Malignant peripheral nerve sheath tumours (MPNST) arise from Schwann cells or within existing neurofibromas and have a strong association with type 1 neurofibromatosis. MPNST with rhabdomyosarcomatous differentiation is also known as malignant Triton tumour (MTT) (Stasik and Tawfik 2006). MTT is aggressive tumour with bad prognosis. In 1932, Mason was the first one to describe rhabdomyoblasts in a peripheral-nerve tumour. The term "Triton tumour" was first described by Woodruff et al. in 1973. It is an extremely rare tumour, with less than 100 cases documented worldwide, and less than 10 in the mediastinum (Cano et al. 2006).

Patients with MTT are usually younger than age 35 (Yimaz et al. 2004). Köstler et al. (2003) reported a 26-year-old patient diagnosed with MTT who developed multiple recurrences despite repeated aggressive surgery, chemo- and radiotherapy during an 8-year period. Northern blotting analysis of an excised in-transit metastasis had revealed expression of retinoid receptors α and γ, and the patient received experimental treatment with retinoid isotretinoin and interferon-α for one year and remained without any evidence of disease for more than three years (Köstler et al. 2003).

Here, we report the case of a 12-year-old boy in Slovakia who was admitted to the University Children’s Hospital with a pain on the right side of his thorax. CT demonstrated tumour with the size of 58 × 53 mm originating from the structure of the side of thorax and osteodystrofe changes of 3rd and 4th costae with no metastasis. Tumour was subsequently excised surgically with partial resection 3rd and 4th costae. The pathological examination after surgery confirmed MTT with focal myeloblastic differentiation. The patient underwent chemotherapy according to the protocol SIOP MMT 95 (vincristine, ifosfamide, actinomycin D, etoposide, carboplatin, epirubicin), which was completed in 27 weeks. Three months after the completion of chemotherapy, CT has shown the first local relapse and tumour (50 × 60 mm) appearing was originating from 3rd costae and adhered to lungs, which was totally excised surgically. Histologically, it was confirmed relapse of MTT with high malignancy. The second line of chemotherapy comprised treatment with Topotecan and Endoxan. After that second cycle of chemotherapy, radiation therapy was added to the same region in TD 56 Gy and paraspinalis on the right side 20 Gy. Later on, CT and MRI of abdomen confirmed mass to all three parts of pancreas – largest was in head, which caused icterus of obstruction of biliaries ducts, which lead to laparotomy with biopsy and cholecystoduodenanoanastomosis. Histologically, the second metastatic relapse of MTT with higher portion of component rhabdomyosarcoma corresponding to embryonal rhabdomyosarcoma has been confirmed. The 3rd line of chemotherapy for the second relapse was performed according to the protocol CWS 91 (Cisplatin and Dacarbazine). Patient underwent two cycles of chemotherapy without any effect, moreover, progression of metastases in abdomen wall was observed.
At the stage of metastasectomy, the MTT tissues have been analyzed in order to get information about expression of all known subtypes of nuclear retinoid and nuclear retinoid X receptors mediating the effects of retinoic acids at the nuclear/cellular level. Determination of mRNA levels encoding all subtypes of nuclear retinoid receptors (RARα, RARβ, RARγ) and nuclear retinoid X receptors (RXRα, RXRβ, RXRγ) has been performed by the reverse transcription and subsequent PCR analyses according to Kimura et al. (2002). The band intensities were measured using the STS 6220I Documentation System (Ultralum, USA) and normalized to the band intensity of PCR product corresponding to the house keeper gene GAPDH. As shown in Fig. 1, both the MTT tissue excised from the patient neck or abdomen expressed all subtypes of RARs or RXRs. Since, retinoid receptors play a role as ligand-activated, DNA-binding, trans-acting, transcription-modulating proteins involved in a general molecular mechanism responsible for transcriptional responses in target genes, retinoids and/or rexinoids might thus represent a potentially powerful alternative to described chemotherapeutic treatments of advanced stages of MTT. Therefore, experimental palliative chemotherapy with 13-cis retinoic acid and interferon α has been indicated. After 6 weeks of that therapy, the next progression of MTT growth has been observed. The subsequent 4th chemotherapy cycle with Cisplatin and Dacarbazine have been shown ineffective and patient died after 34 month of the above treatment.

In conclusion, our goal was to introduce a novel diagnostic approach in clinical oncology based on analyses of expression of retinoid and rexinoid receptors in MTT in relation to potentiality of retinoic acid and its derivatives exploitation in tumour therapy. MTTs are in general infrequent, those found in the head and neck and the upper or lower extremities have a better prognosis than those in the retroperitoneum, buttock, or trunk. It is not clear whether this variation is due to a difference in tumour grade, stage, or resectability, or whether it is a consequence of tumour therapy (Isla et al. 2000).

Ethics approval: The research followed the tenets of the Declaration of Helsinki and informed consent was obtained from the patient and his mother prior to sample collection for research with residual tumour tissue.

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References


Brtko J. (2007): Retinoids, rexinoids and their cognate nuclear receptors: character and their role in chemoprevention of


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