Ring chromosome 22 and Neurofibromatosis type II: a case report

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Introduzione

Ring chromosome 22 is a rare human constitutional cytogenetic abnormality: associated symptoms and findings may be extremely variable from case to case. Neurofibromatosis type 2 (NF2) is a rare autosomal dominant syndrome that is primarily characterized by the presence of bilateral vestibular schwannomas/acoustic neuroma (Fig.1). NF2 results from mutations of a gene on the long arm (q) of chromosome 22 (22q12.2). Clinical features of neurofibromatosis type 1 and 2 as well as different tumor types have been reported in patients with ring chromosome 22[(1)] .

Case report

Here, we report a 29-year-old female who was diagnosed with a vestibular schwannomas of the left acoustic nerve with associated symptoms of tinnitus, hearing loss, and balance dysfunction. No cutaneous signs at the general clinical examination. She underwent surgery for removal of the schwannoma. Her mother presented with multiple meningiomas and died at the age of 52ys for complications of benign brain tumors, her sister died in the first year of life for a brain tumor (Fig.2). The psychometric assessment showed a mild mental impairment. Seven years later, brain MRI showed acoustic neuroma of the right vestibular nerve. While the diagnosis of NF2 was clinically definite, mental impairment was atypical and was investigated by genetic analysis. NF2 gene analysis was performed and no point mutations or intragenic deletion/duplications were detected. Since the anecdotal association between chromosome 22 abnormalities and NF2 clinical features has been described, karyotype analysis on blood lymphocytes was performed and an homogeneous ring chromosome 22 was observed. Array CGH allowed to demonstrate the absence of deletion of chromosomes 22 telomeric regions. The patient is today clinically unchanged.

Discussione e Conclusioni

Ring chromosome 22 is a rare constitutional cytogenetic aberration, in which the formation of a ring with breakage in both chromosome arms leads to a terminal deletion in 22q. Therefore, carriers of a ring chromosome 22 present with most of the features of the 22q13.3 deletion syndrome such as mental retardation. Ring chromosome 22 can also cause multiple meningiomas and vestibular schwannomas fulfilling NF2 diagnostic criteria [(2)]. This is explained by the aptitude of the ring to be lost during mitotic cell division generating a mosaic monosomy for NF2 gene. This peculiar genetic mechanism has to be kept in mind whenever we are facing with a patient fulfilling NF2 diagnosis or in familial occurrence of brain tumors, after exclusion of NF2 gene abnormalities. Furthermore, this case highlights the need to perform a comprehensive evaluation including psychometric tests in patient suspected of having NF2.

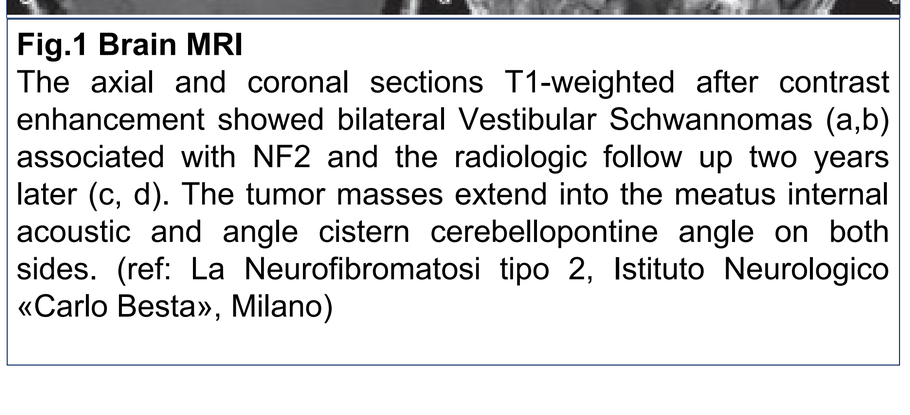

Fig.1 Brain MRI
The axial and coronal sections T1-weighted after contrast enhancement showed bilateral Vestibular Schwannomas (a,b) associated with NF2 and the radiologic follow up two years later (c, d). The tumor masses extend into the meatus internal acoustic and angle cistern cerebellopontine angle on both sides. (ref: La Neurofibromatosi tipo 2, Istituto Neurologico «Carlo Besta», Milano)

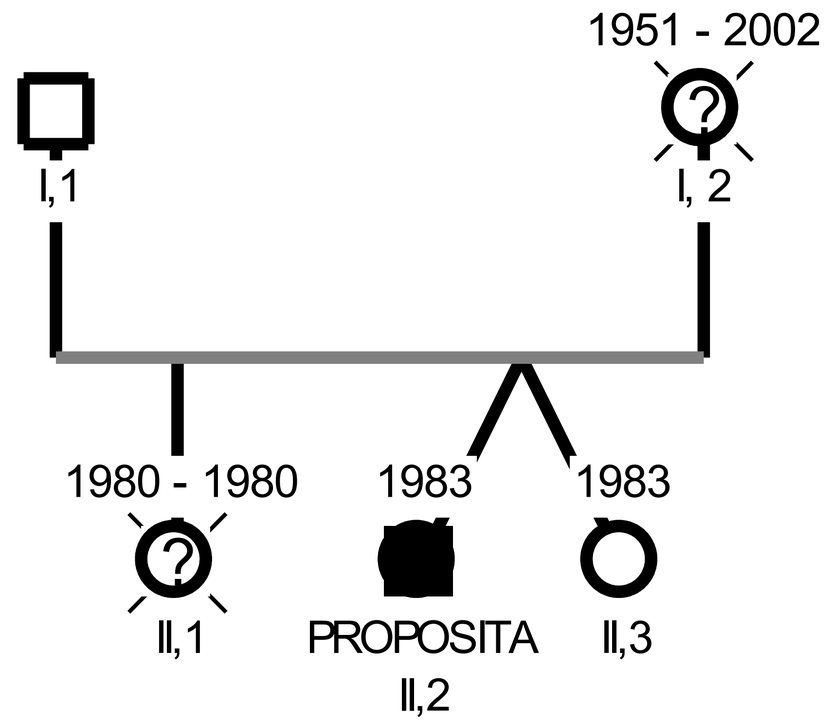

Fig. 2 Family Tree
I, 2: M.G. was born in 1951 and died in 2002 for a posterior fossa tumor. She was probably a carrier for ring chromosome 22.
II,1: V.M. was born in 1980 e died within the first year of life for a subtentorial brain tumor.
II,2 PROPOSITA: she is 33 years old, she presented with multiple acoustic neuromas associated to Neurofibromatosi tipo 2. The karyotype analysis on her blood lymphocytes showed an homogeneous ring chromosome 22.

Bibliografia

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