TOPICAL REVIEW

Results and perspectives of the treatment of skeletal neoplasms

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Abstract

Improvements in the therapy of skeletal neoplasms at the end of the 20th century are the reason for a retrospective view on the development of the therapy of skeletal neoplasms, especially in the Slovak Republic. Up to the sixties years of the 20th century was amputation the imperative in the surgical treatment of malignant tumors, above all tumors of the extremities. Then chemotherapy was introduced into the treatment of these tumors, in Slovak Republic it was later. Bone transplantations were widely used in the 70 and 80 years of 20th century. Autotransplantations of bone grafts were used at the Orthopaedic department in Bratislava already in the year 1953, but low number of appropriate grafts limited their use in clinical practice. In the 70 and 80 years development of bone banks was observed. Results of the treatment of malignant diseases with this technique are considered poor. Only few patients survived more than 5 years after the surgery, mainly due to inappropriate techniques of detection, localization and determination of the size of the tumor. Biopsy played above all at this time an important role in the diagnostics of bone tumors. Apart from basic examinations of the fixed material, processed after it was imbedded in particular medium, perioperative biopsy is recently being performed with the technique of frozen sections from unfixed tissue obtained during the surgery. This type of material processing prolongs the period from obtaining the material till making the diagnosis, but the advantages of this type of examination are undoubted. ***(Ref. 17.)***
Key words: tumors, bones, biopsy, man, therapy.

Final quarter of the 20th century has brought dramatic improvements in the treatment of malignant neoplasms of skeletal system. Present treatment results in longer survival of the patients, improvements of their functional and psychic state and economic situation. Malignant tumors of skeletal system are in comparison with other malignant tumors rare. Statistically their incidence is between 0.2 % up to 1 % (UZIS, 2000). They are considered insidious and the clinical result of the treatment is still uncertain. It is also due to the fact, that they are often arising de novo. The highest incidence is in the childhood and in young adulthood. They are often resistant to radiotherapy and rapidly metastasize, predominantly via lymphatics.

Marked improvements in the treatment of malignant tumors of skeletal system are attributed to 1. Improvement of radiographic techniques for localization of tumors and metastases, 2. Better understanding of the disease course, 3. Improvement of the techniques of skeletal-muscular reconstruction, 4. Extension of the role of radiotherapy and chemotherapy, 5. More aggressive treatment of metastases Marks et al (1996). Up to the sixties years of the 20th century was amputation the imperative in the surgical treatment of malignant tumors, especially tumors of extremities (De Vita et al, 2001; Horsky et al, 1984; Huraj et al, 1985). In these years the use of chemotherapy was introduced. In our country it was much more later due to socioeconomic possibilities of at that time separated world (Horsky et al, 1982). Chemotherapy was administered at orthopaedic departments after consulting with an oncologists and his recommendation. Presently it is obvious from reknown studies that chemotherapy is in comparison with surgical treatment much effective. Miser et al (1998) report survival of 2.5 years in 90 % of patients. With multidisciplinary approach to patients with osteosarcoma is recent survival 5 years

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in 65–70 %. With good response to chemotherapy up to 80 % according to Bacci et al (1993). This observation is in accordance with the results of chemotherapy treatment of other connective tissue tumors (Briele et al, 1992).

70ties and 80ties years of the 20th century are connected with the boom of bone transplantology (Huraj and Paukovic, 1985). Transplantation of grafts of man bones at the Orthopaedic department in Bratislava started in 1953, but low possibilities of harvesting the grafts limited its use in clinical practice. Seventies and eighties years of the 20th century brought the development of bone banks (Huraj a Paukovic, 1982; Judet et al, 1994). The results of the treatment of malignant tumors with this techniques are considered poor (Huraj a Paukovic, 1985). World statistics indicate 5 years survival in 10 % to 20 %. At the orthopaedic department of the University hospital in Bratislava survived from 12 patients undergoing such surgery one patient (Horsky et al, 1984). This low number of survivors is attributed first place to inappropriate techniques of detection, localization and size determination of the tumor with the aim to ensure oncologic radicalism. CT was introduced in the second half of 80ties years of the last century and NMR has not been existing yet. Particularly at that time has biopsy played an important role in the diagnostics of bone tumors.

Biopsy (from the Greek bios life and opsis view) is a term first used by the French dermatologists Besnier in the year 1879 (Galbavý, 1996) to describe the methodical process of diagnostic evaluation of cells, tissues and organs obtained by a medical procedure. The aim of this procedure is to establish the diagnosis and extent of the disease, to observe the dynamics of the disease course and to judge the prognosis. Biopsy enables rapidly and in time to detect the core of the disease surge. Notably for malignant tumors it represents the basis for successful treatment. It can not be replaced with other diagnostic method in the diagnostics of bone tumors. The pathologists is a member of diagnostic team, in which he often decides about further course of the treatment. Without morphologic verification of the malignant tumor it is not possible to perform a mutilating surgical procedure or administer chemotherapy. Undoubtedly, every physician establishing the diagnosis and treating malignant bone tumors must have a positive attitude to biopsy (Cervenansky et al, 1964).

In the biopsy of bone tumors apart from basic bioptic examination of fixed material, prepared after it was imbedded in an appropriate medium also perioperative biopsy, performed with the technique of frozen sections from unfixed tissue obtained during the surgery, is performed (Paukovic et al, 1998). The technical preparation of the bioptic sample is effected by its characteristics. Unlike other tissues important component of the material obtained with bone biopsy are the mineralized components. Processing of this material prolongs the period from taking off the material to establishing the diagnosis. The problem of perioperative bioptic examination from firm material with use of cryostat with high freezing point was solved in favor of perioperative biopsy. Section obtained with this technique has some limitations in comparison to parafinized section, which are due mainly to the thickness, but the quality is sufficient to obtain reliable diagnosis. The experience of Galbavy et al (1994) show, that continence is incorrect. The analysis of the materials of the Institute of pathological anatomy at the Medical school, Comenius University in Bratislava showed, that perioperative diagnostics of bone tumors has its value and can be successfully used when certain rules are kept (Paukovic et al, 1998).

Bioptic examination as other examinations too can be accompanied by mistaken decisions. Mostly they are due to false evaluation of the reactive changes accompanying bone tumors. These changes involve also changes of periost. To prevent false negative results of morphologic evaluation close cooperation of orthopaedist, radiologist and pathologist is necessary. It is recommended to determine the site of the taking off the material with angiography or to perform it under direct X-ray control because malignant tumors often undergo partial necrosis (Makaiova et al, 2001).

If the preliminary X-ray shows high mineralization of all parts of the tumor (e.g. sclerotizing osteosarcoma), to prevent possible devaluation of the picture by decalcification in the acid, it is adviced to perform quick perioperative examination. Comparison of undemineralized sample with demineralized one enables to correct the technical artefacts. Cryostatic sections enable very good evaluation of the cytologic details, because artefacts seen in parafine sections, are in cryostatic sections not occurring at all.

In 2001 were at the Institute of Pathological Anatomy at the Faculty of Medicine, Comenius University, Bratislava, and University Hospital, Bratislava, examined 51 perioperative bone bioptic samples. No false positive results were detected. Two false positive results were corrected after examination of parafine section. Despite of this, if it is possible, we prefer parafine sections of high quality, which provide higher diagnostic confidence. Errors of diagnosis can be reduced, if the diagnosis of bone tumor is seen as a synthesis of clinical findings, X-ray morphology and findings of microscopic examinations. It is irresponsible to consider the histology alone neglecting clinical findings and biologic substrate. This is valid mainly when the bioptic material was obtained at random. Lichtenstein made the following statement to the trepanobiopsy of bone tumors: It is similar to riding a bicycle with hands tied up at the back. This way of riding may also be without accident. But if a barrier emerges, we will fly over the handle-bars and break the neck. In this opinion we see the warning of an experienced morphologist against purely histological orientation of the diagnostic process, with clappers on our eyes. Its limitations and dangers have to be reduced by critical exchange of information with clinicians and by focusing on the benefit of the patient.

The opinions on the etiopathogenesis, diagnostics and treatment of bone tumors underwent dramatic development during the history of orthopaedics. Recently the multidisciplinary management of these patients leads definitely to improvement of the survival of patients with bone tumors. Early diagnosis, neo-adjuvant chemotherapy and above all surgical procedures with the

preserving the extremity and consecutive chemotherapy have essentially contributed to this improvement.

References

Bacci G, Picci P, Ferrari S. Primary chemotherapy and delayed surgery for nonmetastatic oswteosarcoma of the extremities: results in 164 patients preoperatively treated wit high doses of methotrexate followed by cisplatin and doxorubicin. Cancer 1993; 72 (11): 3227.

Birele HA, Walker MJ, Greager JA, Wood DK, Lindsey WF, Das Gupta TK. Combined modality treatment: Limb-sparing surgery plus radiation therapy and adjuvant chemotherapy. 465—471. In: Raaf JH (Ed). Soft Tissue Sarcomas. Diagnosis and Treatment. St. Louis, 1992. Mosby.

Červeňanský J, Škrovina B, Kossey P. Nádory kostí a im podobné afekcie. Bratislava, Veda 1964, 439 p.

De Vita V, Hellman S, Rosenberg SA. Cancer principles and practice of Oncology. 6th ed. Lippincott, Williams and Wilkins 2001, 1518 p.

Galbavý Š, Paukovic, J, Zaviačič M, Danihel Ľ, Porubský J, Babál P. Význam imunohistochémie v diagnostike ochorení osteoartikulárneho aparátu. 24—26. In: Tribulová N, Slezák J (Ed). Pokroky v základnej a aplikovanej histochémii. Bratislava, SAV 1994.

Galbavý Š. Biopsia. 184—189. In: Kadlec O, Hulín I (Ed): Encyklopédia medicíny. Bratislava, Asklepios 1996.

Horský I, Huraj Sen E, Huraj Jr E, Jindrová V, Paukovic J. Liečba ostegénneho sarkómu v detskom veku. Acta Chir Orthop Traum Čech 1984; 51 (5): 388—391.

Horský I, Huraj Sen E, Huraj Jr E, Jindrová V, Sklovský A, Paukovic J. Chemoterapia v komplexnej liečbe malígnych nádorov. Acta Chir Orthop Traum Čech 1982; 49 (1): 83—86.

Huraj Sen E, Horský I, Huraj Jr E, Jindrová V, Sklovský A, Paukovic J. Frekvencia nádorov osteoartikulárneho systému u detí na Ortopedickej klinike v Bratislave. Acta Chir Orthop Traum Čech 1982; 49 (2): 166—169.

Huraj Sen E, Paukovic J. Kostný štep v teréne osteosarkómu. Acta Chir Orthop Traum Čech 1985; 49 (4): 319—324.

Judet T, de Thomasson E, Paukovic J, Arnault O. Rekonštrukcia insuficientných acetábul pri prvotných totálnych endoprotézach masívnymi autoštepmi. Acta Chir Orthop Traum Čech 1994; 61 (1): 29—33.

Lichtenstein L. Bone Tumors. 4th ed. St. Louis, S.V. Mosby Co. 1972, 372 p.

Makaiová I, Makaj F, Kordoš J, Paukovic J, Kopáč C, Švancárová Ľ, Kováčová S, Bahleda R, Studený M, Vivodová M, Veselý J, Pročka V. Využitie gamagrafických metód v diagnostike a monitorovaní muskuloskeletálnych sarkómov. Slov Lek 2001; 11 (3—4): 156.

Marks KH, Belhobek GH, Bauer TW, Duthrie RN. Tumours of the musculoskeletal system. In: Mercker's Orthopaedic Surgery. Arnold et al 1996.

Miser J, Arndt C, Smithson W. Long term follow-up of high grade osteosarcoma treated with preoperative ifosfamide, adriamycin and high dose methotrexate with cisplatin added postoperatively for poor histologic responders. Proc Amer Soc Clin Oncol 1998; 17: 535 a.

Paukovic J, Kováč C, Galbavý Š. Význam cielenej biopsie nádorov pohybového ústrojenstva. Bratisl Lek Listy 1998; 99 (Suppl): 47—48.

Zdravotnícka ročenka Slovenskej republiky 2000. Bratislava, ÚZI 2000, 204 p.

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