Reviewer's report

Title: MAPK activation in mature cataract associated with Noonan syndrome

Version: 2  Date: 14 October 2013

Reviewer: Alexsandra C Malaquias

Reviewer's report:

Major Compulsory Revisions

Case report, second paragraph:
...Genetic analysis revealed a mutation in the PTPN11 gene. The identified PTPN11 mutations (c.188A>G [p.Ser35Thr]) encode alterations located in the N-terminus of SH2 (Src homology 2) domain, catalytic domain in PTPN11...
Please, correct this item: PTPN11 substitution of A>G in position 188 of cDNA (c.188A>G) = p. Tyr (Y)63Cys (C). I do not understand if the position of DNA (c.188A>) is wrong but this variation Ser35Thr has not been described in Ensembl site. Is it a new variation?

Discretionary Revisions

I suggest some alterations to improve the MS (here in red).

1- Introduction, first paragraph:
Noonan syndrome (NS, OMIM 163950) is an autosomal, dominantly inherited disease that results in characteristics such as is a common genetic disorder characterized by congenital heart disease, short stature, thoracic abnormality, cryptorchidism, mental retardation, and a typical facial appearance, among other characteristics [1, 2].

2- Introduction, second paragraph
Gain-of-function mutations in the PTPN11 gene lead to activation of the Ras-mitogen-activated....

3- Introduction, third paragraph
Ocular hypertelorism, blepharoptosis, strabismus, ametropia, and cataract have been reported as eye complications in NS [8]. However, the mechanisms of onset of cataract in this disorder are not clear, and only one case requiring operation has been reported previously [9]. We reported a case of NS associated with mature cataract that required operation. We could also prove MAPK activation and suggested the possible association of MAPK cascade with cataract formations in this disease.

4- Case report, first paragraph:
A 42-year-old man experienced decreased visual acuity in the right eye before 2 years, but did not seek treatment. Later, he became aware of severely Hashida
et al.--6 decreased visual acuity in the right eye several months ago and visited our hospital. The patient was born at 37 weeks of gestation with a weight of 2,300 g and had neonatal asphyxia at birth and had severe jaundice in neonatal period and was suspected of having NS on the basis of his characteristic facial appearance (Fig. 1). The patient has a high arched palate, webbed neck, short neck, ocular hypertelorism, exophthalmos, and dilated cardiomyopathy. These factors led to a clinical diagnosis of NS at the age of 1 year (Fig. 1). Cardiac disease is controlled through the use of oral drugs. Without receiving growth hormone treatments, his final body height was 154 cm, which is below the potential average height of Japanese men.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.