Prenatal Detection of Fanconi Anemia

Fanconi anemia (FA), a clinically heterogeneous disorder with incidence of 1 in 350,000 births, is characterized by bone marrow failure (aplastic anemia), developmental delay, physical abnormalities, and increased risk of solid tumors and leukemia [1,2]. Chromosomal breakage investigation using DNA interstrand cross-linking agents such as diepoxybutane (DEB), and Mitomycin C (MMC) is the gold standard for the diagnosis. Molecular studies have so far identified 15 genes that can have mutations in FA patients [3,4]. We describe prenatal diagnosis of FA by cytogenetic and molecular analysis.

A 5-year-old girl having hypoplastic anemia was referred to us for chromosomal breakage studies. Chromosomal analysis from peripheral blood cultures induced with mitomycin C (MMC) (40 ng/mL) revealed a high frequency chromosomal breakage (8.6 breaks/cell) compared to controls (0.062 breaks/cell) (***Fig.*1**). Western blot for *FANCD2* confirmed the upstream gene defects in FA pathway. Molecular analysis of proband showed heterotzygous c.1303C>T (rs148473140: R/C) mutation in *FANCA* gene. Father was found to be carrier for the mutation and the mother was normal. In the next pregnancy, chorion villus sample was aspirated at 12 weeks of gestation and mutational analysis of *FANCA* gene showed c.1303C>T mutation in genomic DNA of the fetus.

The chromosomal breakage study for the diagnosis of FA is available in few cytogenetic laboratories. However, the diagnosis of FA by chromosomal breakage study from chorionic villi or amniotic cell culture is time consuming and there are chances of getting false positives and negatives. Molecular level study by mutation analysis, on the other hand, is a rapid and accurate method for diagnosis of proband and subsequent pregnancies.

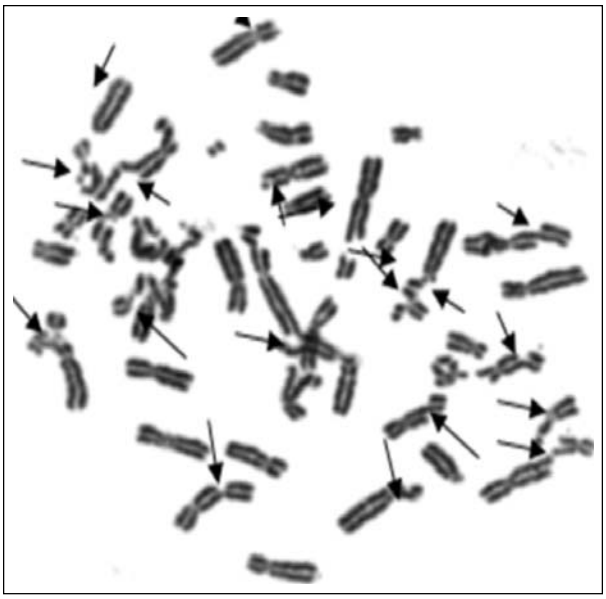

FIG. 1 *Metaphase showing chromosomal breakage and radial formation.*

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Experience of Nutrition Rehabilitation Centers in Management of SAM

Authors of the recent publication [1] need to be commended for documenting the experience of management of severe acute malnutrition (SAM) in public sector. Low mortality or high survival at discharge from Nutrition Rehabilitation Centers (NRCs) is noteworthy. Equally important is the documentation of social determinants of SAM which is considered to be a bio-psycho-social-disorder [2].

This paper reports that nearly two-third children having complicated SAM were discharged without recovery [1]. Organic causes like tuberculosis can lead to development of SAM and using IMNCI protocols (as

stated in the paper) for detecting presence or absence of tuberculosis is a major flaw in NRC protocols. All children with SAM should be screened appropriately (or be referred) for detecting organic causes, especially when they do not have expected recovery in NRC. Since this paper [1] also had an objective of informing future design and implementation of program for care of children with SAM, the readers also expect comments on the strategies other than community based programs to use ready-to-use-therapeutic food (RUTF). This becomes more important in view of a recent Cochrane systematic review [3] which did not found enough evidence favouring RUTF over standard diets. Indian Academy of Pediatrics also recommended RUTF only for a limited time period (4-8 weeks) until child recovers from SAM [4]. Several strategies need to be implemented simultaneously to tackle this bio-psycho-social-disorder (i.e. SAM).

It is surprising to find that a small trial [5] on 70 study subjects comparing liquid and solid RUTF has been referenced as global evidence on effectiveness of RUTF in supporting catch-up growth. The 'survival 6 months after discharge' from NRC is likely to be a better program performance indicator as it incorporates the care both during NRC stay and in community. NRC protocols should incorporate this or other similar performance indicators.

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AUTHOR'S REPLY

Thanks for appreciating the paper, raising some important issues and seeking few clarifications. As stated in the paper, all children who were admitted to the NRCs were examined by a physician to detect the presence/absence of medical complications using the IMNCI criteria for identifying medical complications. Children admitted in the NRCs also underwent investigations (pathology, microbiology, radiology etc.) based on their clinical condition and were treated appropriately along with nutritional rehabilitation; 6.4% of children with medical complications and 2.1% children with uncomplicated SAM were medically transferred. NRCs protocols and training materials describe when to label a child as a non-responder and the steps that need to be taken for such children.

This paper reports that more than half (58.2%) of the children admitted to the NRCs had uncomplicated SAM and such children should be cared for in a community-based program using good quality ready-to-use therapeutic food. This recommendation is in line with a number of references quoted in the paper. The reader would also appreciate that the recommendation is in line with the recently released Consensus Statement of the IAP and WHO.

The reader, would appreciate the limits of a 'NRC Only' strategy; the paper mentions that of all the children discharged from the NRC, only 25% came back for three follow-ups. A 'survival 6 month or 12 month after discharge' is a desirable performance indicator, but such a tracking is possible with a community-based program where the child can be followed up at home by a community worker and does not need to come to the NRC.

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