patient confused and ill treated.

KEYWORDS

Von Recklinghausen's Disesae, Neurofibromatosis, Neurofibromas, NF1

INTRODUCTION

An autosomal dominant disorder, Von Recklinghausen's Disease, commonly known as Neurofibromatosis type 1 (NF1), is a multisystem disorder affecting approximately 1 in 3500 people. The earliest historical evidence first appeared in the 13th century but neurofibromatosis gained recognition as a distinct disorder Friedrich Daniel von Recklinghausen published his landmark paper (in German) On the Multiple Fibromas of the Skin and Their Relationship to the Multiple Neuromas in 1882. More recently, in 1956 Crowe, Schull, & Neel published a milestone manuscript detailing the numerous manifestations of this disorder. [1]

Most of the patients with NF1 are asymptomatic but neurological and bone abnormalities may be the presenting complaint in some. Being autosomal dominant, family members are affected with great variability in expression of disease. These patients sometimes may have cognitive problems and learning disabilities and hence must be dealt with care.

Neurotic excoriations are self-induced skin lesions caused by picking, rubbing, scratching or repetitive itching. Patients have poor impulse control and cannot avoid the desire to scratch. Depression, anxiety and OCD are the most common psychiatric disorders leading to neurotic excoriations. [2]

We hereby report a classical case of Von Recklinghausen's Disease which was missed at many instances and hence mistreated as Neurotic Excoriations thus leaving the patient confused and ill treated.

CASE REPORT

A 17 year old boy was referred to the Neurology OPD of a tertiary care hospital with the chief complaints of excoriated lesions over both arms, legs and abdomen present for 2months as a diagnosed case of neurotic excoriations by psychiatrists in private hospital, taking anti-anxiety medications at the time of presentation.

These lesions first developed over the lower abdomen gradually progressing and patient developed similar lesions over bilateral arms, forearms and spread over legs. He gave history of bleeding from these lesions and some lesions being dark colored. There was severe itching associated with these lesions.

He gave history of similar complaints last year and that lesions cleared completely in winters and aggravated in summers.

Patent was taking treatments from general physicians and psychiatrist for past 2 months for these and was labelled to have neurotic excoriations and was being given SSRIs along with oral antihistaminic for his symptoms.

FIGURE 1

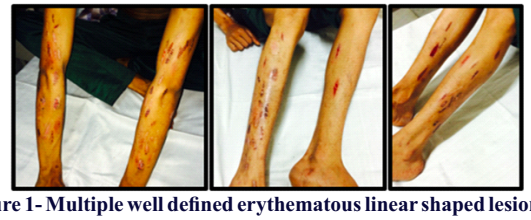


Figure 1- Multiple well defined erythematous linear shaped lesions with crusting (in few) present over bilateral arms, forearms and legs

Patient came to us for a second opinion as his symptoms were persisting despite regular treatment. On thorough questioning, he gave history of multiple asymptomatic nodular lesions over the abdomen developing 7 years back. On examination, we found these to be multiple neurofibromas, immobile and soft in consistency present almost over the same areas as excoriated lesions which were causing him to scratch himself and inflict excoriations. Dermatology opinion was taken for the above, confirming our findings, and suggesting NF along with dermatitis artefacta, as a differential.

FIGURE - 2

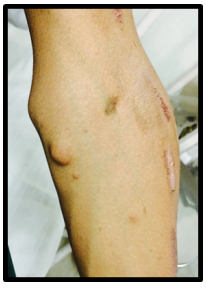


Figure 2 – Single well defined Nodular lesion suggestive of Neurofibroma present over the arm

He also had multiple hyper pigmented macules present over the upper back, palms (CALMs) and Axilla (Axillary freckling, pathognomic sign of NF1, Crowe's sign)

FIGURE -3

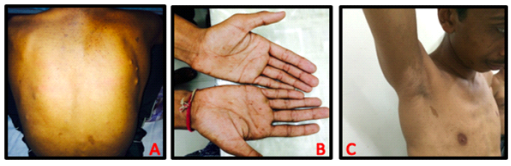


Figure 3 – Multiple Café Au Lait Macules (CALMS) present over A) Upper Back B) Bilateral Palms; C) Axillary Frecking, also known as Crowe's Sign

A detailed neurological examination was conducted and he was found to have no abnormalities (hearing or visual changes, ataxia, weakness, swallowing difficulties or changes in sensation). His blood pressure on multiple occasions was normal though he suffered from occasional headaches.

Ophthalmological examination revealed no evidence of Lisch Nodules. The patient underwent MRI assessment of brain with contrast but encountered no abnormalities.

In addition to these finding, we also found that his 2 brother had similar lesions in their bodies (First degree relatives with Nf1).

FIGURE - 4

Figure 4 – Patient along with his 2 siblings showing characteristic signs of NF

This patient continues in a longstanding monitoring, in particular for further skin changes, neurological symptoms and for the possibility of developing a pheochromocytoma.

A thorough history and examination is thus essential for diagnosis and proper treatment. We must emphasize here that clinical assessment should include examination of all other members of the family.

DISCUSSION

Neurofibromatosis is a multi system autosomal dominant condition affecting 1 in 3500 people, where tumours are developed along the course of peripheral nerves, and soft-tissue and bone deformities can also be present [3,4]. The majority of patients are asymptomatic but some can present with neurological or bone complains. The expression of the disease is highly variable among family members with the same mutation [5].

The NF1 gene encodes neurofibromin, a cytoplasmic protein that is predominantly expressed in neurons, Schwann cells, oligodendrocytes, and leukocytes. It is a multidomain molecule with the ability to regulate several intracellular processes, including the RAS-cyclic AMP pathway, ERK / MAP kinase cascade, adenylyl cyclase, and the cytoskeletal assembly.[6]

The initial manifestation of NF-I is usually café-au-lait macules (CALMs). It is a slowly evolving neurodermic dysplasia. Nodular neurofibromas can appear in peripheral nerves at any regions of the body and have the capability of growing into a large size, whereas, diffuse cutaneous neurofibromas are more common in adults, ranging from several to many thousands. Neurofibromas may involve many organs, including the stomach, intestines, kidney, bladder, larynx, and heart. In the head and neck region, the most commonly affected sites are the scalp, cheek, neck, and oral cavity.[7]

In present case, several soft tissue lesions, comparable to the localized neurofibroma, could be seen all over the patient's body. His siblings also had these lesions, but to a lesser extent.

NF1 has a significant impact on quality of life through alteration of health and appearance. Adolescence is a particularly difficult time when neurofibromas may grow rapidly in response to hormonal changes. [8]

The National Institute of Health Consensus Development Conference in 1988 proposed diagnostic criteria for neurofibromatosis type 1, if a patient has two or more of the following findings:

1. Six or more café au lait macules
2. Two or more neurofibromas of any type or one plexiform neurofibroma
3. Freckling in the axillary or inguinal regions
4. Optic glioma
5. Lisch nodules
6. Distinctive osseous lesion such as sphenoid dysplasia
7. Family history of the first-degree relative with neurofibromatosis. [9]

In our case, the patient has multiple café' au lait macules, multiple neurofibromas all over the body, has axillary frecking along with a definite positive family history with his 2 siblings (younger brothers) being affected.

The majority of patients are asymptomatic but some can present with neurological or bone complains.

Various neurological pathologies can also be found, such as, hamartomas of the iris, neurinomas of the acoustic nerve, tumors of the central nervous system (gliomas, glioblastomas), macrocephalies, and mental retardation (in 40% of cases).[10,11] The third offspring had a history of seizure in his childhood and had an arteriovenus shunt due to operation on his brain. There was no mass or tumor in his CT scan report, but diagnosis was intraventricular obstructive hydrocephaly.

Cognitive problems can be present in 60% of cases including difficulties at school, learning disabilities or attention deficits. Possible associated neurological symptoms include weakness, numbness and paresthesias in any extremities or parts of the body, as well as headaches in 20% of patients and seizures in up to 10% [4].

On account of the fact that neurofibromatosis is an autosomal dominant inherited disease, genetic consulting is necessary before marriage and before becoming pregnant, as well.

In the broadest sense, learning disabilities occur in nearly half of all NF1 patients and are a chief concern of parents. No consistent profile of the specific deficiencies in NF1 exists but an extensive review in 2006 found that patients have academic deficiencies, particularly in math and reading, slightly lower intelligence quotients (Iqs), and a high preponderance of ADHD.[12] These issues are of particular interest to the pediatric practitioner, as early intervention to address these concerns may lead to improved outcomes later in life.

These anomalies often cause patients to experience emotional and psychological trauma, which results in their isolation and withdrawal from society. Counselling and support groups are absolutely imperative in maintaining the psychological well being of these patients.

Therefore, awareness for the condition is absolutely imperative to defeating such discrimination. The emotional turmoil that results can be psychologically disastrous for the patient. It has significant effect on their position in society, and often results in them becoming completely reclusive.

India has still to develop a registered NF support organization of its own. The existence of such an organization, will greatly improve the quality of life for patients suffering from NF, and raise awareness for the condition in India, which is desperately needed.

The Manchester Checklist is widely used in the UK as a guide to patient management (Figure -5). [8]

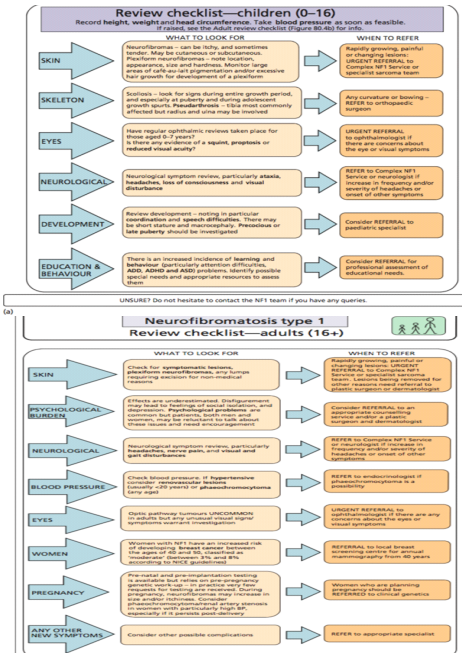
Neurofibromatosis type 1
Review guidelines

Annual Review Recommended

At time of diagnosis, or possible diagnosis, ALL patients should be seen in a genetics department. Those with significant complications will be followed up as appropriate through the nationally funded Complex Nf1 Service. Annual review should be undertaken by a community/district paediatrician and GP throughout childhood, and by a GP in adulthood. Patients, paediatricians and GPs have telephone access to the NF Service in Genetic Medicine for NF-related concerns.

Age	Genetics appointment	NF1 reviews carried out by	Vision checks
<6 and 50% risk	In first year and then at 2 and 5*[1]	Care coordinated by genetics	Symptom check at Nf1 review
<8 affected	Confirmation of diagnosis and assessment. Genetic counselling for family	GP and community/ district paediatrician. Liaison with NF service for complex cases	At least annual with paediatric ophthalmologist
8–15 affected	On request		Annual with optician/orthoptist
16–18 affected	Appointment for counselling re: adult complications and genetics	Care coordinated by GP	Symptom check at Nf1 review
>16 affected*[2]	On request		

*[1] If no café-au-lait spots by 5 years, NF1 can be excluded in the majority of NF1 families.
*[2] Women aged 40-50 should be referred for annual mammography as per 'moderate risk' NICE guidelines.



Multiorgan occurrence of NF1 requires a multidisciplinary approach. As there is no medical treatment for NF1, the management must be toward prevention and control of the complications. Although the rate of malignant transformation of NF1 is low (3 – 5%), these neoplasms can cause other clinical problems, including esthetic and functional compromising.

SUMMARY

Neurofibromatosis type 1 is a multisystem disorder requiring management by multiple disciplines, often coordinated through a primary care physician or a geneticist. The neurologist has a role not only in the diagnosis of NF1 and differentiating it from other similar disorders but also in the recognition of rare but associated manifestations. Genetic testing has increased our ability to make the diagnosis in uncertain cases but has not allowed us to predict a particular patient's natural history based on the mutation. Further research into genotype-phenotype correlations is needed before such predictions can be made. There is a paucity of available medical treatments but ongoing trials hold promise in treating both the cutaneous and non-cutaneous manifestations of NF1.

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