**Isolated testicular relapse in acute lymphoblastic leukaemia of childhood**

Tiedemann et al. have shown this approach to be highly effective at least in the short term, with 100% disease-free survival at 18–54 months for a series of 10 boys. Four of their series were diagnosed early by biopsy of an unenlarged testis. Earlier diagnosis and more vigorous and consistent therapy may well improve the outcome of testicular relapse. At the same time, prevention either by more intensive chemotherapy or perhaps by testicular irradiation may be a better prospect, especially for the poor risk cases. Recent trials are testing these concepts.

We thank all members of the working party who have allowed us to publish data on their patients, and Dr Chessells for helpful advice.

**References**


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**Commentary**

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This article describes the outcome in boys with acute lymphoblastic leukaemia (ALL) who were entered into the first three Medical Research Council UK ALL trials and in whom the first remission ended in an apparently isolated testicular relapse. Twelve years ago testicular leukaemia had been described but the extent of the problem was not fully recognised and, unfortunately, in these early protocols, no clear recommendations for treatment were given. Nevertheless, some guidelines about management and prognosis can be drawn from this retrospective analysis.

Boys who develop overt testicular infiltration while still on chemotherapy have a uniformly poor prognosis and almost invariably develop later marrow relapse. Such patients therefore should receive local and systemic treatment followed by bone marrow transplant if a suitable donor is available.

The majority of patients who develop testicular relapse do so within the first 2 years after treatment has been electively stopped or are found to have occult testicular infiltration on routine biopsy performed before a decision about stopping treatment. The outcome for such patients may be rather better and some, given optimal treatment, may have a chance of long-term disease-free survival.

Effective local control of testicular leukaemia may be achieved by orchidectomy or radiotherapy. A dose of 2400 rad is necessary for local control of testicular disease. One patient in Eden's study developed local recurrence after this dose but details of his systemic treatment are not clear, and we continue to prefer radiotherapy to the more traumatic alternative of orchidectomy. Presumably local control will prove easier in patients with occult (biopsy positive) infiltration. In view of the high incidence of bilateral infiltration radiotherapy should be given to both testicles.

Although the bone marrow and cerebrospinal fluid may be apparently normal at the time of testicular relapse, patients who receive local treatment or minimal additional systemic chemotherapy are at risk of subsequent bone marrow or central nervous system (CNS) relapse. Extensive staging investigations, including lymphography and laparotomy, in a small group of boys with apparently isolated testicular relapse, showed that some had involvement of para-aortic nodes indicating that disease was widespread. It is thus apparent that intensive systemic reinduction, consolidation, further chemotherapy, and further CNS prophylaxis are essential. Despite this evidence that testicular leukaemia is but a 'marker' of residual disease elsewhere, we find at this hospital that boys with a positive biopsy or with late overt infiltration treated with bilateral local irradiation, intrathecal methotrexate, intensive reinduction, and further chemotherapy do much better than those with late bone marrow relapse: 10 of 11 boys so treated remain in second complete remission and off treatment 35 to 70 months from the time of testicular relapse.
The introduction of routine testicular biopsies, by facilitating early diagnosis and treatment, may improve the prognosis of testicular leukaemia; unfortunately it has not, in our experience, reduced the subsequent rate of marrow relapses after treatment has been electively stopped. It is not clear whether this failure to reduce late bone marrow relapses is evidence against re-seeding of the marrow from the testis or of failure to detect minimal residual disease in the testicle. In this context the occurrence of 'false-negative' biopsies has been a worrying problem and one where examination for minimal infiltration with cells which stain for terminal deoxynucleotidyl transferase (a marker for T-ALL and common ALL) may ultimately prove helpful.

Prophylactic testicular irradiation soon after induction of first remission has reduced the incidence of testicular leukaemia but has not decreased the bone marrow relapse rate in boys with ALL. Whether the testis is but a marker of residual disease or a source of re-seeding, it seems clear that protocols with a significant difference in outcome between boys and girls are also those with a high incidence of testicular leukaemia. It is possible that protocols with more intensive systemic chemotherapy may eliminate the difference in outcome between the genders and reduce the incidence of testicular leukaemia. The present generation of UK ALL trials is designed to address this problem and incidentally to provide strict guidelines for the management of extramedullary relapse.

References

With commentary

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