Fanconi's Anemia in Newborn

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Fanconi's anemia (FA) is a paradigm for congenital anomalies, aplastic anemia and predisposition to malignancies. Identification of the disease at birth is based on characteristic physical malformations, as hematologic manifestations at birth are extremely rare. We report a case of FA in a newborn who presented with anopthalmia, unilateral radial ray defect, hemivertebrae and thrombocytopenia.

Key words: *Anopthalmia, Fanconi's anemia (FA), Radial ray defects, Thrombocytopenia.*

First description of Fanconi's anemia (FA) dates back to 1927, where Fanconi described three brothers who had pancytopenia and birth defects(1). Since then more than 1000 cases of Fanconi's anemia have been reported in the world literature(2). However of these only 9 cases were identified in the first month of life.

Case Report

A 36 week, 1380 grams, growth restricted male neonate, born to a third gravida mother, with uneventful antenatal and intrapartum period, was admitted to our NICU on day one of life. Examination of the newborn revealed microcephaly, a small triangular facies, bilateral anopthalmos, hypertelorism, depressed nasal bridge, high arched palate, low set ears, webbed neck, widely spaced nipples, bilateral undescended testis, radially curved left forearm and hypoplastic biphalangial thumb attached to the palm by thin thread like pedicle. Baby had an ecchymotic patch below left eyelid. No café au lait spots were noted. Skeletal roentogenic survey revealed, left hypoplastic radius, hypoplastic two phalanges of left thumb, curved ulna and cervical hemivertebrae. Hematologic profile revealed significant thrombocytopenia - Platelet count 40,000/cmm. Hemoglobin, red blood cell morphology and white blood cell count were within normal limits. Mother's platelet count was normal. Bone marrow aspiration was a dry tap.

Cytogenetic studies were performed on peripheral blood lymphocyte cultures stimulated with Phytohemagglutinin (PHA) induced with Mitomycin C (MMC) (40 ng/mL). Chromosomal preparations were obtained using standard procedure and were subjected to GTG banding. Chromosomal analysis revealed a high frequency of chromosomal breakage (6.0/metaphase) compared to control cultures (0.5/metaphase) (*Fig. 1*). Cultures without MMC induction showed no chromosomal damage. The newborn was diagnosed as a case of Fanconi's anemia. Chromosomal analysis of sib and parents revealed normal karyotype. In view of poor long-term prognosis, parents refused any further treatment and baby was discharged against medical advice on 15th day of life.

Discussion

Diagnosis of Fanconi's anemia (FA) is

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Manuscript received: March 25, 2004.
Initial review completed: Auigust 19, 2004;
Revision accepted: September 27, 2004.

Fig. 1. Metaphase showing chromosome breakage and radial forms.

based on the characteristic chromosomal breaks following clastogenic stress; the presence of physical anomalies or aplastic anemia is not required for diagnosis(2).

Physical anomalies described in FA involve almost all the systems(2). 'Classic' phenotype of FA includes, short stature, abnormality of the thumbs, microcephaly, café au lait and hypopigmented spots and a characteristic facial appearance (a broad nasal base, epicanthal folds, and micrognathia). FA newborns commonly have hypogonadism and renal malformations(2,3). Radial ray abnormality is the most common physical abnormality noted in the patients with FA during infancy. Bilateral radial ray defect is more common (78%) than unilateral (22%)(3). Hematologic abnormality at birth is very rare(4).

Differential diagnosis considered in the present case were, Thrombocytopenia–absent radius (TAR) syndrome, VATER / VACTERAL syndrome, Trisomy 18 and Holt - oram syndrome.

TAR syndrome presents at birth with severe thrombocytopenia with bleeding manifestations and radial ray defects(5). Microcephaly, short webbed neck and skeletal anomalies noted in the present case, though rare, have been reported in patients with TAR syndrome (2,3). In FA, if the radii are affected, the thumbs are always abnormal (absent / hypoplastic); in TAR, in which radii are absent, the thumbs are always present(2). The present case had an abnormal thumb, consistent with the diagnosis of Fanconi's anemia.

FA has considerable overlap in the physical abnormalities with VATER / VACTERAL syndromes. In a large series of FA patients, 10% patients had three principal clinical features and additional 20% patients had two major defects found in VATER syndrome(6). Therefore, FA patient can be easily misdiagnosed as VATER/ VACTERAL syndrome. The present case had vertebral and limb defects. VATER or VACTERAL syndromes are sporadic where as FA has 25% chance of recurrence and misdiagnosis has severe consequences for genetic counseling(7). Therefore it is recommended to rule out FA in patients with suspected VATER / VACTERAL syndromes by chromosomal testing(3,6).

Holt-Oram syndrome has radial ray defects with cardiac defects (100% cases). In the present case there were no cardiac defects(5). Trisomy 18 can rarely have radial ray defects and eye anomalies. However trisomy 18 has host of different physical abnormalities and a typical facies(2). In the present case diagnosis of FA could be established only after chromosomal breakage studies.

Diagnosis of FA requires high index of suspicion as it presents with physical abnormalities involving multiple systems and hematologic abnormalities at birth are extremely rare. Early diagnosis in FA is very

important as long term survival depends on the age of onset of hematologic abnormalities or malignancies(8). If FA is recognize in the preanemic phase, drugs and environmental insults implicated in acquired aplastic anemia or malignancy can be avoided and life span can be prolonged(2). Early diagnosis also offers options of planning next pregnancy; as the umbilical cord blood can be used for stem cell transplantation. Bone marrow or umbilical cord blood transplantation from an HLA identical sibling is now considered the treatment of choice for FA(3,7).

Acknowledgements are due to Dr. Nilima Kshirsagar, Dean, Seth G.S. Medical College and K.E.M. Hospital, for permitting to publish this article.

Contributors: TBP was involved in management of patient, data collection, review of literature and drafting the manuscript, RHU and RNN were involved in management of patient, concept and design of the article and critical revision of the manuscript for important intellectual content. VBR was involved in carrying out cytogenetic studies and helped in preparation of manuscript.

Funding: None.

Competing Interests: None.

REFERENCES

1. Fanconi G. Familiare infantile perniziosaartige Anamie (pernizioses Blutbild und Konstitution). Jahrbuch fur Kinderheilkunde 1927; 117: 257-280.
2. Alter BP, Young NS. The bone marrow failure syndromes. *In:* Nathan DG, Orkin SH (Eds.): Nathan and Oski's Hematology of infancy and childhood, 5th edn., WB Saunders, Philadelphia. 1998; pp. 259-272.
3. Giampietro PF, Alder-Brecher B, Verlander PC, Pavlakis SG, Davis JG and Luerbach AD. The need for more accurate and timely diagnosis in Fanconi Anemia: A report from the International Fanconi Anemia Registry. Pediatrics 1993; 91: 1116-1120.
4. Butturini A, Gale RP, Verlander PC, Adler-Brecher B, Gillio AP, Auerbach AD. Hematologic abnormalities in Fanconi anemia: An International Fanconi Anemia Registry study. Blood 1994; 84:1650-1655.
5. Jones KL. Thrombocytopenia - absent radius syndrome. *In:* Jones KL (Ed.) Smith's Recognizable Patterns of Human Malformations, Philadelphia; WB Saunders Company, 5th edn, 1997; pp. 322-323.
6. Porteous MEM, Cross I, Burn J. VACTERAL with hydrocephalus: One end of the Fanconi anemia spectrum of anomalies? Am J Med Genet 1992; 43: 1032-1034.
7. Auerbach AD. Fanconi anemia: Prenatal diagnosis in 30 fetuses at risk. Pediatrics 1985; 76: 794-800.
8. Alter BP. Annotation - Fanconi's anemia and its variability. Br J Hematol 1993; 85: 9-14.