

LETTER TO THE EDITOR

Association Down Syndrome-Retinoblastoma: A New Observation

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Dear Editor,

A significant subset of cancers is due to a variety of constitutional genetic susceptibilities. The study of particular causative associations has allowed an understanding of the genetic mechanisms involved in the process of carcinogenesis and, in particular, of the role of the Rb gene in retinoblastoma development.¹ Here, we report on a new case of retinoblastoma in an infant with Down syndrome that we believe could be another example of non-random association.

A bilateral retinoblastoma was discovered in an 11-month-old infant with progressive pendular horizontal nystagmus since the age of seven months. Anisocoria and enlargement of the right pupil appeared later. The parents, a 32-year-old mother and a 37-year-old father, were non-consanguineous and in good health. There was no familial history of eye disease, cancer, or malformation, including the three-year-old brother of the patient. A comprehensive ocular examination revealed a bilateral group V (according to Reese-Elworth classification) exophytic retinoblastoma with a total of four primary tumors: three in the right eye and one in the left eye. Metastatic evaluation was negative. The child was treated with four cycles of chemoreduction (Carboplatine and Etoposide) followed by a bilateral stereotac-

tic conformal radiotherapy (50.4 Gy). Currently, eight months after the diagnosis, tumor control has been achieved in both eyes.

During the course of hospitalization facial dysmorphism (round flat face, brachycephaly, bilateral epicanthus, small and round ears), left single palmar crease, short fingers and toes, hypotonia, and developmental delay led to the diagnosis of Down syndrome. The karyotype of peripheral lymphocytes showed a mosaic constitutional trisomy 21: mos 47,XY,+21[6]/46,XY [24]. FISH analysis excluded a constitutional 13q14 deletion. The mutational screening of RB1 is in progress. Magnetic resonance imaging disclosed a pineal cyst that will be followed to exclude a trilateral retinoblastoma. No other anomaly was found.

Establishing a link between Down syndrome and retinoblastoma is of importance for good medical surveillance of infants and children with Down syndrome and for an early diagnosis. It would also shed additional light on the process of retinoblastoma oncogenesis.

Two epidemiological studies (see Satgé et al.²) on childhood cancer conducted in Norway and Denmark suggested a positive link, although based on only one case each. Given the rarity of Down syndrome (around 1/800 at birth) and the rarity of retinoblastoma (about 1/15000 birth), we should expect the co-occurrence of the two conditions once every 12×10^6 births. Yet, the present report is the 20th such confirmed association, with 15 cases of retinoblastoma in children with Down syndrome reported in a recent review² and four other published cases.^{3–5} Thus, only a large international

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epidemiological study would have the power to test the hypothesis of a causative link between Down syndrome and retinoblastoma. Such a study is highly desirable and we encourage interested persons to contact us for the gathering of data. Finally, if the association is real, the underlying link between the two disorders remains to be elucidated at the molecular level.

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