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Original research

Conservative strategy in infantile fibrosarcoma is possible: The European paediatric Soft tissue sarcoma Study Group experience

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Abstract ***Background:*** Infantile fibrosarcoma (IFS) is a very rare disease occurring in young infants characterised by a high local aggressiveness but overall with a favourable survival. To try to reduce the total burden of therapy, the European pediatric Soft tissue sarcoma Study Group has developed conservative therapeutic recommendations according to initial resectability.

Material and methods: Between 2005 and 2012, children with localised IFS were prospectively registered. Initial surgery was suggested only if possible without mutilation. Patients with initial complete (IRS-group I/R0) or microscopic incomplete (group II/R1) resection had no further therapy. Patients with initial inoperable tumour (group III/R2) received first-line vincristine-actinomycin-D chemotherapy (VA). Delayed conservative surgery was planned after tumour reduction. Aggressive local therapy (mutilating surgery or external radiotherapy) was discouraged.

Results: A total of 50 infants (median age 1.4 months), were included in the study. ETV6-NTRK3 transcript was present in 87.2% of patients where investigation was performed. According to initial surgery, 11 patients were classified as group I, 8 as group II and 31 as group III. VA chemotherapy was first delivered to 25 children with IRS-III/R2 and one with IRS-II/R1 disease. Response rate to VA was 68.0%. Mutilating surgery was only performed in three cases. After a median follow-up of 4.7 years (range 1.9–9.0), 3-year event-free survival and overall survival were respectively 84.0% (95% confidence interval [CI] 70.5–91.7) and 94.0% (95% CI 82.5–98.0).

Conclusions: Conservative therapy is possible in IFS as only three children required mutilating surgery, and alkylating or anthracycline based chemotherapy was avoided in 71.0% of patients needing chemotherapy. VA regimen should be first line therapy in order to reduce long term effects.

1. Introduction

Although infantile fibrosarcoma (IFS) is a rare tumour, it is the commonest soft tissue sarcoma in children less than 1 year of age. IFS is currently classified as a soft tissue tumour of intermediate malignancy characterised by a quite specific t(12;15)(p13;q25) translocation coding for a ETV6-NTRK3 gene fusion [1–3]. It arises below the age of 2–5 years with survival rates between 80 and 100% [1,4,5]. It often presents with initial rapid growth, sometimes with indolent evolution and metastatic spread is uncommon (1–13%). Local recurrence may occur after initial conservative surgery (17–43%), the latter being the mainstay of treatment, aiming for a conservative resection. However, IFS may present with locally advanced disease and surgery maybe mutilating or cause functional damage [4,5]. Since IFS is a chemosensitive tumour, chemotherapy may play a major role in the treatment strategy [1,6,7]. Recently, the VA regimen (vincristine-actinomycin-D), has confirmed its efficacy and allows important tumour reduction [1]. The International Society of Pediatric Oncology–Malignant Mesenchymal Tumour Committee and the Associazione Italiana Ematologia Oncologia Pediatrica–Soft Tissue Sarcoma Committee (previously called the Italian Cooperative Group) founded the European-paediatric-Soft-tissue-Sarcoma-Study Group (EpSSG) in 2005. The group developed treatment guidelines for IFS, with the major goal to make uniform the treatment of IFS patients across Europe, according to a conservative approach based on non-mutilating surgery and alkylating-anthracycline-free chemotherapy (EpSSG non-rhabdomyosarcoma soft tissue sarcomas [NRSTS] 2005 study – European Union Drug Regulating Authorities Clinical Trial No. 2005-001139-31) This present paper reports the results of a prospective cohort of IFS patients treated between 2005 and 2012 aiming to propose a conservative strategy in this disease.

2. Patients and methods

2.1. Study population

All infants aged from birth to 24 months with localised IFS were prospectively registered in the EpSSG database using a web-based system, from October 2005 to 30th June 2012. Patients were classified according specific tumour sites [8]. Clinical staging was defined according to the tumour node metastases system: T1 or T2 according to the invasion of contiguous organs; N0/N1, and M0/M1 according to the presence of lymph node or distant metastases [8]. Lymph node involvement was evaluated clinically or by imaging and confirmed when necessary by cytological or histological biopsy. The status of resection margins was classified according to the UICC-R classification and the Intergroup