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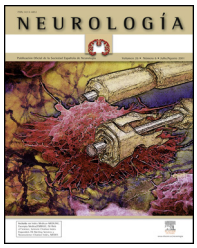

ORIGINAL ARTICLE

Clinical and neuroradiological signs in adults with type 1 neurofibromatosis☆

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KEYWORDS
Type 1 neurofibromatosis;
Brain tumours;
Brain magnetic resonance imaging;
Neurofibromas;
Age;
Sex

Abstract
Introduction: Type 1 neurofibromatosis is the most common neurocutaneous syndrome. Most published case series study the paediatric population.
Material and methods: Cross-sectional study of cases of type 1 neurofibromatosis from neurology departments that were recorded in a database. We analysed the different clinical variables providing the diagnosis as well as demographic and neuroradiological variables.
Results: We found a total of 31 patients with type 1 neurofibromatosis. The mean age was 28.9 years and 58.4% were women. Subjects with unidentified bright objects (UBOs) were younger than those without them (22.45 ± 8.22 years vs. 32.5 ± 10.64; $P = .011$). In contrast, subjects with neurofibromas were older than those without them (30.56 ± 10.68 years vs. 18.25 ± 4.34; $P = .032$). No sex differences were found in the presentation of clinical or radiological variables. Seven patients (22.6%) had tumours; 3 were optic pathway gliomas (1 bilateral), 3 were plexiform neurofibromas, and 1 was a pilocytic astrocytoma in the brainstem.
Conclusions: Patients with type 1 neurofibromatosis presented both peripheral neurofibromas and tumorous lesions of the central nervous system. Subjects with neurofibromas were older than those who did not present them, while subjects with UBOs were younger than those without such lesions.

PALABRAS CLAVE
Neurofibromatosis tipo 1;
Tumores cerebrales;

Manifestaciones clínicas y neurorradiológicas en los adultos con neurofibromatosis tipo 1

Resumen
Introducción: La neurofibromatosis tipo 1 es el trastorno neurocutáneo más frecuente. La mayoría de las series de casos publicadas son sobre la población pediátrica.

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Resonancia magnética cerebral;
Neurofibromas;
Edad;
Sexo

Material y métodos: Estudio transversal de los casos de neurofibromatosis tipo 1 en las consultas de neurología recogidos en una base de datos. Se han analizado las diferentes variables clínicas que conforman el diagnóstico, así como las variables demográficas y neurorradiológicas.
Resultados: Se han encontrado un total de 31 pacientes con neurofibromatosis tipo 1. La edad media ha sido de 28,9 años y el 58,4% son mujeres. Los sujetos con lesiones tipo *Unidentified bright objects* (UBO) son más jóvenes que los que no las presentan ($22{,}45 \pm 8{,}22$ años vs. $32{,}5 \pm 10{,}64$; $p = 0{,}011$), por el contrario, los sujetos con neurofibromas son mayores que los que no los tienen ($30{,}56 \pm 10{,}68$ años vs. $18{,}25 \pm 4{,}34$; $p = 0{,}032$). No hay diferencias de sexo en la presentación de las variables clínicas ni radiológicas. Siete pacientes presentaron tumores (22,6%), 3 fueron gliomas del tracto óptico (uno de ellos bilateral), 3 neurofibromas plexiformes y un astrocitoma pilocítico del troncoencéfalo.
Conclusiones: Los pacientes con neurofibromatosis tipo 1 no solo presentan lesiones tumorales a nivel periférico en forma de neurofibromas, sino también a nivel del sistema nervioso central. La edad de los sujetos que tienen neurofibromas es mayor que la que no los presentan, sin embargo, los que presentan UBO son más jóvenes que los que no poseen estas lesiones.

Introduction

Type 1 neurofibromatosis (NF1) was first described by von Recklinghausen in 1882. NF1 is the most common neurocutaneous syndrome and its approximate incidence is 1 per 3000 to 3500 live births.[1] It affects both sexes equally. This autosomal dominant inherited disorder has high penetrance and markedly variable clinical expression. About 30% to 50% of the cases are due to de novo mutations. In 1990, the gene responsible for this disease was detected in the long arm of chromosome 17. The protein produced by this gene, neurofibromin, was also identified.[2]

Diagnosis of NF1 is based on the presence of at least 2 of the criteria established by the National Institute of Health Consensus Development Conference in 1988 (Table 1). However, it is currently diagnosed by identifying the gene mutation of NF1, which is present in 95% of all cases. Most NF1 manifestations are strongly age-dependent; neurofibromas do not usually appear before adolescence and their frequency increases with age. Café-au-lait spots, in contrast, are usually present by the age of 5, but their number begins to decrease at about the age of 50.[3] Some studies reveal that NF1 patients present a shorter life expectancy.[4]

In addition, T2-weighted MRI signal changes known as unidentified bright objects (UBOs) have been described in 43% to 93% of children with NF1.[5] UBOs are uncommon in NF1 patients older than 20. They are usually located in the globus pallidus, thalamus, hippocampus, and brainstem. Although most of these lesions may remain stable or even disappear, some may transform into gliomas.[6]

Given that most series examining NF1 cases include paediatric patients, our aim is to ascertain the clinical and neuroradiological characteristics of a series of adults with NF1.

Table 1 Diagnostic criteria for type 1 neurofibromatosis. Two or more of the following criteria are required.

1. *Six or more café-au-lait spots with the following diameter:*
   ≥5 mm before puberty
   ≥15 mm after puberty
2. *Two or more neurofibromas of any type or one plexiform neurofibroma*
3. *Axillary or inguinal freckling (Cowden syndrome)*
4. *Optic pathway glioma*
5. *Two or more Lisch nodules (benign hamartomas of the iris)*
6. *Typical bone lesions:*
   Sphenoid dysplasia
   Dysplasia or thinning of long bone cortex (pseudarthrosis)
7. *First-degree relatives with NF1*

Materials and methods

This cross-sectional study of patients diagnosed with NF1 and treated in neurology consults. Data from patients' routine clinical assessments were kept in a database. NF1 was diagnosed according to the criteria of the National Institute of Health Consensus Conference. Patients monitored in our consults were aged 14 years and older.

We recorded the following demographic and clinical data: sex, age, family history, referring department, and the presence of café-au-lait spots, neurofibromas, axillary or inguinal freckling, Lisch nodules, skeletal changes, or neurological symptoms. Similarly, patients' neuroimaging tests were checked in order to confirm the presence of UBOs,[5] optic pathway gliomas, cerebral astrocytoma, stenosis of the aqueduct of Sylvius, and vascular lesions. In patients with lesions, we monitored lesion changes using serial neuroimaging tests.

Quantitative variables were expressed as means and standard deviations, whereas qualitative variables were expressed as percentages. Means and cross tabulations were compared using the chi-square test to determine whether the patients' clinical and neuroradiological characteristics reflected age or sex differences. We used SPSS software® v. 15.0. The level of statistical significance was set at $P < .05$