Unusual chromosomal features in a child with gradual disappearance of right ulna (mono ostolic osteolysis)

Hit K. Goswami,[1] Nirhhay Shrivastava,[2] Shiv Kumar Gopal,[2] Sanjay Sharna,[2] Manoj Chandorkar,[3] In Hwan Lee[4] and Sung Ik Chang[4]

A nine month old male child presenting degenerating right ulna (massive osteolysis) has been followed up for two years. The bone completely disappeared due to abscesses on the right forearm and without orthopedic or haematological complications. Repeated lymphocyte cultures showed somatic pairing (mostly chromosome pair 5), end to end association involving chromosome 14, 21, 21 and 16, and satellite enlargement in a high proportion of cells with an otherwise normal 46,XY karyotype. These observations are compared with 13 other types of orthopaedic patients, and we opine that cumulative picture of chromosomal aberrations appears to correspond with the present rare anomaly "Mono Ostolic Osteolysis" involving right ulna. None of the controls or any other orthopaedic anomaly studied hereunder exhibits this chromosomal picture.

Keywords: human, osteolysis, karyotype

INTRODUCTION

Disappearance of a bone termed as "Osteolysis" is one of the most intriguing anomalies affecting the human body. The specific cause is yet unknown although a definite mode of angiomatosis of bone as the commonest offending lesion has been supported by several workers over a long period of time (Aston, 1958; Butler *et al.*, 1958; Branco and Horta, 1958). The child described hereunder is of unusual significance because disappearance of ulna has never been reported as sequestrated material and contrarily to earlier reports on osteolysis (Turek, 1984), there were no signs at all of new bone formation. Additionally, this paper reports the first chromosomal study on a patient of osteolysis referable to a new syndrome associated with chromosomal features.

MATERIALS AND METHODS

Clinical study

A 9 month old male child was admitted to the orthopaedic ward of Gandhi Medical College and associated Hospital, Bhopal, with a discharging sinus on his right forearm. He had a brief history, as revealed by his parents, of occasional extrusion of bone chips over a period of 3 months. The child had developed three swellings over different parts of the body along with a high fever. The swellings, diagnosed as abscesses, were incised and drained off. The pus cells on culture demonstrated the presence of *Staphylococcus aureus*, which responded to cloxacillin. On oral administration of this antibiotic, the child improved fast and his surgical wounds healed up within a fortnight, but right forearm continued to discharge.

After relevant investigation (Table 1 and 2), the patient was taken for excision of the sinus and biopsy from the sinus tract and the underlying bone. Following the surgery, the wound was healed but osteolysis continued for another year (Fig. 1), resulting in complete disappearance of the right ulna (Fig. 2-7).

Chromosomal studies

Chromosomal studies were performed on peripheral blood lymphocytes in TC 199 and RPMI media from three independent cultures in one year period. Slides were analyzed blindly after routine Giemsa staining (10%, pH 8) (Goswami, 1986; Goswami et al., 1990; Goswami and Goswami, 1993). A few slides from all cultures corresponding to patients, sibs and normal control population including other orthopaedic patients (Table 3) were trypsin Giemsa banded for comparative studies. Number of metaphases scored on each category of persons with pertinent aberrant features

[1] Department of Genetics, Bhopal University, Bhopal, India
[2] Department of Orthopedics, Gandhi Medical College and associated Hospitals, Bhopal, India
[3] Genetic Institute for Human Welfare, Bhopal, India
[4] Department of Anatomy, Keimyung University School of Medicine, Taegu, Korea
Correspondence: In Hwan Lee, Department of Anatomy, Keimyung University School of Medicine, 194, Dongsan-dong, Jung-gu, Taegu 700-412, Korea
Tel: 82-53-250-7472, Fax: 82-53-250-7471, E-mail: ihl5510@dsmc.or.kr

are presented in Table 3 with respective frequencies.

RESULTS

Observation

The propositus is now a 2 year old healthy male child (Fig. 1). With a history of normal neurological, motor and psychological examination of the affected limb, there was a scar mark with puckering, situated over the dorsal aspect of the right forearm at the junction of the middle and lower thirds. The elbow handed down from the arm. The patient moved his fingers normally. On palpation, only one bone was palpable, which by its contour and broad lower end could be inferred as a normal radius. The elbow joint was flail and could be passively hyperextended, hyperadducted and hyperabducted. Olecranon was not felt and only the 2 condyles of humerus and the head of radius could be palpated.

Clinical findings

Haematological and biochemical investigations were carried out at intervals of every 6 months i.e., on admission. Discharging sinus, 6 months later when osteolysis was underway, was completely disappeared (Table 1). Radiological observations are indicated in Table 2. Histopathological study of biopsy material showed only a chronic nonspecific inflammatory process. By and large, no pathological or osteological findings could be correlated with the disappearance of the right ulna in the child.

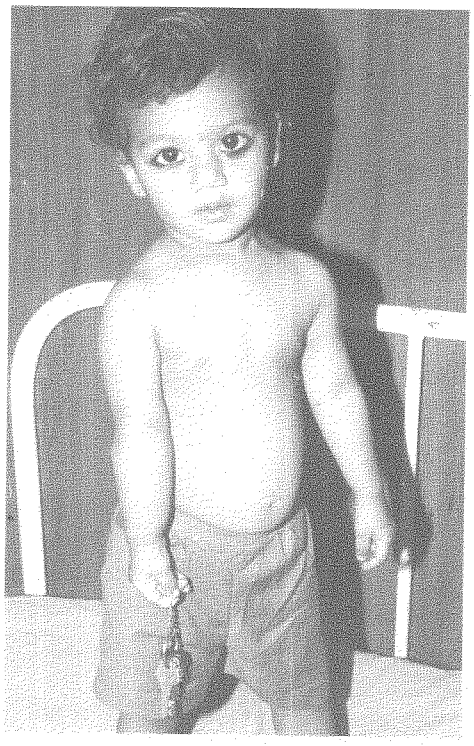

Fig. 1. The child holding key bunch in the right palm after the total disappearance of ulna.

Cytogenetic features

Repeated chromosomal studies have indicated that though there is no specific chromosomal feature which could be categorically associated with the gradual disappearance of the whole bone in the propositus, there is ample evidence that a group of rare and common features do characterise the patient. Somatic pairing (Fig. 9, 10, and 11) and enlargement of satellite, sometimes showing tandem duplication and end to end association of chromosomes assisted with terminal translocations thus forming a short chain of 4 or 5 chromosomes (Fig. 11c), are features not so far encountered in any specific anomaly (see discussion). Simultaneous culture study on other patients and blind scoring in search of these features further confirm that about 52% of the metaphases are exactly normal with remaining ones exhibiting some or the other aberrant feature.

Table 1. Relevant investigations for the patient

Investigations	Date		
	on admission 18-2-92	6 months 15-9-92	1 year 10-3-93
Haemoglobin	8.6 gm%	9.6 gm%	10.2 gm%
Total	9400/cmm	7900/cmm	8000/cmm
Differential	P 60%	P 60%	P 68%
Leucocyte counts	L 37%	L 35%	L 30%
	E 03%	E 04%	E 02%
		M 01%	
Serum alkaline phosphatase	18 KA	28 KA	16 KA
ESR	40 mmFHR	26 mmFHR	15 mmFHR
Serum calcium	14 mg%	14 mg%	12 mg%
Serum phosphorus	2 mg%	4 mg%	4 mg%
Festing blood sugar	–	78 mg%	–

Table 2. Radiological findings for the patient

Investigations	Remarks
Roentogenography	Chronologically arranged skiagrams taken after an interval of 3 months reveal gradual elimination of Ulna in right forearm.
Skeletogram	Nothing abnormal
Arteriography	Brachial arterography for visualising any haemangiomatosis has been normal

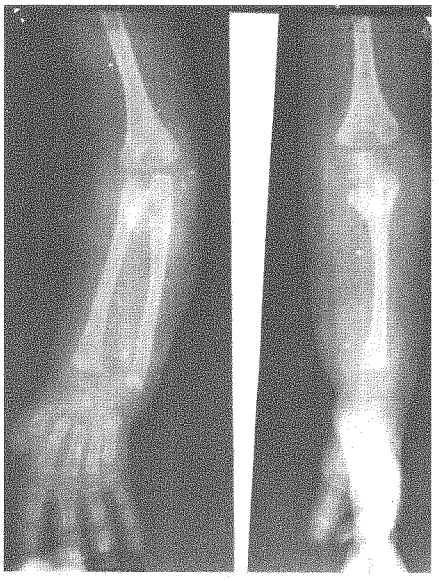

Fig. 2. Photograph of X-ray plate at the initial abscess stage indicating slight erosion of superior area in ulna.

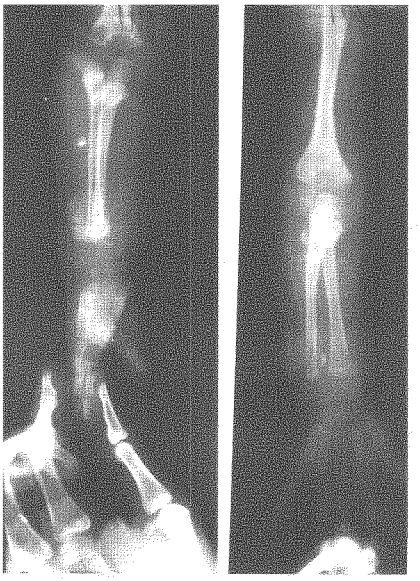

Fig. 3. Photograph of X-ray plate after 1 month showing increase in erosion (abscess drained).

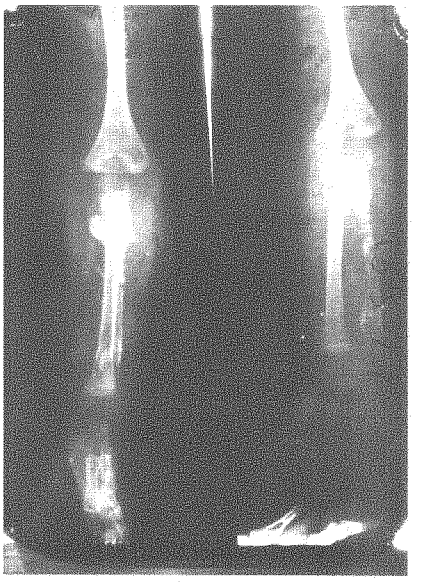

Fig. 4. X-ray plate exhibiting erosion of whole ulnar shaft.

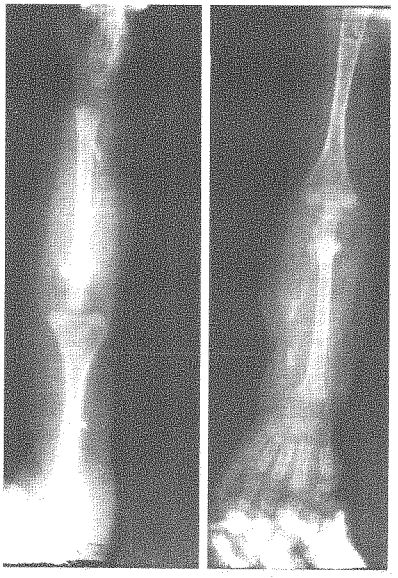

Fig. 5. X-ray plate exhibiting only small pieces (sequestrated) of ulna ; major portion has disappeared.

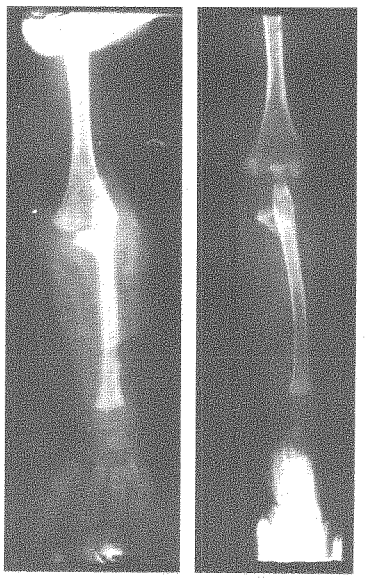

Fig. 6. X-ray plate showing only piece of ulna.

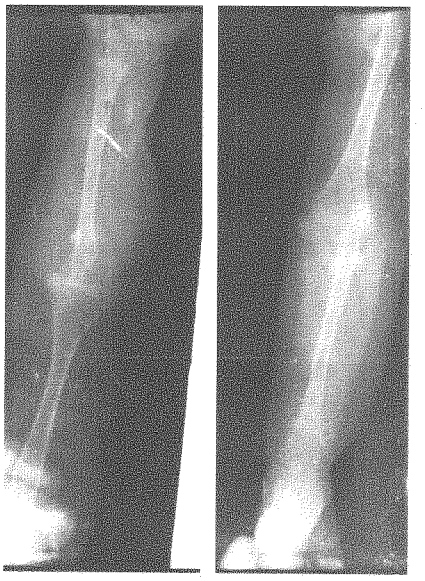

Fig. 7. Whole ulna has disappeared ; deformed radial head area seen.

DISCUSSION

As far as we know, an infection leading to complete disappearance of a whole bone has never been published in the medical literature. It is known however, that infection leads to the death of a bone and its ultimate rejection by the body is a part of the natural history of most bone infections. Also, few cases have been reported where disappearance of the bone took place after trauma (Butler *et al.*, 1958; Jones, 1958). Thus clinically, this patient is exceedingly interesting for the following reasons: 1) This disappearance of bone was reported in a boy of five years of age, the degeneration starting when the boy was 8 or 9 months old; 2) Such a continuous degeneration of the bone is unknown to medical literature which did not respond to any surgical treatment (Fig. 2-7); 3) Chromosomal profile of this patient has been compared with simultaneously investigated cases as well as routine normal cases. We strongly opine these features to

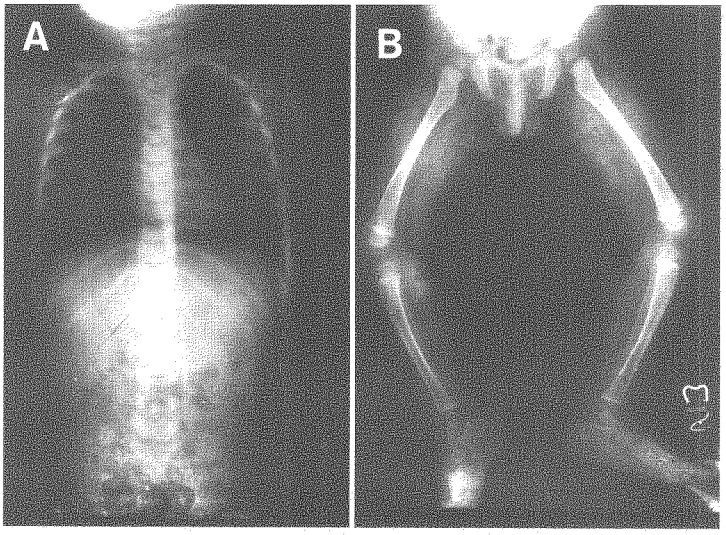

Fig. 8. Photograph of the X-ray plate **A)** Showing normal spine and chest of the child. **B)** Showing normal pelvic and lower limb bones.

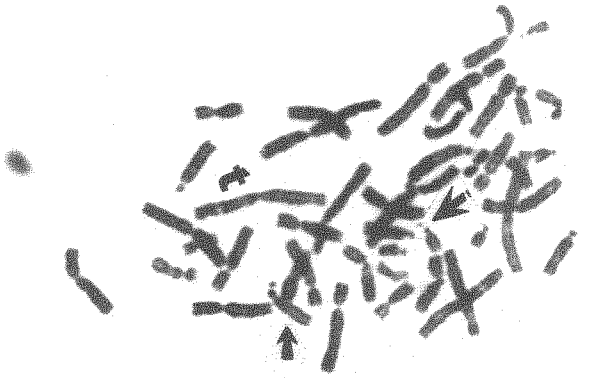

Fig. 9. Giemsa stained metaphase showing acrocentric chromosome with enlargement of satellites (arrow) of the satellites (x2500) 't' shows terminal association.

Table 3. Chromosomal aberrations in lymphocytes of the child (Mono ostolic osteolysis)

	Total number of metapahases scored(240)	Oct-92 (112 metaphases)	Feb-93 (92 metaphases)	June-93 (36 metaphases)	Remarks
Enlargement of satellite	45	17 (0.070)	18 (0.075)	10 (0.041)	Fig. 9
Somatic pairing (inclusive of terminal pairing)	45	25 (0.555)	12 (0.266)	08 (0.177)	Fig. 11A,B,C
Acrocentric association	28	11 (0.045)	14 (0.058)	03 (0.0125)	
Normal metaphases	122	59 (0.245)	48 (0.2)	15 (0.062)	

be typical to this patient (Table 3).

Surprisingly, other investigations revealed results that were either normal (Fig. 8A and 8B) or were only minimally deranged during the process of active osteolysis. These derangements, namely elevated ESR, and slightly elevated serum alkaline phosphates and serum calcium levels, only confirm the ongoing process of infection and destruction of bone respectively. These substances returned to normal levels on the cessation of the process. Elevation of serum alkaline phosphates and serum calcium are features also formal in massive osteolysis (Thompson, 1974). Arteriography is completely normal, a finding also reported earlier. Thompson (1974) found stretching or vascular branches of the right circumflex artery in a case of disappearance of the right ilium and femur. Biopsies performed in the cases reported by Aston (1958) and Thompson (1974) showed angiomatosis of bone. In this patient, however, no evidence of the same process was found and only chronic, nonspecific inflammatory cells were present.

Structural instabilities in chromosomes have been described in association with some syndromes, as the star shaped configuration in ICF syndrome formed by the four copies of the long arm of chromosome radiating from the centromeric region; the multiple chromatid interchanges induced by nitogen mustard in Fanconis anemia (Howell and Taylor, 1992) and the symmetrical interchanges between homologous chromosomes observed in Bloom's syndrome (Therman and Susan, 1993). The cytogenetic features of our patient were recorded after the X-ray plate confirmed degeneration process in right ulna. Since that time, the patient had not been treated, the chromosomal aberration (Fig. 10 and 11) viz. enlargement of satellites and somatic pairing (chromosome 5) becomes of special significance. Acrocentric association can be understood partly due to either duplication or enlargement of the satellites. Still, such a feature is found in many other, totally unrelated cases (Goswami *et al.*, 1992). Homologous chromosomes forming a terminally attached chain cannot be designated as trans-

location and simple hitherto known nomenclature can be pseudo Renner complex (Renner complex is a formation of ring involving many chromosomes in the plant family onagraceae, obviously due to terminal translocation). We presume that the massive osteolysis of right ulna must have been related with the extremely rare phenomenon of somatic paring (chromosome 5) and terminal associations of chromosomes 13, 22, 22 & 17. Several banded and Giemsa stained metaphases have documented these features along with noticeable increase in the size of satellites. A very similar situation also leading to tandem duplication of satellites was reported by Hayashi and Schmid (1975) in ataxia telangiectasia syndrome, but the tandem duplication of satellites was confined to chromosome 14 only.

End to end "fusions" of chromosomes are also described in ataxia telangiectasia syndrome. However, somatic or mitotic crossing over is a remarkable features in Bloom syndrome (Therman and Susman, 1993) which is an extremely rare phenomenon. Multiple telomeric fusions and chain configurations in human somatic chromosomes have also been observed by Dutrillaux *et al.*(1977). Chromosomally, our patient, therefore, appears to be of a great significance. Table 4, based on unpublished data, compares metaphases of 13 patients of different orthopedic disorders with respect to the prevalence of enlargement of satellites and somatic pairing. Observations on acrocentric associations have been too frequent in several instances (Goswami *et al.*, 1990; Goswami *et al.*, 1992), but enlargement of satellites and somatic pairing are not that common. Nevertheless, these structural variations do indicate pathological significance (Mckusick, 1978).

We do not intend to exclusively associate somatic pairing of chromosome pair 5 (more frequent) and enlargement of satellite (more frequent, chromosome 14 and 15) with the present case of disappearance of the right ulna, but there

Fig. 10. Giemsa stained metaphase exhibiting direct chromosome translocation (t).

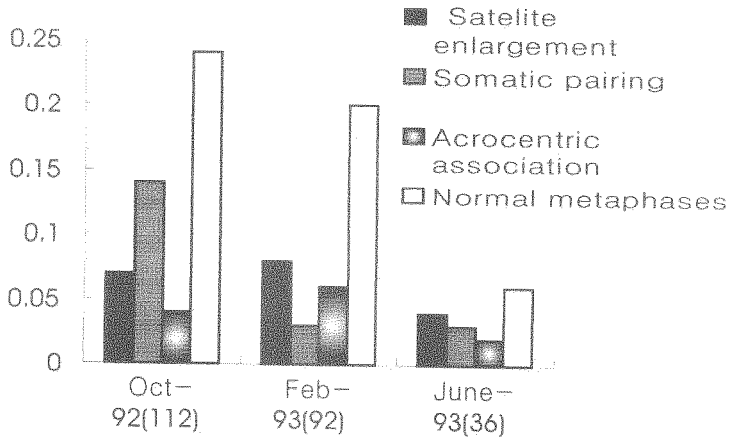

Fig. 12. Computerized profile showing somatic pairing and tandem duplication (satellite enlargement ?) to be main features.

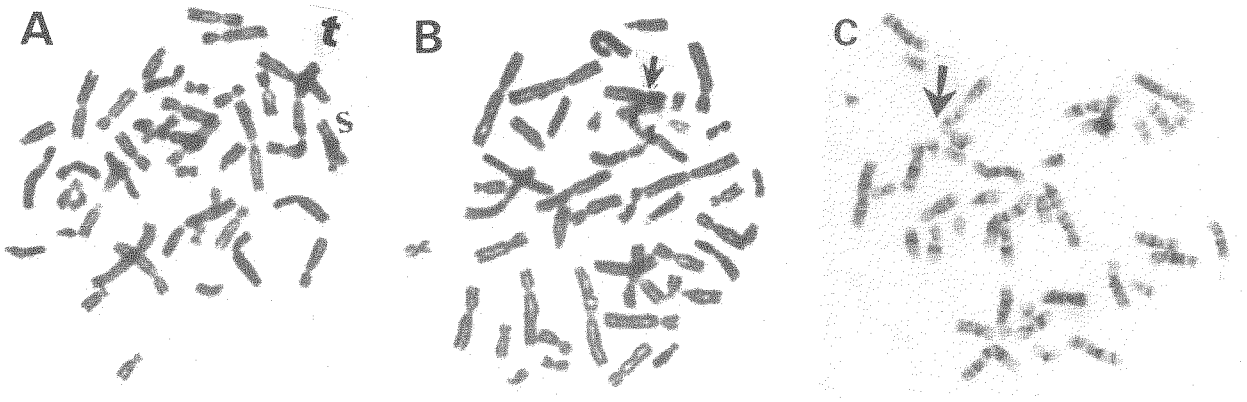

Fig. 11. Giemsa stained metaphase **A)** Showing somatic pairing in chromosomes 5 (labelled as S). Whole chromosome translocation to result end to end association (as 't') in two chromosomes (group A and C) is also seen. **B)** Somatically paired chromosomes 5 and terminally (T) paired of attached chromosome (x2500). **C)** Exhibiting terminally paired pseudo Renner complex (end to end translocation) involving 4 chromosomes (chromosome 13, 22, 22, and 17).

Table 4. Comparative data on somatic pairing and enlargement of satellites in metaphases of orthopaedic patients (Unpublished data)

Orthopaedic Conditions	Number of cases studied	Number of metaphases scored Total (Normal[1])	Enlargement of statellite N (%)	Somatic pairing N (%)	Acrocentric association N (%)
Normal controls	30	740 (702)	4 (0.5)	16 (2.1)	17 (2.2)
Arthogyopsis multiplex cogenital	2	48 (31)	– (–)	– (–)	7 (14.58)
Apert syndrome	1	24 (18)	2 (7.5)	– (–)	– (–)
Bilateral congenital dislocation of knee	2	88 (67)	– (–)	8 (9.09)	2 (2.27)
Congenital fermoral deficiency	2	140 (127)	– (–)	– (–)	– (–)
Phocomelia (Acheiria)	5	76 (59)	– (–)	– (–)	9 (11.84)
Mono ostolic dsteolysis (Present case)	1	240 (122)	45 (18.75)	45 (18.75)	28 (11.67)

[1]Normal includes those metaphases with other features.

has not been any other patient or a person where above features have been observed in his/her lymphocytes among simultaneously run controls (Table 4). There have been only a few cases of normal persons exhibiting somatic pairing but none (Goswami *et al.*, 1990; Goswami *et al.*, 1992) having both features in their metaphases. Thus, the somatic pairing along with the enlargement of satellite should obviously and tentatively be associated with this rare feature. This is because that any disease or syndrome is not necessarily associated with classical descriptions of chromosomal aberrations (deletions, translocations etc.). Earlier, we have described more prominent telomeric ends in a patient of Mullerian duct syndrome (Rangnekar *et al.*, 1990; Borgaonkar, 1991).

Additionally, observation on telomeric "fusion" (end to end association) involving 4 to 5 chromosomes and rarely though, attenuation of chromatin at the telomeric ends (Goswami, unpublished) should also account for such a hitherto unknown pathogenesis of complete disappearance of the right ulna in a child. The present case may be the first chromosomal profile for such an orthopedic anomaly.

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