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CASE REPORT

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Post-chemotherapy microscopic residual prostate rhabdomyosarcoma: long-term conservative follow-up

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Abstract In spite of advances in the treatment of childhood bladder and prostate rhabdomyosarcoma (RMS), the ability to detect minimal residual disease correlates imperfectly with the ultimate outcome. We report the long-term follow-up of a child with microscopic residual RMS after chemotherapy. The correct interpretation of the histologic findings spared the child unnecessary additional therapy and raises enigmatic questions about the biology of minimal residual disease.

Keywords Rhabdomyosarcoma · Bladder · Chemotherapy · Microscopic residual disease · Histopathologic changes

Introduction

Of all patients with childhood bladder and prostate rhabdomyosarcoma (RMS) treated with chemotherapy, 70% survive over 5 years. It may therefore be considered a curable disease [1, 2]. Bladder preservation is indicated when no residual tumor is found macro- and microscopically following chemotherapy. Controversy exists regarding the therapeutic approach to those children who have no evidence of macroscopic disease following chemotherapy, but still have microscopic findings of tumor cells. Our report addresses this issue.

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Case report

A 16-month-old boy presented in 1994 with severe difficulty in urination. Ultrasonographic (US), radiologic, and endoscopy studies revealed a botryoid tumor in the bladder neck and prostatic urethra. Histopathology revealed embryonal RMS. Chemotherapy was commenced with vincristine, actinomycin D, and cyclophosphamide every 3 weeks for 36 weeks. After completion of the chemotherapy, radiologic and endoscopic findings revealed no macroscopic disease, however, a few residual tumor cells were found in the prostatic urethra in one of several biopsies. As the tumor cells appeared degenerated with large-vacuolated cytoplasm and smudged chromatin (Fig. 1), the absence of biologically malignant behavior was presumed and no further therapy was administered. The child was followed periodically by repeated US and computerized tomography examinations. Repeat cystoscopy and multiple biopsies 3 years later revealed normal bladder mucosa with no evidence of tumor. He is now 7 years old and free of disease.

Discussion

Aggressive treatment with either radiotherapy or cystoprostatectomy has been advocated when microresidual bladder RMS exists following chemotherapy [3]. A few reports raise the issue of microscopic residual disease leading to unnecessary therapy [4–6]. In one, the presence of microscopic RMS following chemotherapy led to a cystoprostatectomy in three patients, but no tumor was found in the resected specimen [1]. The same authors reported another three patients who had no further therapy despite positive microscopic residual disease and were found to be free of the disease over 65 months of follow-up. This suggests that even though these patients may have rhabdomyoblast-like cells in biopsy specimens, they do not require additional therapy. No subsequent histopathologic data were presented in this report.

To our knowledge, ours is the first report that demonstrates repeated histopathologic findings that clearly show the different stages of tumor-cell degeneration and the loss of malignant potential of this tissue during-long

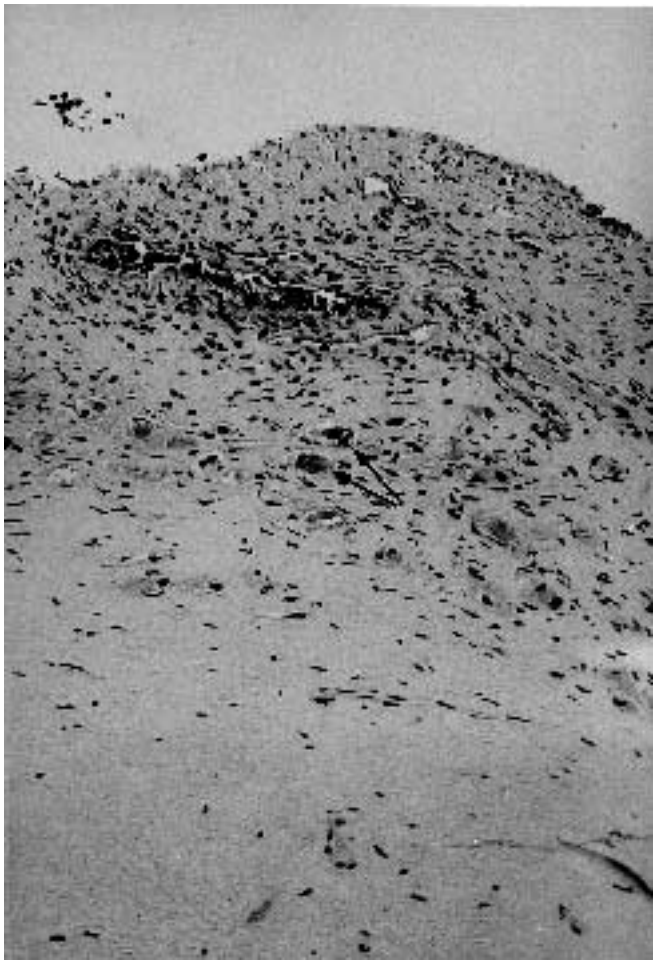

Fig. 1 Biopsy specimen following chemotherapy shows the tumor cell with vacuolated cytoplasm (*arrows*) and smudged chromatin

follow-up period. We hypothesize that the tumor cells lose their malignant potential under the influence of chemotherapy and require no additional therapy. In doubtful cases the histologic studies should be complemented by molecular studies. The most useful molecular marker for embryonal RMS is loss of heterozygosity (LOH) at 11p15 in cases where this was expressed in the original tumor [4–6].

The surgeon should be aware that repeated biopsies may miss the area of malignancy. To avoid this problem, we took multiple biopsies from the area of the original tumor, thereby reducing the possibility of missing an ongoing pathological process to a negligible level. We suggest that careful assessment based on pathologic results is crucial, and conservative, bladder-preserving management should be considered when only microscopic residual disease is found following chemotherapy. This report does not resolve the issue of microscopic residual disease, but raises intriguing questions about the biology of RMS. The answers to these questions will help to spare patients from unnecessary bladder surgery, such as radical cystoprostatectomy, or radiotherapy.

References

1. Atra A, Ward HC, Aitken K, Boyle M, Dicks-Mireaux C, Duffy PG, Mitchel CD, Plowman PN, Ransley PG, Pritchard J (1994) Conservative surgery in multimodal therapy for pelvic rhabdomyosarcoma in children. Br J Cancer 70: 1004–1008
2. Heyn R, Newton WA, Raney RB, Hamoudi A, Bagwell C, Vietti T, Wharam M, Gehan E, Maurer HM (1997) Preservation of the bladder in patients with rhabdomyosarcoma. J Clin Oncol 15: 69–75
3. McLorie GA, Abara OE, Churchill BM, Greenberg M, Mancer K (1989) Rhabdomyosarcoma of the prostate in childhood: current challenges. J Pediatr Surg 24: 977–981
4. Ruymann FB, Grovas AC (2000) Progress in the diagnosis and treatment of rhabdomyosarcoma and related soft tissue sarcomas. Cancer Invest 18: 223–241
5. Scholl FA, Betts DR, Niggli FK, Schafer BW (2000) Molecular features of a human rhabdomyosarcoma cell line with spontaneous metastatic progression. Br J Cancer 82: 1239–1245
6. Dehner LP (1998) The evaluation of the diagnosis and understanding of primitive and embryonic neoplasms in children: living through an epoch. Mol Pathol 11: 669–685