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Cytogenetic characterization of congenital or infantile fibrosarcoma

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Abstract. Chromosome analysis of a congenital or infantile fibrosarcoma from the lower left leg of a 3-week-old baby girl showed only numerical changes involving chromosomes 11, 17 and 20. As three more cases with similar combinations of trisomies of the same chromosomes have been described, this report confirms that adult and congenital fibrosarcoma are cytogenetically different and trisomy 11 may be the key-event.

Key words: Congenital or infantile fibrosarcoma – Numerical chromosome changes – Chromosome 11

Introduction

After rhabdomyosarcoma, fibrosarcoma is the second most common soft tissue tumour in children [9], one third being congenital or infantile occurring most commonly in the extremities [5]. Because of it's more favourable outcome, congenital or infantile fibrosarcoma has been considered as an entity separate from adult fibrosarcoma, although it is histologically similar [7]. Adult and congenital fibrosarcomas also seem to be cytogenetically different. Random structural chromosome changes have been observed in adult fibrosarcomas [4, 14, 15, 23], while in congenital fibrosarcoma, similar combinations of trisomies of the same chromosomes, such as 8, 11, 17 and 20 have been described so far [1, 16, 21]. We here describe the fourth case, carrying a new combination of the same numerical chromosomal changes.

Case report

A 3-week-old baby girl presented with a painless swelling of the lower left leg. She had been born at term, after a normal delivery, with a birth weight of 3 kg. No abnormality was noted at birth. Three days prior to presentation the parents noticed a swelling below the knee latero-externally, which on examination was hard and measured 5 × 3 cm. The overlying skin was red and warm. The rest of the clinical examination was normal. Ultrasound, computerized tomography scan and magnetic resonance imaging of the left lower limb revealed a soft tissue tumour. On further investigation tumour markers were negative and no metastases were found.

After open biopsy a diagnosis of congenital fibrosarcoma was made histologically.

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Pathologic studies

The tumour consisted of fusiform cells, with plump nuclei having a prominent nucleolus (Fig. 1). Up to 15 mitoses were observed per high power field. There was no appreciable matrix production. The tumour was not well delineated, and invaded the adjacent muscle and fat, with abrupt destruction rather than progressive atrophy of the muscle fibres.

Immunohistochemical stains for cytokeratins, desmin, S100, and neurofilaments were negative. Vimentin was strongly positive.

The tumour belonged to the group of infantile fibrous proliferations. Differential diagnosis was between infantile fibromatosis and fibrosarcoma. In view of the numerous mitoses and the pattern of invasion of the muscle, a diagnosis of infantile fibrosarcoma, was made.

Cytogenetic results

Thirty-three G-banded metaphases were obtained from a 3-day-old culture of a biopsy sample, as previously described [13]. A normal female karyotype, 46,XX, was found in 8 cells. All the remaining cells displayed only numerical chromosome changes including loss of one X-chromosome. Two related clones were identified. The major one had tetrasomy 11 (+11,+11), trisomy 17 (+17) and trisomy 20 (+20) (18 out of 25 cells) (Fig. 2). The minor one did not exibit trisomy 20 (3 out of 25). In the remaining cells, 1 showed only trisomy 11, 1 trisomy 20, 1 trisomy 11 with trisomy 20, and 1 trisomies of chromosomes 11, 17 and 20. Therefore, the karyotype of this tumour can be described as: 49,X,−X,+11,+11,+17,+20/48,X,−X,+11,+11,+17/46,XX.

Discussion

The histological appearance of fibrosarcoma is identical in adults and children; however, congenital or infantile

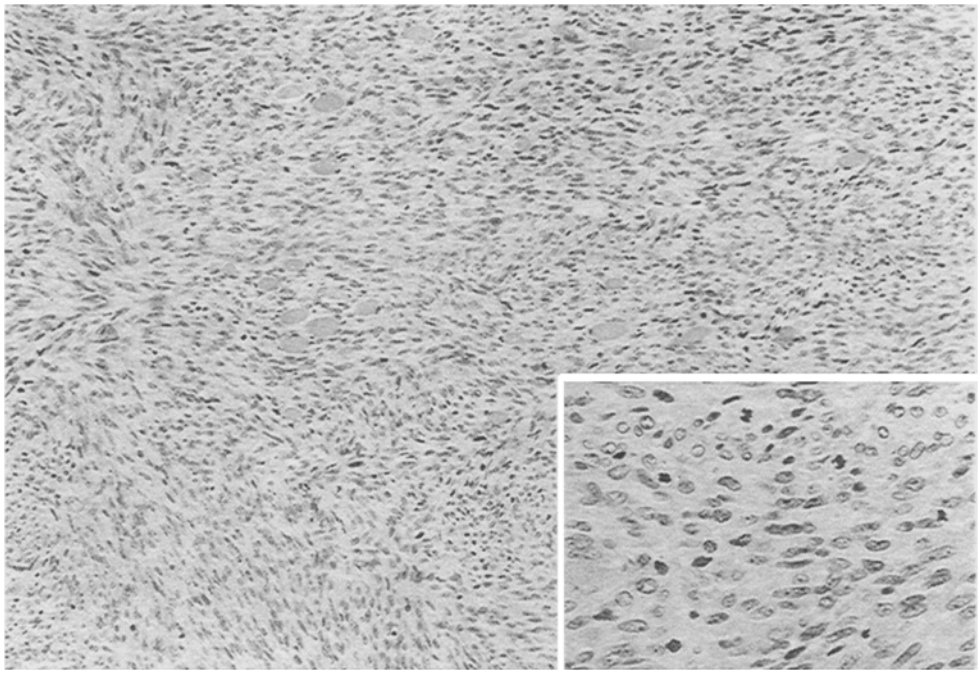

Fig. 1. Interlacing bundles of spindle cells, infiltrating striped muscle. Numerous mitoses in the tumour cells (Hematoxylin and Eosin, × 120). *Inset*, a higher magnification (× 310) of the tumour cells, showing the ovoid nuclei with distinct nucleoli. Several mitoses are present

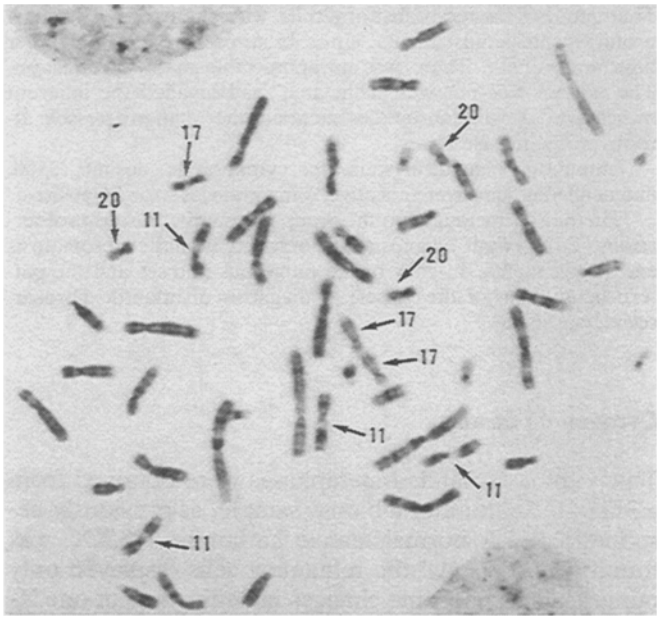

Fig. 2. Metaphase from the major clone with tetrasomy 11 and trisomy of chromosomes 17 and 20

Table 1. Cytogenetic findings in congenital or infantile fibrosarcomas

Patient	Age at cytogenetic investigation	Tumour site	Karyotype	Reference
1	65 days	Left proximal tibial epiphysis	49,XY,+8,+11, +20/48,XY, +8,+11	Speleman et al. [21]
2	5 months	Lower leg	46,XY/49,XY, +8,+11,+20/50, XY,+8,+11, +17,+20	Mandahl et al. [16]
3	At birth	Right calf	48,XY,+11,+20	Adam et al. [1]
4	15 days	Lower left leg	49,X,−X,+11, +11,+17,+20/ 48,X,−X,+11, +11,+17/46,XX	Our patient

fibrosarcoma has been considered as a separate entity because of its different clinical behaviour [6]. Excellent survival is achieved after wide local excision, or amputation alone, and mortality from the tumour is reported as only 7%–8% despite a local recurrence rate of 17%–43% [6, 20]. In addition to a different clinical behaviour, adult and congenital fibrosarcoma seem also to differ cytogenetically. Trisomies of chromosomes 8, 11, 17 and 20, in different but similar combinations, were identified as the only chromosome changes in the four congenital or infantile fibrosarcomas so far cytogenetically investigated (Table 1). Trisomy 11 (+11) was present in all abnormal clones (7/7), followed by trisomy 20 (+20) (5/7), trisomy 8 (+8) (4/7) and trisomy 17 (+17) (3/7). Trisomy 11 with trisomy 20 is the combination more frequently seen (5/7), followed by trisomy 11 with trisomy 8 (4/7). Therefore, trisomy 11 may be the key-event in congenital fibrosarcoma and the presence of the other trisomies (+8,+17, +20) may reflect tumour progression. Trisomy 8 and trisomy 11 have been reported as the only change in several leukaemias. They occur more frequently as secondary changes in both leukaemias and solid tumours, though

less often than trisomy 17 and trisomy 20 [17]. Isolated trisomy 8 with trisomy 11 has been reported in three cases of acute non-lymphocytic leukaemia [17]. Other combinations of trisomies have not been previously described in cancer cytogenetics, except for a very similar karyotype found in a congenital mesoblastic nephroma. Kovacs and coworkers [12] cytogenetically analysed the fibromatous component and the cellular area of this tumour from a 1-day-old child. A normal male karyotype, 46,XY, was found in the cultures from the fibromatous component, and only numerical chromosomes changes (+7,+8,+8,+9,+11,+17,+20) in cultures from the cellular one.

Little is known about the possible effect of numerical changes (gain or loss of a whole chromosome), but one could invoke a simple dose effect of gene(s) on these chromosomes. Recently, Scrable and coworkers [18] reported that the loss of constitutional heterozygosity at loci on chromosome 11 was apparent only in embryonal rhabdomyosarcomas, and cytogenetic analysis of the samples tested revealed trisomy 11 and not structural abnormalities of chromosome 11. Loss of heterozygosity of chromosome 11 was associated with Wilms tumour, rhabdomyosarcoma, hepatoblastoma [10, 11], transitional cell carcinoma of bladder [8] and "breast" tumour [2].

So far, cytogenetic findings have been reported in only six cases of adult fibrosarcoma [4, 14, 15, 23]. Mandahl and coworkers [14] reported a normal female karyotype, 46,XX, and an extra ring chromosome in two myxoid fibrosarcomas. In all the other cases only structural and numerical chromosome changes were observed [4, 15, 23].

The recent developments in the cytogenetics of childhood solid tumours are of importance to the clinician both in the diagnosis and estimation of prognosis of these tumours. Little or nothing is known about the cytogenetics of infantile fibromatosis which is generally considered to be a benign lesion. However its clinical course is locally aggressive and distant metastases have been reported in 4/54 cases by Stout [22] with a total of seven cases [19], described by 1989. The histopathological difference between aggressive infantile fibromatosis and congenital fibrosarcoma is unclear [3]. It is necessary to analyse chromosomes in more cases of infantile fibromatosis to define those two entities.

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