Ewing’s sarcoma: long term favourable outcome in children with combined modality therapy and conservative surgery

Standard treatment: chemotherapy and surgery avoiding radiotherapy

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From November 1985 to January 2000, 21 children aged 4.5 to 18 were treated by EWDD protocol for localized Ewing’s sarcoma.
TUMOR LOCATIONS

- Femur: 4
- Iliac: 5
- Rib: 4
- Tibia: 3
- Fibula: 1
- Spine: 1
- Sacral: 1
- Radial: 1
- Mandibular: 1
PROGNOSTIC FACTORS

18/21 PATIENTS HAD AT LEAST ONE CLASSICAL BAD PROGNOSTIC FACTOR (tumoral volume >100ml or central location).

13 INITIAL TUMOR VOLUMES > 100 ml

12 central locations
EW DD2 INDUCTION CHEMOTHERAPY

0     1      2     3    4      5     6 WEEKS

BIOPSY

CPX 150mg/m²/d 7 days

THPA 35 mg/m²

ADR 1.2 g/m²/d 5 days

RESECTION

IFX
18 y old girl with a huge pleural infusion leading to discovery of a rib tumor with little pain. Very impressive radiologic response in 6 weeks.
Response to preoperative chemotherapy

Decrease of tumoral diameter: 38%
Decrease of tumoral volume: 76%
Response to preoperative chemotherapy

Decrease of tumoral diameter: 28%
Decrease of tumoral volume: 63%
Response to preoperative chemotherapy

Before chemotherapy

After 6 weeks chemotherapy

Decrease of tumoral diameter: 50%

Decrease of tumoral volume: 88%
Response to preoperative chemotherapy

Before chemotherapy

After 6 weeks chemotherapy

Decrease of tumoral size: 66%

Decrease of tumoral volume: 95%
In this protocol early extra tumoral en bloc resection without radiotherapy was the standard local treatment.

It was performed in all cases without risk of neurological sequellaes.

3 patients with contaminated margins received postoperative radiotherapy.
In the literature, risk of local recurrence following radiotherapy reaches 20% to 50%.

Why all our patients were operated?

Mean published risk: 36%
In our surgical experience (1) early resection is a significant prognostic factor. All patients were operated EARLY. 

All limb tumors were resected

Some cases of reconstructive procedures used after resection of femoral Ewing
All pelvic tumors were resected

16 Y old girl with a huge IIB tumor of iliac wing.
En bloc resection after 6 weeks chemotherapy.
Skeletal reconstruction using cement. Excellent oncologic and fonctionnal results with 15 years follow up
Even huge pelvic tumors were resected

Resection of huge tumors are challenges but most important for prognosis.

Early resection of huge tumoral mass can prevent chemoresistance
Even sacroiliac tumors

17 years remission after en bloc resection and reconstruction with cement
Postoperative chemotherapy alternated:

6 IPA (Ifosfamide 6 gr/sqm, Cisplatinum 125 mg/ m², Pirarubicine 35 mg/ m²)

3 Cyclophosphamide(150 mg/m² 7d)
+Pirarubicine (35 mg/m² d 8)

12 weeks of Vincristine (2 mg/ m² x 12), Actinomycine D (2 mg/ m² x 6)
EW.DD2 PROTOCOL.

POST OPERATIVE CHEMOTHERAPY

CPX+THP          ACT D             VCR         ACT D+VCR                I.P.A.

EW.DD2 PROTOCOL.

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TREATMENT TOLERANCE

Tolerance of preoperative chemotherapy is excellent and permits best conditions for the surgery.

Toxicity of postoperative chemotherapy is heavier
1. 20% Vincristine induced multineuritis.
2. 1 Vesical grade 4 toxicity induced by Ifosfamide.
3. 1 Renal toxicity following a course of IPA.
4. Anthracyclines (pirarubicine) low toxicity: only two ECG transitory anomalies.
Late complications related to treatment

We observed two colic cancers in patients treated by this protocol.

Patients were even free survivors when colic cancer occurred, respectively 13 years and 15 years following treatment.

Both patients received post operative radiotherapy after contaminated resection of sacroiliac tumors.

Both patients are in CR for the second cancer.
Oncologic results

EW DD. 21 children with localized Ewing. Median follow up: 10 years (min 5, max 19.5). 20/21 patients are DFS. (15/04/2005)
CONCLUSION 1

This series shows the excellent long term prognosis of children with localized Ewing’s sarcoma treated by this protocol derived from Hayes, with shorter (6 weeks) bidrug induction.

and systematic conservative surgery.

followed by six drugs postoperative chemotherapy.
This serie confirms the results of Hayes on patients treated by surgery: 10/11 operated patients were DFS.

This series also confirms the good prognosis of young patients observed in the multicentric Italian SE 91 study published by Rosito P. et al. Cancer, 1999; 86: 421-428.
CONCLUSION 3

- It emphasizes the low toxicity of this chemotherapy.
- And underlines the risks of radiotherapy even at mild doses (2 second cancers out of 3 patients irradiated) and the need to avoid it as often as possible.