CASE REPORTS

LATE-ONSET NEUROFIBROMATOSIS (NF-7): A CASE REPORT

GEÇ BAŞLANGIÇLI NÖROFİBROMATOZİS (NF-7): OLGU SUNUMU

Mehmet YILDIRIM, M.D., Demet KESİCİ, M.D., Vahide BAYSAL, M.D.,
Özden ÇANDIR*, M.D., Ahmet AKKAYA**, M.D.

Suleyman Demirel University Faculty of Medicine, Departments of Dermatology, Pathology* and Pulmonology, Isparta, Turkey.**
Gazi Medical Journal 2004; 15: 107-110

SUMMARY: We present a 68-year-old man with late-onset neurofibromatosis (NF-7), a very rare form characterized by the development of neurofibromas at a later adult age and by the occasional occurrence of malignant tumors. Common characteristics, such as café au lait spots, axillary freckling, and Lisch nodules, were not present.

***Key Words:** Neurofibromatosis, Type-7, Meningioma.*

ÖZET: İleri yaşlarda nörofibromların gelişmesi ile karakterize olan ve nadiren malign tümöral oluşumlarla seyreden 68 yaşındaki geç başlangıçlı nörofibromatozisli (NF-7) bir olgu sunuyoruz. Olguda nörofibromatozisin sık görülen özelliklerinden café au lait lekeleri, aksiller çillenme ve Lisch nodülleri yoktu.

***Anahtar Kelimeler:** Nörofibromatozis, Tip-7, Meninjiom*

INTRODUCTION

Neurofibromatosis (NF) is an autosomally dominant, inherited syndrome manifested by developmental changes in the nervous system, bones, and skin. Several types have been described. NF-1 (classic form) is the most common form, with a disease prevalence in population-based studies of approximately 1/ 4500 (1-3). The responsible gene (NF-1 gene) is located near the centromere of chromosome 17. NF-1 includes the development of multiple cutaneous neurofibromas and café au lait spots. NF-2 (central or acoustic) is genetically different from type 1 and results from the alteration of a gene located in chromosome 22. Type 2 NF is distinguished by bilateral acoustic neuromas (1,4,5). Our patient suffered from the very rare late-onset form (NF-7), characterized by the development of neurofibromas at a later adult age.

CASE REPORT

A 68-year-old man was referred to the dermatology department because of multiple tumoral lesions on his abdominal region. He had had multiple tumoral lesions that had not bothered him except cosmetically for twenty years. The tumors were 1-2 cm, small, skin colored, pandulous, cutaneous tumoral lesions on the abdomen (Fig. 1). He had no axillary freckling or café au lait spots. No one else in his family suffered from NF. Lisch nodules and optic glioma were not seen in an ophthalmologic examination. Neurologic and other systems were normal. Laboratory findings including a test for tumor markers were normal. Chest radiography, abdominal ultrasonography, thoracal and abdominal computed tomography (CT) scans were also normal. The skeletal system was normal upon radiological examination. Cranial CT showed a 35x30x36 mm mass that was considered a meningioma in the anterior fossa

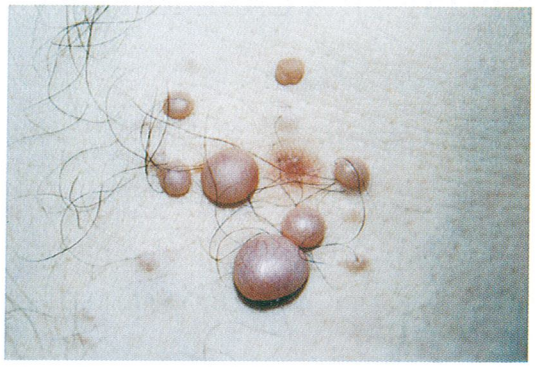

Fig. 1: Clinical appearance of the case.

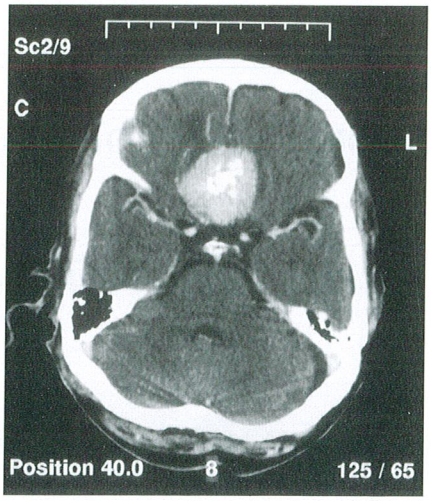

Fig. 2: The patients' cranial CT is showing the meningioma.

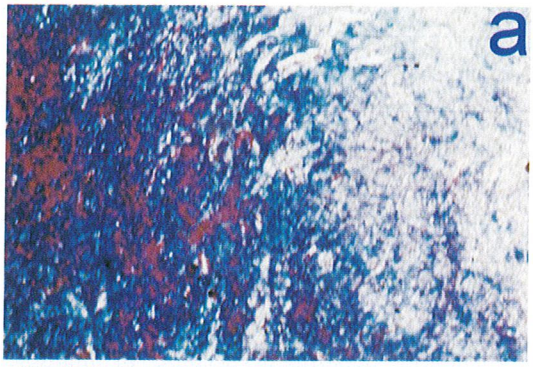

Fig. 3A: Red stained nerve tissue and blue stained fibrous tissue components (MT, X40).

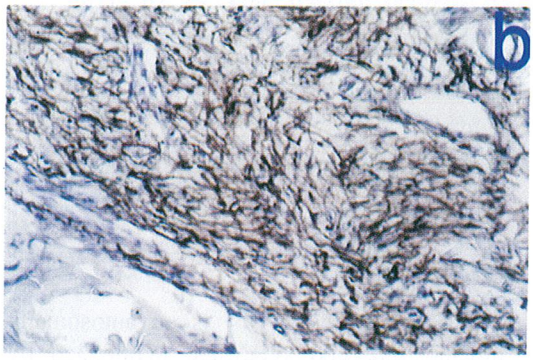

Fig. 3B: Positive stained nerve fibers in tumoral tissue (S 100, X40).

(Fig. 2). One of the tumoral lesions in the skin was surgically excised and histopatologically examined. Light microscopy showed spindle-shaped tumor cells arranged in interlacing fascicles with Masson trichrome staining, with which fibers of fibrous tissues are blue-stained and nerve tissues are red-stained (Fig. 3a). Immunohistochemical analysis of the tumor cells showed immunoreactivity for S-100 protein (Fig. 3b) and vimentin (Fig. 3c). Smooth muscle actin was not expressed in the tumor (Fig. 3d).

DISCUSSION

NF, an autosomally dominant disease arising from maldevelopment of the neural crest, is localized on chromosomes 17 (NF-1) and 22 (NF-2). The major features of NF-1 are multiple café au lait spots, multiple peripheral neurofibromas, axillary freckling, optic gliomas, Lisch nodules (iris hamartomas), and osseous lesions (6). NF-2 is characterized by acoustic neurinomas and is much less common than NF-1. NF-2 causes significantly more morbidity and mortality than other forms of NF (3).

Atypical forms are uncommon (Table 1). Riccardi categorized eight types of NF, including NF-1 (von Recklinghausen NF), NF-2 (bilateral acoustic NF), NF-3 (mixed NF), NF-4 (variant NF), NF-5 (segmental NF), NF-6 (multiple familial café au lait spots), and NF-7 (late onset NF). Moreover, there are also cases of an

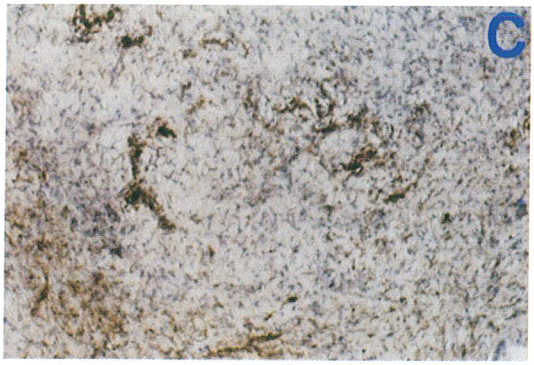

Fig. 3C: All components of tumoral tissue are positive stained (Vimentin, X200).

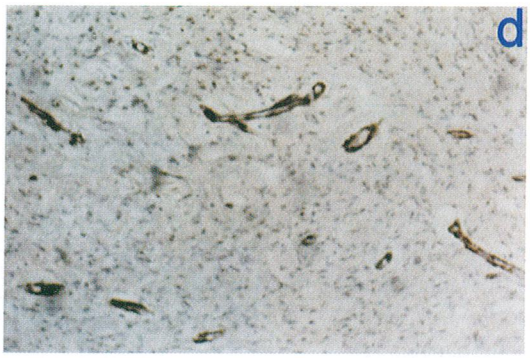

Fig. 3D: Tumoral tissue is SMA negative and positive stained tunica muscularis of the vessels of tumoral tissue (SMA, X40).

Table 1. Typical and atypical forms of neurofibromatosis (NF) according to Riccardi's classification (4,6,7)

Type	Designation	Characteristic features
Typical forms		
NF 1	Classic form	Six or more café au lait spots, two or more neurofibromas, freckling (axillary or inguinal), Lisch nodules, optic gliomas, pseudarthrosis (at least two of these features have to be present), short stature, mental retardation, kyphoscoliosis.
NF 2	Central form	Acoustic neurinomas (bilateral in 90%)
Atypical forms		
NF 3	Mixed form	Café au lait spots, neurinomas or neurofibromas, multiple central nervous system tumors (glioma, meningiomas)
NF 4	Variant form	Café au lait spots and neurofibromas (in at least two large or noncontiguous body regions), no other features of NF 1
NF 5	Segmental form	Café au lait spots and neurofibromas (confined to a small region of the body)
NF 6	Spot form	Café au lait spots
NF 7	Late onset NF	Development of neurinomas and neurofibromas in the third decade of age or later, malignant transformation of neurofibromas
NF 8	Unspecified form	Typical features of NF that do not fit into one of the above-mentioned categories.

unspecified type (NF-8). NF-3 represents a mixture of NF-1 and NF-2 and is characterized by small numbers of café au lait spots, bilateral acoustic neuromas, and various other neural tumors. Type 5 is characterized by restriction of café au lait spots and neurofibromas to one part of the body without crossing the midline. Type 6 is characterized by the presence of café au lait spots as the primary or sole feature, with no Lisch nodules, neurofibromas, or other neural crest tumors. In type 7 neurofibromatosis, neurofibromas do not become apparent before the end of the third decade. It is not yet known whether it is inherited or not (1,4,6,7).

The late-onset (NF-7) form begins in the third decade or later, with the development of multiple cutaneous and deeper neurofibromas and/or neurinomas, whereas the first clinical features of other types appear in early childhood or, at the latest, during puberty. Our patient's

neurofibromas developed after the fourth decade. Common characteristics, such as café au lait spots, axillary freckling and Lisch nodules, are not present in this type (4). Our patient showed none of these findings either. He had no family history of NF. NF-7 is characterized by occasional occurrence of malignant tumors associated with a poor prognosis. Based on Riccardi's classification, we consider this case to be an example of NF-7. Only a few cases of this type have been reported to date (4).

There is no treatment for the neurofibromas except excision. Deaths have been reported from intracranial meningiomas and gliomas, peripheral nerve sarcomas and other associated malignancies (1).

The intracranial mass in our patient was excised and histopathologically examined. The diagnosis of meningioma was confirmed. The patient has no other complaints at present.

Correspondence to: Mehmet YILDIRIM, M.D.
Süleyman Demirel Üniversitesi
Tıp Fakültesi,
Dermatoloji Anabilim Dalı,
32100, ISPARTA-TÜRKİYE
Tel: 246- 211 25 03
Fax:246- 237 17 62
E-mail: yildirim@med.sdu.edu.tr

REFERENCES

1. Odom RB, James WD, Berger TG. Andrews' Disease of the Skin Clinical Dermatology. 9th ed. Philadelphia: WB Saunders Company; 2000.
2. Ruggieri M. The different forms of neurofibromatosis. Childs Nerv Syst 1999; 15: 295-308.
3. Ruggieri M, Huson SM. The neurofibromatosis: An overview. Ital J Neurol Sci 1999; 20: 89-108.
4. Drews G, Emmrich P, Hauss J, Spiegel H. Malignant schwannoma and late-onset form neurofibromatosis (NF VII) in a patient with skeletal manifestations. Langenbecks Arch Surg 1999; 384: 441-444.
5. Pivnick EK, Riccardi VM. The neurofibromatosis. In. Freedberg IM, Eisen AZ, Wolff K, (eds): Dermatology in General Medicine. 5th ed. New York: McGraw-Hill; 1999. p. 2152-2158.
6. Ogose A, Hotta T, Imaizumi S, Saito H, Homma T, Takahashi HE. Deep-seated segmental neurofibromatosis without café au lait spots. Skeletal Radiol 2000; 29: 543-547.
7. Lin AN, Carter DM. Hereditary cutaneous disorders. In. Moschella SL, Hurley HJ (eds): Dermatology. 3rd ed. Philadelphia: WB Saunders Company; 1992. p. 1335-1380.