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# ALL THE DIAGNOSTIC CRITERIA OF NEUROFIBROMATOSIS TYPE-1 IN ONE FAMILIALCASE

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**Abstract**

Neurofibromatosis also known as von Recklinghausens disease, is an autosomal dominant condition caused by mutation, of the neurofibromatosis gene. The neurofibromatosis gene is located at chromosome 17q11.2. The expression and features of this genetic disorder are variable. The diagnosis of neurofibromatosis is based on the established criteria of National Institute of Health Conference and are met by an individual who demonstrates two or more of the criteria. This study demonstrate more than six well developed unique signs, and a huge plexiform of right arm world wide. The huge plexiform of arm with all its complications, disfigurement, and discomfort ness at its superlative degree of botheration. The familial case show Lisch nodules, glycoma, café-au-lait spots, skin freckling, café- au-lait bands, groin freckling, body tumors of different types and shape, bands of pendactile tumors, sprouting tumors, skeletal deformities, short stature, sever photophobia. and a very huge multilobular plexiform of several kg, weight with all its complications (Follow up study case).

**Keywords**: Lisch nodules, Photophobia, Café-au-lait spots, Plexiform.

## 1. Introduction

Neurofibromatosis type one, is the most common in human. Neurofibromatosis is an autosomal dominant disease with complete penetrance and extremely variable expression. It has one in three thousand to four thousand individual. The main clinical features of neurofibromatosis are Café-au-lait spots, cutaneous neurofibromas and Lisch nodules (Riccardi, 1992, Huson *et al.,* 1994). Other clinical manifestations are abnormalities of the cardiovascular, gastrointestinal, renal, and endocrine, facial and body disfigurement, cognitive deficit, and malignancies of the peripheral nerve sheathes and central nervous system. The neurofibromatosis gene was mapped to chromosome 17q 11.2 it was positionally cloned by (Cawthon, *et al.*,1990).

The neurofibromatosis gene spans at 350kb of genomic DNA, it contains 60 exons (Danglot, *et al.,* 1995). The neuriofibromin protein is responsible, which contains eight amino acids Marchuk *et al.,* (1991). The neurofibromin has a high similarity to ras–specific (GTPs) are activating proteins (GAPs) called the GAP-related domain (GRD), which under ras activity (Ballester, *et al.,* 1990).

In this study we have characterized phenotype variation and peculiarities of neurofibromatosis. This study also gives maximum signs and criteria for the diagnosis of this genetic autosomal dominant disorder and the aggressiveness and the discomfort. The study also show a very typical plexiform huge plexiform ever seen in the literature.

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## 2. Materials and Methods

The neurofibromatosis diagnosis was based on the National Institute of health consensus Conference criteria (Mulvihill *et al.*, 1990). The family belongs to Sindh. All the participants were well informed about the, and consent was obtained from all patients study their relatives, even neighbors. Taking a family history is a very important ingredient in making the diagnosis of a genetic disease, (Levitan *et al.*, 1997). The family history was taken from patients, and was repeatedly confirmed by asking questions from the relatives and neighbors. Pedigree was constructed according to the information data collected. Pedigree was constructed, and arranged in symbols. Photographs of affected areas showing Lisch nodules, Café-u-lait spots, skin freckling, groin freckling tumour band on the belt, Tumour strips at the spine and color bone, sessile tumours, pedunculated tumours, and a huge plexiform having unbearable weight, were taken. The clinical description of the genetic defect and case documentation conveys surgery removal of neurofibromatosis tumor and plexiform and histopathology. Surgeries were done by surgeon for tumours excession and the tissues were kept in 10% formalin. Blocks were made in paraffin wax and section cutting was done at 2mu. The sections were stained with Hematoxylin and counterstained with eosin. Eye examination (eye examination was made by eye specialist using slit lamp to confirm lisch nodules). Cafe-au-lait, spots were also examined carefully, according to National Institute of Health consensus conference neurofibromatosis.

## 3. Results and Discussion

This study focused on a familial case, suffering neurofibromatosis, type one, mainly and its complications such as plexiform (**Fig.1)**, with all its aggressiveness an observation which is in accordance with previous studies (Samuelsson 1981, Husen, 1989a, Riccardi, 1992). The study indicates that severity of neurofibromatosis with plexiform puts the patient in miserable condition with social andpsychological stress. These findings are consistent with the studies of Ablon (1999) Wolkenstein *et al.*,(2001).

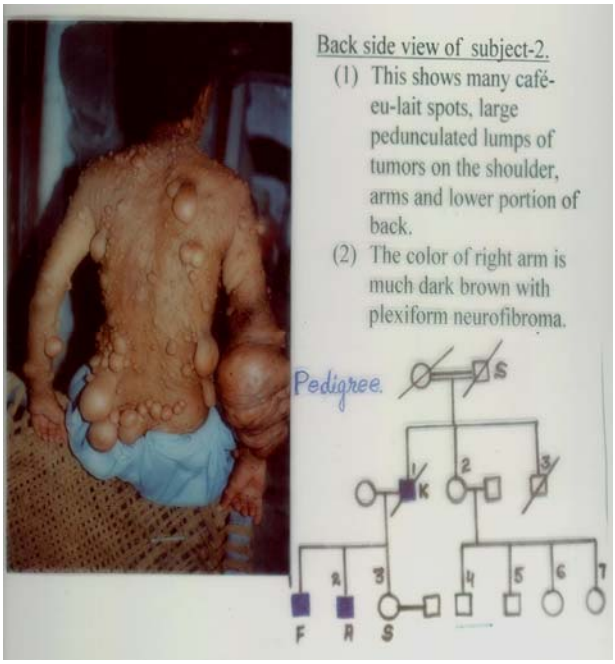


**Fig. 1. Back view of arm plexiform and pedigree.**

**Plexiform,**
**Belt tumors,**
**Café-au-lait band**

The analysis of familial case of neurofibromatosis revealed that in three generations there are three cases of neurofibromatosis (**Fig.2)**, and all are male members. The pedigree chart shows that the patient, in first generation II-3 was married with a female have no neurofibromatosis neither any genetic disorder signs. while the male was suffering with neurofibromatosis showing tumors on the chest. The third generation two female and two male, both the female were normal while the male were having neurofibromatosis. In III-1 and III-2 was suffering with neurofibromatosis with some initial signs right from birth such as Café-au-lait spots.

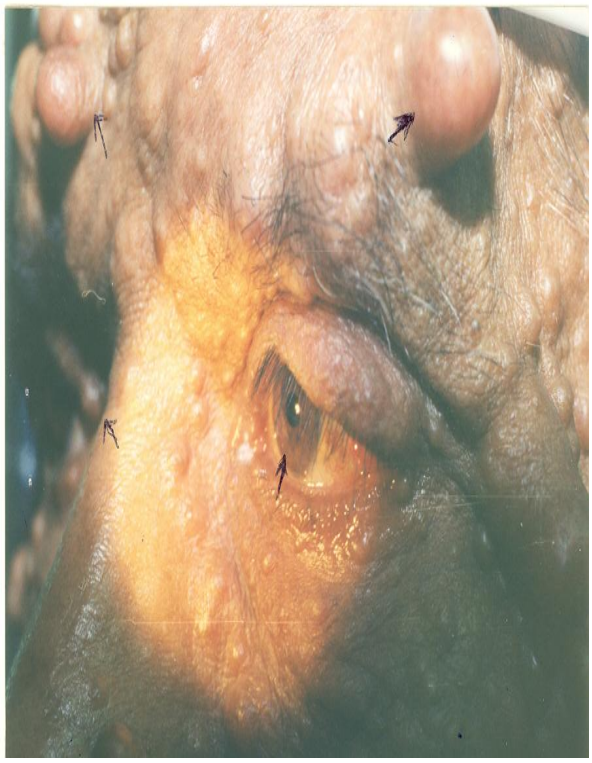

**Fig. 2. Lisch nodules**

**a. Horn neurofibroma.**
**b. Lisch nodules**

The signs of neurofibromatosis appear right from child hood. The photographs show (**Fig -3).**

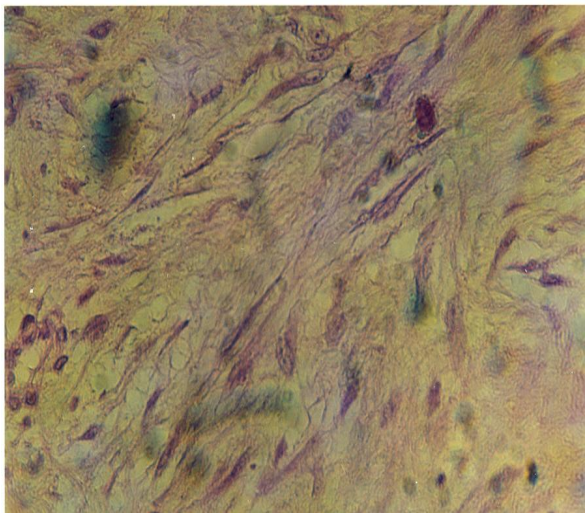

**Fig. 3. Histopathology of tumors**

**Nerve fibers,**
**Chronic cells inflammatory cells,**
**Spindle cells.**

many types of nerve tumors on skin. The patient III-2 gradually developed showing many types of tumors i.e. small tumors, large tumors, sessile tumors and pedunculated tumors, Large tumors start bleeding with slight hitting any pressure, or itching The wound healing, in epidermal neurofibromatosis, has suggested that trauma could play a part in the formation of the skin manifestations associated with neurofibromatosis, such as neurofibromatosis (Friedman *et al.*, 1999 Karvonen, 2000) and Café-au-lait spots. The tumors were ranging from 0.1cm to 36cm and showing a huge plexiform the picture shows line of large pedunculated tumors on belt, on spine on head appears as horns. Skin freckling appears as a band due to its high degree of expression. The subject no III-2, showing a big plexiform on the arm, with multinodular lumps putting several kg extra weight on the arm. The plexiform weight was unbearable. The study reveals all the features of neurofibromatosis which are given by NIH (1988) as diagnostic criteria. NIH confirms neurofibromatosis confirmation if two signs are positive. Messiaen *et al.*, (2000) studied many unrelated neurofibromatosis one patients fulfilling the NIH diagnostic criteria Stumpf *et al.*, (1988) Gutmann *et al.*, (1997). This confirms our study more authencity that many diagnostic criteria are well prominent in one familial case, which is very rare. The subjects III-1 and III-2 both showing Lisch nodules, short stature, husky voice, neurofibromatosis in the nostrils. The subject III-1 developed severe photophobia and scoliosis was also seen.

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