NOWOTWORY 2001/ tom 51
Zeszyt 3 / 245–248

Desmoid tumour in paediatrics: a radiotherapeutic approach

Anna Skowrońska-Gardas, Izabella Śliwowska

Aim and purpose. Desmoid (fibromatosis aggressiva) is a rare, histologically benign but locally aggressive tumour. Radiotherapy has an important place in the treatment of this disease, but the value of this method in paediatric patients is not established and published results are sparse. The aim of this study is to present our experience in treating paediatric desmoid tumours and to consider the most optimal treatment for these patients.
Material and methods. Between 1991 and 2000, 9 children in age 4-14 years with desmoid tumours, were treated in the First Radiotherapy Department of the Warsaw Cancer Center of Oncology. All patients were irradiated after nonradical surgery and 6 due to the first or next local recurrence. The aggressive chemotherapy regimes were applied in 8 children. All patients received local irradiation for tumour bed with total doses of 50-60 Gy.
Results. All children are alive from 10 to 112 months after completing radiotherapy. In 2 patients local relapses after 8 and 18 months were observed. Five patients are living with no evidence of disease more than two years after radiotherapy. The growth arrest and other serious complications after radiotherapy were not observed.
Conclusions. The treatment of a child with desmoid tumour should be considered individually. Surgery is a treatment of choice, and adjuvant radiotherapy with doses of 50-60 Gy should be applied when the potential morbidity of a second operation is high. Chemotherapy with „low toxicity" agents could be considered in patients with gross residual disease and in those with recurrent tumours.

Desmoid tumor w pediatrii: zastosowanie radioterapii

Podstawa i cel pracy. Desmoid (włókniakowatość) jest rzadkim, histologicznie łagodnym, lecz miejscowo agresywnym guzem. Radioterapia zajmuje istotne miejsce w leczeniu tego schorzenia, ale ocena roli tego typu terapii u dzieci nie jest ustalona, a doniesienia w literaturze są rzadkie. Celem tego opracowania jest przedstawienie doświadczeń Zakładu Radioterapii w leczeniu pacjentów pediatrycznych i rozważenie najbardziej optymalnego sposobu leczenia dla tych chorych.
Materiał i metody. W latach 1991-2000, w I Zakładzie Radioterapii Centrum Onkologii w Warszawie leczono 9 dzieci w wieku od 4 do 16 lat, z rozpoznaniem desmoidu. Wszyscy pacjenci byli napromieniani, po nieradykalnym zabiegu operacyjnym, a 6 z powodu pierwszej lub kolejnej wznowy. U 8 dzieci zastosowano również agresywną chemioterapię. Pacjenci byli napromieniani na obszar loży guza w dawkach 50-60 Gy.
Wyniki. Wszystkie dzieci żyją przez okres od 10 do 112 miesięcy od zakończenia radioterapii. U 2 pacjentów stwierdzono wznowę po upływie 8 i 18 miesięcy. Pięcioro dzieci żyje bez objawów nawrotu ponad 2 lata po napromienianiu. Nie obserwuje się u nich zaburzeń wzrostu, ani innych poważnych komplikacji po radioterapii.
Wnioski. Leczenie dziecka z rozpoznaniem desmoidu powinno być rozpatrywane indywidualnie. Leczenie chirurgiczne jest metodą z wyboru; uzupełniająca radioterapia w dawkach 50-60 Gy powinna być zastosowana u pacjentów z wysokim ryzykiem okaleczenia po reoperacji. Chemioterapia z zastosowaniem leków o „niskiej toksyczności" może być rozpatrywana u małych dzieci z dużą pozostałością guza oraz w przypadkach nawrotu.

Key words: desmoid tumour, fibromatosis aggressiva, radiotherapy, children
Słowa kluczowe: desmoid, włókniakowatość, radioterapia, dzieci

Desmoid tumours or Fibromatosis aggressiva are rare, slow growing, histologically benign tumours of soft tissue. Despite their benign appearance, they are locally aggressive and tend to invade surrounding structures [1]. Desmoid tumour is a relatively rare lesion, representing less than 0.1% of all neoplasms, with reported annual incidence 2-4 cases/1 mln population [2]. About 2% of desmoids are FAP (Familial Adenomatous Polyposis) associated, with mutation of APC gene and about 1000 fold increased risk of developing desmoids compared to the

The First Radiotherapy Department
The Maria Skłodowska-Curie Memorial Cancer Center
and Institute of Oncology, Warsaw, Poland

general population, especially with intraabdominal localisation [3]. An association between trauma and hormonal status (pregnancy) has been also reported [4, 5]. Desmoid tumours are localised most often in the extremities, neck, trunk, abdominal wall and in the small bowel mesentery [3, 6, 7]. The treatment of choice for most of these tumours is a wide local excision, but local failures after surgical treatment are often observed, from 5 to 50% after microscopically complete resection to 60-90% after incomplete surgery [6, 8-10]. For patients treated with combined incomplete resection and radiotherapy, relapse rate is diminished to 20-40% [1, 5-7, 9, 10]. The role of adjuvant chemotherapy has not been established in any prospective, randomised study, although some authors reported stabilisation and remission in single cases [4, 6]. A number of drugs that are not classical antineoplastic agents have been used: nonsteroid anti-inflammatory drugs, ascorbic acid, vitamin K, antiestrogens etc. with occasional benefit in largely anecdotal reports [11, 12]. Most published articles included adult patients alone or adult and paediatric population together; reports related to treatment of desmoid in children are sparse [4, 8, 12].

The aim of this study is to present our experience in treating paediatric patients with desmoid tumours, and to consider the most optimal ways of treatment.

Material and Methods

From 1991 till 2000, 9 children, aged 4-16 (median 12) with histopatollogically confirmed diagnosis of desmoid tumour (*Fibromatosis aggresiva*) received irradiation in the First Radiotherapy Department of the Warsaw Cancer Center. In all cases microscopically or macroscopically nonradical excision was performed. Three children were irradiated immediately after nonradical surgery, in remaining 6 radiotherapy was applied due to first or next relapse. Two girls were treated with multiple surgery procedures for 5 times. Eight children but one were treated before radiotherapy with aggressive chemotherapy regimes, usually used in malignant sarcomas. This treatment was applied in paediatric oncology departments before they were reffered to our Center.

All patients received radiotherapy with Co-60 or mixed photon and electron beams. The treatment was planned with the use of simulator, and 2 opposite or oblique beams with wedges were applied. In 4 patients treated after 1996, the conformal radiotherapy was performed, with CT and 3-D treatment planning and individual shielding. The total doses were 50-60 Gy, and fractionation doses 1.8 Gy. The tolerance of treatment was good, only mild skin reactions (RTOG I) in all patients were observed.

Results

All patients are alive from 10 to 112 months after completing radiotherapy. In 2 children local recurrences after 8 and 18 months were observed, one of them is living after forearm amputation, the second after next nonradical resection, with stable disease. Two patients, treated with multiple surgery and with gross residual tumours, are observed up to 12 months, with slow partial regression of tumour. Patients' characteristics, methods of treatment and results are presented in Table I.

Late side effects of treatment are mostly connected with surgical treatment. The growth arrest and serious soft tissue complications after radiotherapy were not observed. Two girls, treated with mutilating surgery and intensive chemotherapy, suffer from serious postsurgical complications, one of them has a shortening and deformation of leg.

Discussion

Desmoid tumours (*Fibromatosis Aggressiva*) are a heterogeneous group a benign fibrous proliferation. Multiple recurrences often occur, but deaths due to this disease are rare (in 0-8% cases) mostly in head and neck or mesenteric localisation [3, 8]. There are many reports describing prognostic factors and methods of treatment. The treatment of choice is surgery, but recurrence rate is high. Groups of patients, (from 13 to 190 cases), presented in the literature consist of adults and children together. In many reports the most important prognostic factor, that independently predicts for local recurrence is a surgically positive margin [5-9]. However some authors do not confirm this observation [1]. Adjuvant radiotherapy is connected with improvement of local results in patients with positive surgical margins, after partial surgery, and also in patients treated nonsurgically [5-7, 9, 10, 13]. A sufficient portals of irradiation, encompassing whole tumour bed for avoiding „geographical misses" and doses range 50-60 Gy are mandatory [1, 5, 7, 9, 10, 13]. The group of 9 patients, treated with combined surgery and radiotherapy, was presented in Polish literature [14]. The local control was obtained in 7 patients. Authors suggested doses of 56 Gy in radiation therapy when used as only modality of treatment, and of 50 Gy in postoperative irradiation. Some authors, emphasize also young age (below 18 or 30 years) and plantar localisation as a negative prognostic factor [4, 6, 10]. The largest paediatric series (63 children) with desmoid tumour was reported from Memorial Sloane Kettering Cancer Centre [8]. The basic method of treatment was surgical resection. Recurrence at 3 years was observed in 75% of patients. Radiotherapy was applied in 11 patients, but only in 5 with doses higher than 50 Gy. Four children recurred, including 2 of 5, who received doses above 50 Gy. Six patients received chemotherapy, and of the four patients with at least 3 years follow-up, two recurred. Authors from St. Jude Children's Research Hospital presented long-term results with radiation therapy in 13 children with desmoid tumours [15]. Up to now it is the largest series of paediatric patients, treated with radiotherapy and with median follow-up of 198 months. In this group 10/13 children recurred, but only 1 later than 32 months after irradiation, and 3 have died from their disease. The failure rate with radiation therapy in this group was high, and authors speculate, that these tumours in children are biologically different from their adult counterpart.

In our material all patients were irradiated due to nonradical excision and 6 with recurrent tumour. Two girls were treated with multiple surgery, and in one of them this treatment was a cause of serious morbidity. In these patients we observed a slow partial regression of

Tab. I. Patients' characteristics, methods of treatment and results in children with desmoid treated in Radiotherapy Department, Center of Oncology, Warsaw

N	Age	Sex	Localisation	Treatment before RT / year		Recurrence before RT / year		RT year	Recurrence after RT /months		Treatment of recurrence	Present status	Months after RT
1	12	M	shank	NS Chth	1990 1990	no		1991	no		-	NED	112
2	9	M	buttock	RS NS	1988 1993	yes	1993	1993	no		-	NED	89
3	5	M	forearm	NS Chth	1993 1993	no		1993	yes	8	amputation	NED	86
4	7	F	groin	NS Chth NS	1991 1995 1995	yes	1995	1995	no		-	NED	57
5	4	M	abdominal wall	Chth NS	1996 1996	no		1996	no		-	NED	50
6	16	F	popliteal fossa	NS Chth NS	1997 1998 1998	yes	1998	1998	yes	18	NS	SD	32
7	11	M	arm	NS Chth NS	1997 1997 1998	yes	1998	1998	no		-	NED	25
8	14	F	extremites inferior (plantar to buttock)	NS NS 4x Chth	1994 1995-1999 1999-2000	yes	1995-1999	2000	no		-	PR	12
9	14	F	abdominal wall	NS Chth NS 3x Chth	1992 1992 1998 2000	yes	1998	2000	no		-	PR	10

Abbreviations: RS – radical surgery, NS – nonradical surgery, Chth – chemotherapy, RT – radiotherapy, NED – non evidence disease, SD – stable disease, PR – partial regression

residual tumour. The slow response of desmoid tumour after radiotherapy has been reported [15]. In all children but one aggressive chemotherapy was applied, without any therapeutic effect. Relapse free survival >2 years was obtained in 5/7 patients, in 2 children follow-up is shorter. These results are similar as presented by others [3-6, 9, 10] and better than reported by St. Jude Hospital team [15], but long-term observations are necessary. The doses ranging from 50 to 60 Gy were well tolerated, and up to now we do not observe any serious complications related to radiotherapy.

According to our experience and literature data we suggest, that treatment for children with desmoid should be considered individually. Surgery is a treatment of choice, and, when negative margins can be achieved, no additional therapy is indicated. Even if the surgical margins are minimally positive, many patients will not have a recurrence.Tumours that are incompletely resected are treated adjuvantly, when the potential morbidity of a re-excision is high. Under these circumstances adjuvant radiation therapy is used and the doses above 50 Gy are recommended. Radiation portals should be adequate to encompass whole tumour bed with 5 cm margin. Chemotherapy could be an alternative to radiation therapy especially for young children, but the systemic use of such toxic drugs as alkylating agents and anthracycline is difficult to justify for a tumour that is only locally aggressive. Alternative to these agents are drugs with relatively „low toxicity", such as vinblastine and methotrexate. These agents are the subject of Pediatric Oncology Group trial for patients with gross residual tumour after surgery and for those with recurrence.

Conclusions

The treatment of pediatric desmoid tumour should be considered individually by a multidisciplinary team. Surgery is a treatment of choice, and adjuvant radiotherapy in doses 50-60 Gy should be applied after nonradical surgery, when the potential morbidity of a second operation is high. Chemotherapy with „low toxic" agents could be considered in young children with gross residual disease and in those with recurrent tumours.

Anna Skowrońska-Gardas Ph.D., M.D.
The First Radiotherapy Department
The Maria Skłodowska-Curie Memorial Cancer Center
and Institute of Oncology
Wawelska 15
00-973 Warsaw
Poland

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Paper received: 7 February 2001
Accepted: 13 March 2001