

Original Article

Evaluation of Phenotypic Characteristics of 53 Cases of Neurofibroma in Hazrat Fatemeh Hospital during the Years 1994-2005

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ABSTRACT

Background and Objective: Neurofibromas occur as solitary and multiple forms. The solitary ones are extraneural and more common, histologically exhibiting spindle cells with wavy nuclei, scattered among collagen fibers. Multiple neurofibromas are seen in neurofibromatosis (types I and II), including intraneural (plexiform, cutaneous deep circumscribed) and extraneural (cutaneous, deep diffuse) variants and various combinations of the above mentioned forms. In reviewed literature, solitary localized neurofibromas are mentioned to affect the genders equally, most develop in persons between the ages 20 and 30 years and evenly distribute over the body surface. Since Hazrat Fatemeh hospital is the referral center of dermatology, it seemed that evaluation of patients with neurofibroma within 11 years could be helpful.

Materials and Methods: The present study included 53 patients with neurofibromas who referred to department of pathology of Hazrat Fatemeh Hospital during the years 1994-2005. Their lesions were diagnosed as neurofibromas by the pathologist. Lesions were categorized into solitary or multiple neurofibromas, then sex and age distributions and the involved areas were compared in each group.

Results: In solitary group, neurofibromas were distributed in order of frequency over face (48%), upper extremities (13%), scalp, trunk, and lower extremities each one 9%, and neck (4%). The frequencies of distribution for neurofibromatosis were face (40%), upper extremities (23%), trunk, and lower extremities each one 14%, and scalp and neck each one 6%. Solitary neurofibromas of face, trunk, and upper extremities predominated in females, but lesions of scalp, neck, and lower extremities were more common in males. In contrast, neurofibromatosis of face, scalp, and neck were more frequent in males, the reverse was true for lesions of trunk and extremities. The peak incidence of solitary neurofibroma was within the ages of 15 and 30 years. In comparison, the peak incidence of neurofibromatosis was between 9 and 13 years. One third of neurofibromatosis developed plexiform neurofibromas, but no single case was observed in solitary group. None of the solitary or multiple neurofibromas were transformed to malignancy up to the time of current study.

Conclusion: The solitary neurofibromas of head ($p < 0.04$) and multiple neurofibromas of face ($p = 0.04$) were more prevalent in males, while multiple neurofibromas of upper extremities ($p < 0.03$) were more frequent in females. Age distribution of solitary neurofibromas as compared to references and lower incidence age of neurofibromatosis in the study were in concordance with references.

Key words: Neurofibroma, Neurofibromatosis, Plexiform

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Introduction

Neurofibroma is one of the most prevalent of benign tumors (1). It occurs as solitary or multiple forms. Its growth pattern can be limited, diffuse, and/or plexiform. Solitary form that is the most common one (90%) appears soft, polyploid, adjacent to small nerves, and its color is similar to skin or to some extent mustard-like. This form is rarely greater than 1 cm in size, its growth is limited, usually seen at an age range of 20-30 years and has a uniform distribution over the body surface (2,3). The presence of at most 4 small solitary cutaneous neurofibroma in the absence of other symptoms can not be an indication of neurofibromatosis (3). Neurofibroma is usually eosinophilic, with marked margin, without capsule, is extraneural, and is a combinational growth of all parts of peripheral nerve including axon, Schwann cell, and fibroblasts. Schwann cells are usually the predominant parts and appear as spindle cells with wavy nuclei that intersperse regularly between wavy thin collagen fibers (3,4). These fibers are usually as both dense and separated in a diffuse background. Although they have apparently a nodular appearance, but can invade neighboring adipose and cutaneous tissues (5). Meanwhile, neurofibroma background usually contains many mast cells. In addition, rare cases of solitary neurofibroma may be composed of numerous separated stellate and spindle cells in a mixed pattern. It is not an important sign to have focalized dispersed cells with large hyperchromatic nuclei in the absence of mitosis. Epidermal appendices are regularly maintained in dermal neurofibroma. Sometimes, an involvement of small nerves has been observed with their enlargement and higher cellularity.

Multiple cutaneous neurofibroma is usually a characteristic of neurofibromatosis (von Recklinghausen's disease). Other lesions of this syndrome with regard to their incidence include plexiform neurofibroma (intraneural), deep diffuse (extraneural), peri-areolar multiple neurofibroma, Lisch intraocular nodule, macular dermal hyperpigmentation, and bilateral axillary alopecia. Milky brownish spots exist in all cases of neurofibromatosis. Number of spots greater than 6 and each one larger than 1.5 cm can indicate the presence of neurofibromatosis.

Although type I neurofibromatosis (peripheral or NFI) can be inherited through a dominant autosome, but approximately half of the cases have a mutation.

Dermal neurofibroma develops some times before puberty or during puberty and its size and number gradually increases. In this disorder, there is an involvement of superficial and deep nerves, nerve roots, visceral autonomic nerves, and blood vessels (3). Meanwhile, it can occur in axilla, buttock, thigh, deep soft tissue, orbit, mediastinum, retroperitoneal space, tongue, gastrointestinal system, and many other places (2). Range of neurofibroma is very widespread in type I neurofibromatosis including extraneural dermal types (like solitary kind), superficial or deep with marked boundaries (intraneural), plexiform (intraneural), deep diffuse (extraneural), and a combination of these conditions (3). Plexiform and diffuse neurofibroma is closely associated with type I neurofibromatosis. Plexiform type is almost always pathognomonic (2) and 10% of patients with diffuse lesions have neurofibromatosis (5). The appearance of large plexiform neurofibroma resembles a wormy network and at low magnification shows itself as small nodules with dense eosinophilic pattern that is residues of lesioned nerve (5). In regional or limited neurofibromatosis that is a subtype of dermal neurofibroma, there is lower dermal neurofibromas and with a negative family history (3). In addition, there is a low probability for neurofibromas of type I neurofibromatosis to differentiate into malignant tumors of nerve sheath (with an incidence of 3.6-4.6%) (5). It may occur at lower ages than usual and more frequently seen in lower extremities (6). The incidence of malignancies related to neurofibromatosis including sarcomas, carcinomas, and melanomas is higher than other causes in normal population (7-9).

The genetics of type II neurofibromatosis (central or NFII) is different from type I and about half of its cases is due to new mutations (10) with milky brownish spots, neurofibroma, and various intracranial tumors including bilateral auditory nerve Schwannoma.

Although in most studies, age and sex distribution and metastasis pattern of lesions in solitary neurofibroma (as a common benign neoplastic lesion) has been reported alike (2-4), but it seems that their prevalence is different between males and females and for different parts of the body and its incidence appears to be higher in men and in extremities (11). Therefore, this study was conducted to evaluate the related parameters in referrals of department of pathology, Hazrat Fatemeh hospital with a diagnosis of neurofibroma.

Materials and Methods

The present study was conducted on 53 patients with neurofibromas who referred to department of pathology of Hazrat Fatemeh Hospital during the years 1994-2005 with a diagnosis of neurofibroma. Lesions were categorized into solitary or multiple neurofibromas, then sex and age distribution, involved areas, plexiform cases, and malignancy rate for each group were analyzed. For statistical analysis, χ^2 test was used.

Results

In this study, 60% (31) and 40% (22) of patients had solitary neurofibromas and neurofibromatosis respectively. In solitary neurofibroma group, 56% (18) of cases were female and 44% were male and the frequency for neurofibromatosis in females and males was 46% (10) and 54% (12) respectively. In addition, frequency of plexiform neurofibromas in patients with neurofibromatosis was 33% (7) and none of the solitary group had such a condition. In solitary group, neurofibromas were distributed in order of frequency over face (48%, n = 15), upper extremities (13%, n = 4), scalp, trunk, and lower extremities each one 9% (n = 3), neck (4%, n = 2), and unreported cases as 3% (n = 1). The frequencies of distribution for neurofibromatosis were face (40%, n = 9), upper extremities (23%, n = 5), trunk and lower extremities each one 14% (n = 3), and scalp and neck each one 6% (n = 1) (Figure 1).

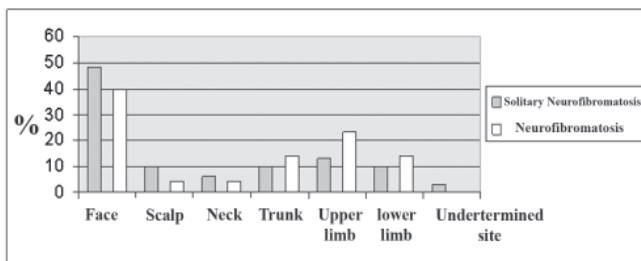


Figure 1. Frequency distribution of solitary and multiple neurofibroma

In cases of solitary neurofibromas with regard to sex distribution for males and females, the frequency was 33% (5) and 66% (10) for face, 100% (3) and 0% for scalp, 100% (2) and 0% for neck, 0% and 100% (3) for trunk, 25% (1) and 75% (3) for upper extremities, and 66% (2) and 33% (1) for lower extremities. In cases of neurofibromatosis with regard to sex distribution for females and males, the frequency was 11% (2) and 89% (7) for face, 0% and 100% (1) for scalp and neck,

100% (3) and 0% for trunk, 80% (4) and 20% (1) for upper extremities, and 66% (2) and 33% (1) for lower extremities (Figure 2).

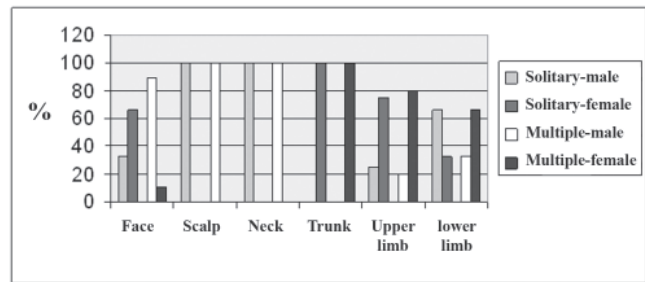


Figure 2. Frequency distribution of solitary and multiple neurofibroma with regard to sex

The peak incidence of solitary neurofibroma was within the ages of 15 and 30 years. In comparison, the peak incidence of neurofibromatosis was between 9 and 13 years (Figure 3). In addition, none of the referred patients had any malignancy at the time of follow up until study conductance.

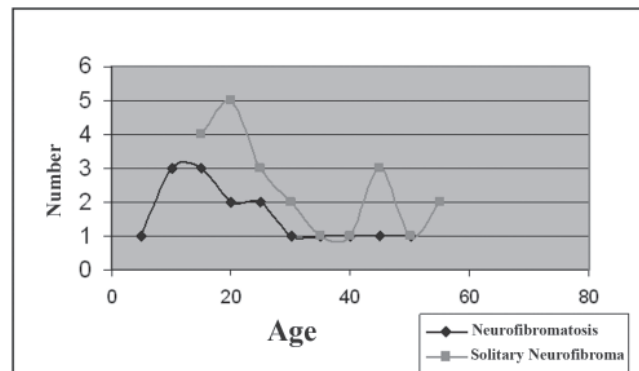


Figure 3. Age distribution of patients with solitary neurofibroma and neurofibromatosis

Discussion

Neurofibromas are common benign tumors that with regard to prevalence are next to lipomas, fibrosis histiocytoma, nodular fasciitis, hemangioma, and fibromatosis (1). Therefore, studying age, sex, and metastasis pattern of this tumor is clinically important.

In studied references, solitary dermal neurofibromas comprise 90% of cases and its sex distribution is uniform for body parts and its common age of occurrence for dermal region is also uniform (2-5) and type I neurofibromatosis predominates in men and is more common in extremities (11).

Since Hazrat Fatemeh hospital is a skin reconstruction (plastic surgery) referral center, therefore, a higher incidence of dermal solitary neurofibromas (60%) was

obtained in this study as compared to other studies (2-3). In addition, a higher incidence of solitary neurofibroma was obtained for females that is due to limited number of samples is not statistically significant ($p>0.05$). The same fact is also true for higher incidence of neurofibromatosis in men in this study that is consistent with another study (11). It appears that a larger sample size is required for a more accurate conclusion on its sex predominance.

On the other hand, higher prevalence of solitary lesions of head ($p<0.04$) and multiple lesions of face in men ($p=0.04$) and greater incidence of upper extremity lesions in women ($p<0.03$) was statistically significant. Meanwhile, higher metastasis of lesions in face for both groups was also significant ($p<0.05$) and more studies are warranted to be performed to determine its metastasis pattern in other regions of body. In this study, prevalence of lesions of type I neurofibromatosis was highest for face and in the next order, for extremities that is contrast to another study. Meanwhile, in the latter study, prevalence of plexiform neurofibroma was reported as 8%, while in our study it was obtained as 33%. In addition, in that study, prevalence of malignancies due to type I neurofibromatosis was 3%, while in our study no such cases was found out (11) that may be due to differences in used sample size and indifferention of types II and III neurofibromatosis. Finally, age distribution of solitary neurofibroma in this study was 15-30 years that is consistent with references (20-30 years). In addition, a lower age of incidence of neurofibromatosis was also consistent with references (2-5).

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