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The effectiveness of radiotherapy for painful humeroscapular periarthritis (PHS)

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Study aim. The analysis of radiotherapy effectiveness as a treatment modality for periarthritis humeroscapularis (PHS)
Material and method. 30 patients irradiated because of PHS (1 Gy per fraction up to 6 Gy). Follow-up ranged from 1 to 216 months. The arm mobility and pain relief were assessed at the completion of radiotherapy and during follow-up examinations. Correlation between some biological factors evaluated before radiotherapy and the aforementioned endpoints was assessed using Spearman's test.
Results. The mean degree of pain relief ranged from 42% to 93%. Mean improvement of arm abduction, flexion and reflexion angles ranged from 24° to 83°, from 47° to 91° and from 4° to 13°, respectively. The sole prognostic factor found in this study was the degree of orthopedic disability before the treatment. Small impairment at the onset correlated with significant improvement after radiotherapy. No radiation toxicity or secondary malignancies were observed.
Conclusion. Radiotherapy of PHS is an effective, safe and economical treatment modality, which could form an alternative for standard orthopedic and pharmacological treatment in recurrent or persistent disease.

Skuteczność radioterapii w leczeniu zespołu bolesnego barku

Materiał i metoda. Przeanalizowano wyniki leczenia grupy 30 chorych na PHS, napromienianych dawką frakcyjną 1 Gy do dawki całkowitej 6 Gy. Czas obserwacji zawierał się w przedziale od 1 do 216 miesięcy. Oceniano stopień ustąpienia bólu oraz ruchomość w stawie ramiennym przy zakończeniu leczenia oraz podczas kolejnych kontroli. Zależności pomiędzy niektórymi czynnikami biologicznymi, a uprzednio wspomnianymi ocenianymi cechami sprawdzano przy użyciu testu Spearmana.
Wyniki. Średni stopień ustąpienia bólu zawierał się w przedziale od 42% do 93%. Kąt poprawy odwodzenia, zginania i prostowania ramienia wyniósł odpowiednio od 24° do 83°, od 47° do 91° oraz od 4° do 13°. Jedynym znalezionym czynnikiem prognostycznym był stopień niesprawności w stawie ramiennym przed rozpoczęciem radioterapii – niewielka niesprawność wiązała się z dużą poprawą po leczeniu. Nie zaobserwowano żadnych objawów ubocznych, ani wtórnych nowotworów w czasie obserwacji.
Wniosek. Radioterapia zespołu bolesnego barku jest skuteczną, bezpieczną i względnie tanią metodą leczenia, mogącą być alternatywą dla chirurgicznych i farmakologicznych metod leczenia w nawrotowych i przetrwałych postaciach tego schorzenia.

Key words: benign disease radiotherapy, painful shoulder, PHS, periarthritis humeroscapularis
Słowa kluczowe: radioterapia schorzeń nienowotworowych, bolesny bark, PHS

Introduction

Periarhritis humeroscapularis (PHS) is chronic periarticular inflammation of the humeral joint encompassing soft tissues, with extraskeletal ossification, shoulder pain and joint disability.

The treatment of periarhritis humeroscapularis causes many controversies due to the unsatisfactory results of different treatments modalities.

A number of treatment methods are applied in this disease. The most popular is pharmacological treatment using anti-inflammatory non-steroid drugs applied in oral [1] and topical form [2]. Other, rarely applied kinds of pharmacological treatment include a form of immunotherapy using thymopentin [3] and biphosphonate therapy reducing extra skeletal calcification [4].

Another commonly performed treatment modality is percutaneus injection of steroids and/or local anesthetics used as intra-articular injections [5] and nerve blocks [6]. This is an effective and relatively low-priced treatment modality, which allows to achieve satisfactory, but only temporary results, significantly better than the placebo effect [7].

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Surgery is used relatively rarely, because of the complex nature of PHS and due to the limited efficacy of this method. For these reasons surgical treatment is applied rather as a form of anaesthetic treatment (denervation), rather than to alter the anatomy of the shoulder region [8, 9].

In painful cases without significant shoulder dysfunction superficial and deep acupuncture may be performed [10].

Another rarely used treatment modality for PHS, which, however, offers functional improvement and pain relief, is extracorporeal shock-wave therapy [11].

Due to the limited efficacy of these treatment modalities, a relatively important treatment method, despite the non-malignant character of this disease, is radiotherapy. Radiotherapy in case of PHS has been performed from the first half of the last century and until the present time, and it remains a quite popular choice in such clinical circumstances [12-16]. The application of PHS radiotherapy is based on its high efficacy (pain relief and arm mobility improvement in more than 80% [14] and mean pain relief exceeding 80% [16]) and on its safety (application of small fraction doses ≤1 Gy and lack of adverse effects [14-16]).

In this kind of radiotherapy the anti-inflammatory effect is the basic issue [17-19]. The mechanism of this effect is complicated an, to a great extent unclear. It is probably based on phenomena completely different than those, which are used in classic oncological radiobiology. There is no evidence to prove that radiobiological effects used in benign disease radiotherapy depend upon the inhibition of clonogenic cell repopulation [20]. The anti-inflammatory effect of low fraction doses is probably based on the modulation of E-selectin liberation and the activation of endothelial cells, which decreases leukocyte adhesion [17], on blocking the oxidative burst in macrophages [19] and on blocking nitric oxide synthase expression in irradiated tissues [18].

Aim of the study

The aim of the study was to assess the value of radiotherapy in the treatment of patients with periarthritis humero-scapularis (PHS).

Material

The material consisted of 30 patients suffering from periarthritis humero-scapularis (PHS) (13 women and 17 men); (age: 32 – 76 years; mean 59). The time from the onset of the disease to the start of radiotherapy ranged from 1 to 120 months (mean 18). Eight patients had concomittant cancer and another five had been previously treated because of neoplastic disease. Two patients had haemangiomas of the cervical vertebrae. In 15 cases the disease was located in the right; and in 15 – in the left shoulder. In 32% of cases the pain of the shoulder rendered sleep difficult. Before radiotherapy 19% of patients took non-steroid anti-inflammatory drugs, 12% – tramadol and 8% – narcotics. Three of these patients were previously treated by periarticular steroid injections, and two – by physiotherapy. The mean degrees of arm abduction, flexion and reflexion at the treatment beginning were respectively 85°, 83° and 31°.

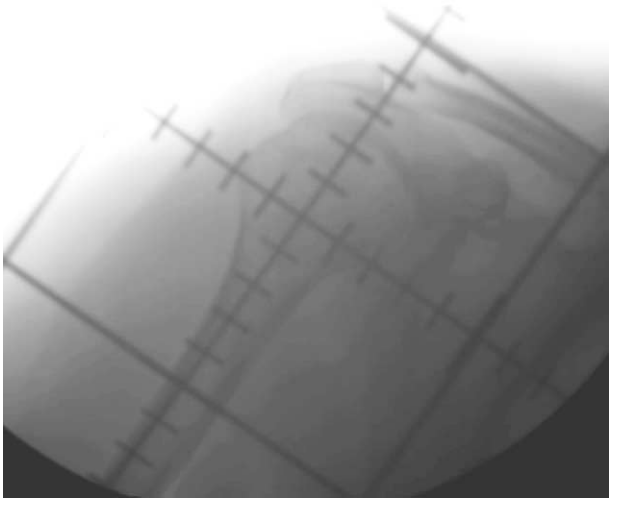

Figure 1. The irradiated field in the case of PHS

Patients were irradiated between November 1999 and September 2003 at the Department of Radiotherapy of the M. Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology in Gliwice. All were treated from two opposite (AP-PA) fields, using gamma ^{60}Co beams, 1 Gy per fraction, up to a total dose of 6 Gy. The irradiated fields comprised the shoulder and the surrounding soft tissues (Figure 1). The mean area of the irradiated field was 106 cm^2 (range from 42 cm^2 to 189 cm^2) and the mean thickness of the shoulder was 14 cm.

Follow up ranged from 1 to 216 months (mean 54).

Method

All patients were examined before radiation treatment, at the end of radiotherapy and on week 1 and 7 and month 6, 12 and 24 after treatment complation. Some patients were controlled longer. During examination the angle of arm abduction, flexion and reflexion were measured and the degree of pain relief was expressed in percentages, as compared to the level from before the onset of radiotherapy. The impact of shoulder pain on sleep and the intake of analgesics was evaluated

Means and ranges of the abduction, flexion and reflexion angles of arm and the percentages of pain relief evaluated during particular controls and during the last control were calculated.

The percentages of patients with pain relief, with major pain relief (≥50%) and with complete pain relief were calculated at the end of radiotherapy and during the follow-up examinations.

The percentages of patients with significant improvement (≥20°) of arm abduction at the end of radiotherapy and during following controls were calculated.

The character of data distribution was evaluated using the Shapiro-Wilk test.

Correlation between patient age, symptom duration, and the abduction, flexion and reflexion angles were evaluated before radiotherapy, pain decrease at the end of radiotherapy and abduction, flexion, reflexion angles and level of pain relief was evaluated during follow-up (analysis: Spearman's test).

Table I. Means and ranges of pain relief and abduction, flexion and reflexion angles during control examinations

Measured feature name	Time of control						
	Radiotherapy completion	Week 1 after treatment	Week 7 after treatment	Month 6 after treatment	Month 12 after treatment	Month 24 after treatment	Final control
Pain relief	42% (0-100%)	70% (0-100%)	77% (0-100%)	80% (20-100%)	93% (50-100%)	78% (30-100%)	74% (0-100%)
Abduction angle	109° (30-180°)	111° (30-180°)	132° (15-180°)	148° (50-180°)	168° (120-180°)	Too poor data	142° (30-180°)
Flexion angle	130° (30-180°)	133° (30-180°)	131° (15-180°)	164° (90-180°)	174° (150-180°)		153° (30-180°)
Reflexion angle	35° (10-50°)	35° (10-50°)	35° (10-45°)	44° (30-45°)	42° (30-45°)		37° (10-45°)

Table II. Analgesic intake during follow-up

Drug	Percentage of patients					
	Radiotherapy completion	Week 1 after irradiation	Week 7 after irradiation	Month 6 after irradiation	Month 12 after irradiation	Final control
Non-steroid anti-inflammatory drugs	13%	19%	6%	7%	11%	4%
Tramadol	6%	12 .5%	12%	13%	11%	11%
Narcotics*	6%	12 .5%	6%	13%	33%	8%

* in all cases narcotis were taken by patients with active neoplastic disease because of cancer pain provoked by cancer

Results

The mean abduction angle before radiotherapy was 85° (range: 10° – 180°). The mean flexion and reflexion angles before the treatment were 83° and 31°, and ranged from 5° to 180° and from 5° to 90°, respectively.

Means, ranges of pain relief degrees and angle improvements are presented in Table I.

At the end of radiotherapy pain rendered sleep difficult in 15% of cases, one week later – in 6% and seven weeks after radiotherapy – in 7%, six months after the treatment in 8%, 12 months after the treatment in 8% and during the final control – in 4% of cases.

Evaluation of sleep disturbances and analgesic intake two years after radiotherapy was neglected because of poor data.

The analgesic intake during follow-up is presented in Table II.

The percentages of patients with different degrees of pain relief during follow-up are presented in Table III.

Significant improvement of arm abduction (≥20°) at the end of radiotherapy was noted in 44% of patients. In the following control examinations these percentages were 31%, 31%, 57%, 50% and 41% during control performed one and seven weeks, and six and twelve months after radiotherapy, and during the final control, respectively.

Spearman test showed, at the end of radiotherapy, statistically significant correlations between abduction, flexion angles and abduction angle before the treatment ($p=0.0007$, $R=0.76$, $p=0.004$, $R=0.85$ respectively), reflexion angle and reflexion angle before the treatment ($p=0.045$, $R=0.68$).

One week later correlations between pain relief and pain relief at the end of radiotherapy ($p=0.02$, $R=0.5$), abduction angle and abduction, flexion, reflexion angles before the treatment, pain relief at the end of radiotherapy ($p=0.000009$, $R=0.92$, $p=0.046$, $R=0.72$, $p=0.008$, $R=0.84$, $p=0.03$, $R=0.58$ respectively), flexion angle and abduction, reflexion angles before the treatment ($p=0.00004$, $R=0.98$, $p=0.039$, $R=0.73$ respectively), were found.

Seven weeks after radiotherapy correlations between abduction angle and reflexion angle before the treatment ($p=0.001$, $R=0.93$), flexion angle and abduction, reflexion angles before the treatment ($p=0.047$, $R=0.71$, $p=0.0498$, $R=0.75$ respectively), reflexion angle and duration of symptoms ($p=0.013$, $R=0.75$), were found.

Table III. Percentage of patients with different degrees of pain relief during follow-up

Degree of pain relief	Any pain relief	Major pain relief (50≤)	Complete pain relief
Radiotherapy completion	77%	50%	12%
Week 1 after radiotherapy	91%	83%	39%
Week 7 after radiotherapy	95%	84%	37%
Month 6 after radiotherapy	100%	87%	47%
Month 12 after radiotherapy	100%	100%	78%
Month 24 after radiotherapy	100%	80%	40%
Final control	90%	73%	47%

Six months after treatment completion we found only one statistically significant correlation i.e. that between pain relief and the reflexion angle before the treatment ($p=0.04$, $R=0.89$).

An analysis of correlations during the last control showed statistical significance between pain relief and patient age ($p=0.04$, $R=0.39$), abduction angle and abduction, reflexion angles before the treatment ($p=0.013$, $R=0.6$, $p=0.01$, $R=0.73$ respectively), flexion angle and abduction angle before the treatment ($p=0.046$, $R=0.54$), reflexion angle and abduction, reflexion angles before the treatment ($p=0.026$, $R=0.59$, $p=0.04$, $R=0.63$, respectively).

No acute and late radiation toxicity or secondary malignancies were observed.

Discussion

Pain relief

Our results presented in this paper are similar to those obtained earlier. In a paper published in 2001 [16] we reported pain relief at a level of 27%, 72% and 85% at the end of radiotherapy, one and seven weeks later respectively. These results were observed in a group of PHS patients irradiated identically as in the present study.

It is rather difficult to compare our results with those published in literature. The reason for this situation arises from the different evaluation criteria used by different authors, however a majority of researchers report significant pain relief. Keilholz described significant pain reduction in 81% of patients, and complete pain relief in 49% of patients irradiated with two 3 Gy courses, 0.5 Gy per fraction up to 6 Gy of total dose [14]. He also reported major pain relief in 16% of cases and complete pain relief in 14% of patients irradiated with two 6 Gy courses, 1 Gy per fraction up to 12 Gy [15]. Seegenschmiedt reports similar results – 75% of cases with major relief and 46% of cases with complete relief after two series of 6x0.5 Gy (total dose 6 Gy) [21].

In view of the previously cited results [14], and results described in this article (73-100% of major effect, i.e. pain relief ≥50%, and 37-78% of complete pain relief, depending upon the time of follow-up) we could expect the negative impact of an increased total dose on the degree of pain relief. Other authors also report better values of pain relief – from 73 to 76% [12, 13]. On the other hand Valtonen et al. have presented a double blind trial based on 104 patients divided in two groups: radiotherapy versus sham irradiation, in which no gain from this treatment was found (improvement in 59% and 65% of cases respectively) [22]. This publication suggests the lack of a radiotherapy-dependant anti-inflammatory effect, but the relatively low percentage of irradiated patients with pain relief does call for attention.

Orthopedic improvement

Despite the excellent results as regarding pain relief, the decrease of orthopedic disability observed among our patients was smaller than that described in other articles. Kelholz reports the percentage of patients with marked mobility improvement (abduction at least 20° more than before treatment) as equal to the percentage of patients with marked pain relief, i.e. 81% [14]. Our results are not as good – according to controls – from 31% to 57%, and are similar to the results which we have published previously (17%-60%) [16]. The exact assessment of orthopedic changes after PHS irradiation based on the published literature and their comparison is difficult because of different endpoints used in the different studies. In some of them the arm mobility is evaluated as a percentage of improvement [14, 16], in others it is evaluated on special orthopedic scales, for example acc. to the Constant and Murley score [15, 21].

Radiotherapy modalities

A majority of contemporary irradiation schemes used in radiotherapy of benign inflammatory diseases is based on the Trott concept that the best effect could be achieved with a fraction dose of ≤1 Gy [20]. Only such a small fraction dose assures all the anti-inflammatory effects of irradiation, such as leukocyte adhesion decrease, blocking the oxidative burst in macrophages and blocking nitric oxide synthase expression in irradiated tissues [17-20]. Higher fraction doses (especially those exceeding 2 Gy), may even increase inflammation in the irradiated tissues (acute radiation toxicity). This is the reason why the most popular PHS radiotherapy schemes are 6x1 Gy or 12x0.5 Gy [14, 16]. The sequences of fraction doses delivery are different. The total dose could be delivered as five times a week [16] or a three times a week irradiation up to 6 Gy given in two series of 3 Gy with an 8-week gap [14]. Some papers report irradiation to higher dose (12 Gy). For example Keilholz irradiated patients three times a week using 1 Gy fraction doses up to 12 Gy delivered in two 6 Gy series [15]. Seegenschmiedt reported radiotherapy delivered three times a week in 0.5 Gy fractions up to a 12 Gy total dose given in two series [21]. Higher total doses, such these in two last aforementioned publications, exceeding 6 Gy, are not recommended by Trott, because of the plateau-like effect appearing in this kind of radiotherapy [20]. These variations may explain the differences in pain relief observed after different total doses described in the first part of the discussion.

Prognostic factors

Symptom duration, the independent prognostic factor reported in literature [13, 15, 21] was not confirmed on in our study. We did not observe the negative impact of disease duration on treatment results understood as pain relief or functional improvement.

The only one prognostic factor found in this study was the degree of orthopedic disability before the onset of treatment. Slight impairment at the beginning correlated with greater improvement after radiotherapy.

Adverse effects

We did not observe any local radiation injuries, neither acute nor late and neither are they reported in the literature. The only widely discussed issue, referred to in numerous publications, is the probability of carcinogenesis [12, 15, 16, 21, 23]. There were no secondary malignancies in the irradiated patient group, but the relatively short follow-up (mean 54 months) appears to be inadequate for such an assessment. The quite common statement regarding the high risk of carcinogenesis after radiotherapy for benign diseases is rather an archetype based on observations made in the course of the radiation treatment of Bechterew's disease – i.e. radiotherapy delivered in a huge volume to adolescent patients and comprising the bone marrow of the spine [21, 24]. Considering the small total dose delivered for PHS, the relatively small target volume, the patient age (mean: 59 yrs) and the fact that literature data fails to confirm the high risk of carcinogenesis we should not fear the development of malignancies secondary after this treatment [16, 21, 23].

Economical aspects

It is extremely difficult to discuss the economical aspects of different treatment modalities without the context of the insurance system. Radiotherapy cost calculation is probably different in different countries. Generally, radiotherapy is considered to be an expensive treatment modality. However, such a statement is true for radical conformal oncological therapy, while short, six fraction irradiation from two opposite fields is considerably less expensive. If we consider the lengthy treatment with non-steroid anti-inflammatory drugs or repeated invasive procedures such as intra- or periarticular injections, the overall cost of radiotherapy would appear rather encouraging.

Conclusion

Basing on our results and discussion we may conclude that radiotherapy of periarthritis humeroscapularis is an effective, safe and relatively inexpensive treatment modality, which could be considered as an alternative to standard orthopedic and pharmacological treatment in case of recurrent or persistent disease.

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