results in the common axial length range (when *A* constants are customised separately for IOL Master or ultrasound biometry), it is of interest to note, for example, that an eye with an axial length of 21.00 mm and *K* values of 7.80 mm, the Hoffer *Q* and SRK/T formulae recommend IOL powers of 32D and 31D, respectively, to achieve emmetropia, which suggests that for short eyes different formulae are not likely to be equally accurate. Large data sets of short or long eyes are needed to prove the superiority of one or other formula for eyes at the extremes of the axial length range and the Cataract National Dataset in the UK will be one way of achieving such data sets.

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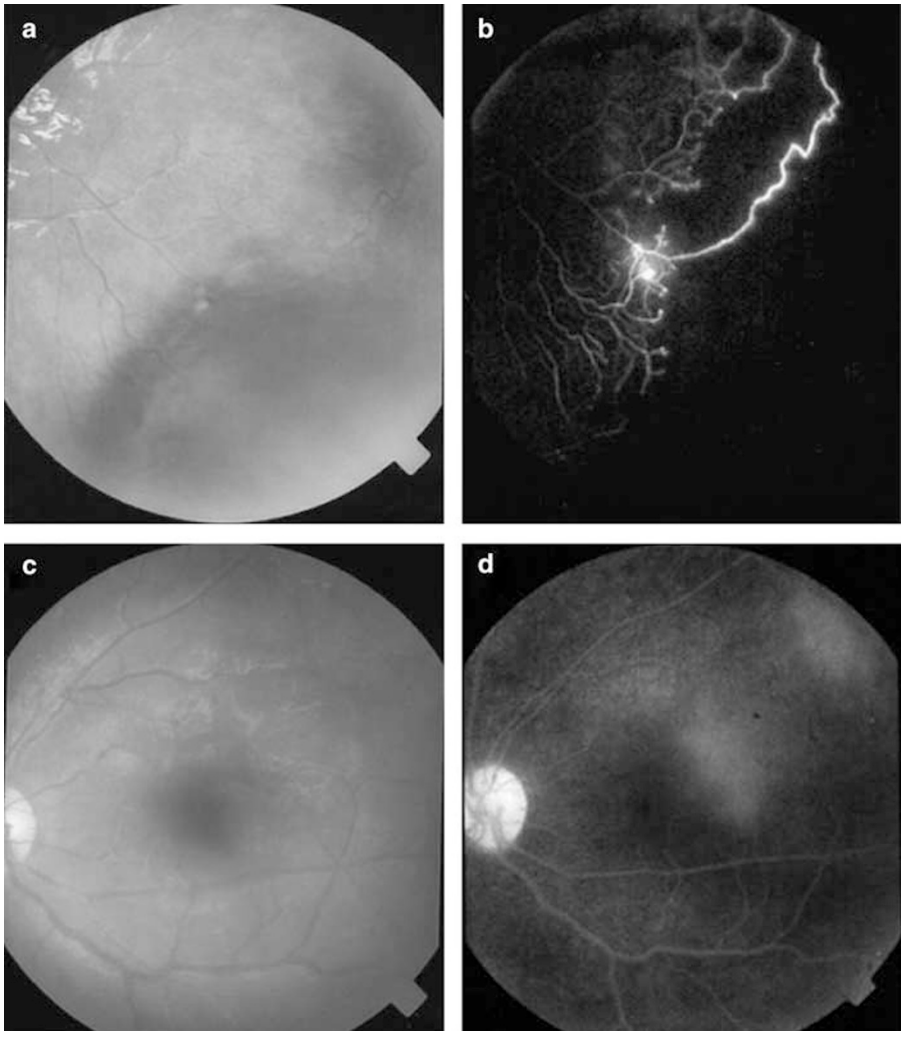
Sir,

NEMO mutational analysis in a Japanese family with incontinentia pigmenti

Incontinentia pigmenti (IP), also known as Bloch–Sulzberger syndrome, is an X-linked



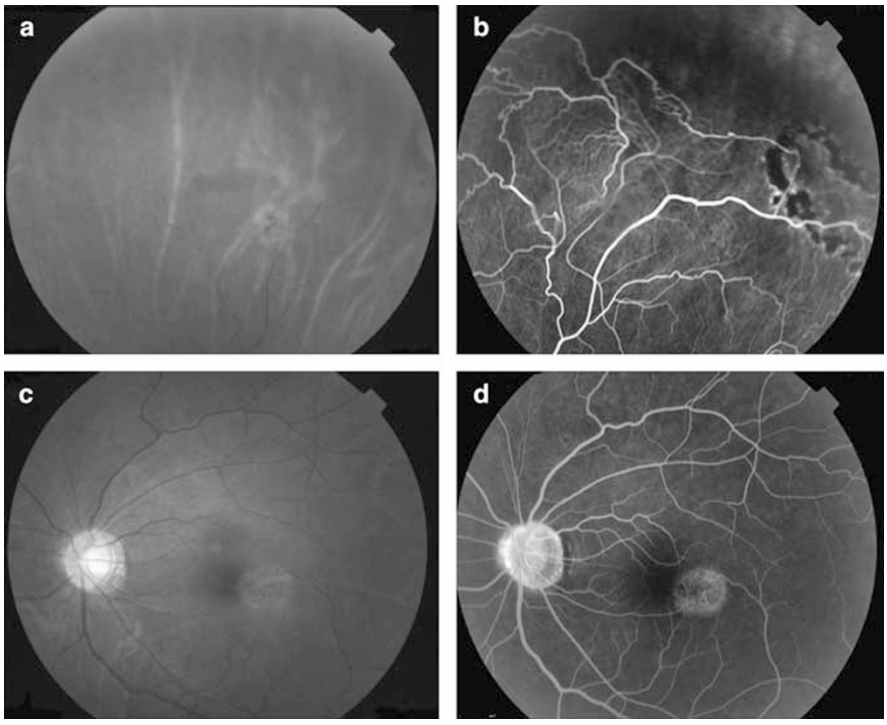


Figure 2 Fundus photograph and FAG of the mother. (a) Peripheral retina of the left eye was consisted of an aberrant retinal vascularization. (b) The tortuous vessels filled with fluorescein in early stage, later leaked from them a little. Photocoagulation scars were also seen performed by another ophthalmologist. (c) Fundus photograph of posterior pole of left eye of the mother. The 1 PD size of hypopigmentation spot was seen. (d) FAG of the same lesion showing hyperfluorescent spot without leakage.

dominant disorder. Ocular complications are associated in about 35% of the cases. Most IP is caused by mutations in a gene called *NEMO*, which encodes a regulatory component of the IκB kinase complex that is required to activate the NF-κB pathway.[1] Although several cases of IP have been reported in the Western world, the genetic aetiology is unknown in the Eastern world.

The proband was a 1-year-old Japanese girl who was diagnosed with IP by a paediatrician. Fundus examination revealed arteriovenous anastomosis, meridian running, and ghost vessels with outlying wide avascular areas at the periphery of the left eye (Figure 1a and b), and only approximately 0.5 PD size avascular areas in the right eye. Fluorescein angiography (FAG) revealed parafoveal hyperfluorescence at the macular lesion (Figure 1d), and an oozing spot although the fundus of the same lesion appeared normal (Figure 1c).

Her 29-year-old mother, who was also diagnosed with IP, requested to have her eyes examined. She had no subjective eye symptoms, but had been told she had retinal abnormalities and had laser photocoagulation by another ophthalmologist. On initial examination, her visual acuity was 20/20, and fundus examination revealed abnormalities of vessels at the peripheral retina in both eyes similar to that in her daughter (Figure 2a and b). A 1 PD size retinochoroidal atrophy was detected at the inferotemporal quadrant of her left eye (Figure 2c). FAG showed leakage from the vessels of terminal dilated segments, and there was a hyperfluorescent window defect pattern in the macular area (Figure 2d).

To determine the genetic defect in the mother and daughter, molecular genetic analysis of the *NEMO* gene was performed after obtaining informed consent. Direct sequence of all the coding regions of *NEMO* did not disclose any disease-causing mutations, but Multiplex-PCR[2] subsequently identified a common exons 4–10 deletion of *NEMO* (Figure 3). This deletion was not detected in the proband's unaffected father and 56 healthy controls.

Figure 1 Fundus photograph and FAG of the affected proband. (a) Peripheral retina of the left eye showing terminal arborization of vessels, meridian running with outlying avascular areas. (b) Fluorescein angiography of the same lesion showing the arteriovenous connections. The tortuous vessels and terminal dilated segments were filled with fluorescein in early phase with late leakage from them. (c) Central retina of the left eye of the same patient. At macular lesion, the fundus seemed normal. (d) FAG revealed parafoveal hyperfluoresceint, oozing spot.

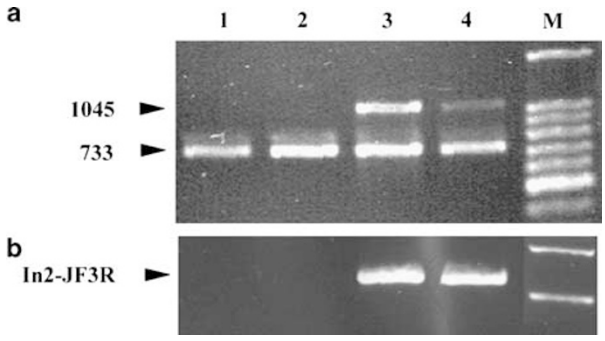


Figure 3 Multiplex PCR to detect *NEMO* gene deletion of exons 4–10. (a) Using primers Int3s, Rep3s, and L2Rev, which determine deletion of exons 4–10 in either *NEMO* or delta *NEMO*, double bands at 733 and 1045 bp each were seen in mother (lane 3) and proband (lane 4), whereas single 733 bp band in her unaffected (lane 2) father and healthy control (lane 1). (b) Subsequent PCR using *NEMO*-specific primers In2 and JF3H. Single band was obtained only in the affected two individuals (lanes 3 and 4) indicating the deletion is originated from *NEMO* gene. No band was seen in her father and healthy control (lanes 1 and 2). M = size marker.

One of the most common ocular lesions in IP is vascular abnormalities in the peripheral retina.[3] The similarities of avascularization in both patients suggest that *NEMO* may be involved in angiogenesis of the human retina. The formation of retinal vessels involves either vasculogenesis or angiogenesis, and the latter may be responsible for the formation in the perifoveal and peripheral regions.[4] Therefore, we postulated that the perifoveal degeneration observed in the mother may be a result from perifoveal vascular abnormality. This is consistent with our previous report[5] that NF-κB signalling is closely associated with retinal angiogenesis. In contrast, phenotypic variations suggest the presence of other genetic factors.

It was recently reported that in the West, an identical genomic deletion accounted for 90% of the identified mutations in the *NEMO* gene. Because the same gene deletion was found in Japanese, the deletion may be the most common mutational hot spot irrespective of race, although further genetic analysis of Japanese IP patient is required.

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Sir,

Bevacizumab: a compassionate way of doing business?

We agree with Canning and Lotery[1] that a clinical trial of bevacizumab in the treatment of neovascular age-related macular degeneration (AMD) could reveal important safety issues, but for rarer diseases randomised controlled trials are not always appropriate.

Neovascular glaucoma is another disease where bevacizumab is promising. It is, however, uncommon compared with AMD, and fortunately most cases respond to panretinal photocoagulation (PRP) when timely performed.[2] For the minority in whom PRP is either not possible or not effective, the prognosis is dire.

Bevacizumab has several possible roles in the management of this vexing condition. Used early it may prevent intractable glaucoma; later when the angle is closed, it may be used as an adjunct to glaucoma drainage surgery reducing the risk of intraocular bleeding. Finally by causing regression of new vessels and reducing leakage of inflammatory mediators, it may help in the treatment of painful blind eyes.[3]