

Potential role of PET-CT in chemotherapy efficacy assessment and recurrence diagnosis in a patient with a Wilms' tumour

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Abstract

BACKGROUND: Wilms' tumour is the most frequent renal malignancy in children. There is no worldwide consensus regarding treatment and PET-CT role in this neoplasm. The aim of this report is to demonstrate the potential role of PET-CT in chemotherapy efficacy assessment and recurrence diagnosis. **CASE description:** a 7-year-old boy was diagnosed with blastemic type Wilms' tumour and underwent neoadjuvant chemotherapy, nephrectomy, and adjuvant chemotherapy in compliance with SIOP protocol. Three years later the patient underwent surgical resection of the metastasis and chemoradiotherapy. Nine months later tomography and PET-CT were performed (during the third month of the treatment due to a second recurrence). The results were equivocal but within four months the boy underwent surgical resection of a third recurrence. Fourteen months later a second PET-CT revealed an active disease with

extensive involvement of the left lung and pleura. The patient was referred to oral palliative chemotherapy.

DISCUSSION: Equivocal PET-CT results during chemotherapy should be interpreted with caution. The first, during third line chemotherapy, was equivocal; however, an early massive recurrence three months later indicates that treatment was ineffective. The second PET-CT examination fourteen months later, as the only modality, depicted massive progression of the disease. This suggests the value of this examination in recurrence diagnosis. **CONCLUSIONS:** PET-CT seems to be valuable technique in recurrence detection in patients with histologically unfavourable tumours. Equivocal results of PET-CT should raise suspicion of recurrence even in recently treated patients. The timing of CIM and PET-CT should be considered individually — no universal and reliable schedule exists.

Key words: Wilms' tumour, PET-CT, chemotherapy

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Introduction

Wilms' tumours account for 5–7% of all neoplasms in paediatric patients [1–3]. In Poland these tumours accounts for 60–80 new cases per year [2, 3].

Prognosis depends mostly on stage at diagnosis and histological components of the lesion. Over the last three decades overall survival has increased from approximately 30% up to 91.7% [1, 5]. There is no worldwide consensus regarding treatment and follow up procedures, and two main approaches have emerged over the years. National Wilms' Tumour Study (NWTs) recommends surgical treatment in the vast majority of patients prior to chemotherapy. On the other hand, the International Society of Paediatric Oncology (SIOP) endorses neoadjuvant chemotherapy. Such discrepancies exist not only in the field of primary treatment but also in recurrence and resistant disease treatment. No sig-

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nificant difference in survival or recurrence rates between these protocols has been found.

The role of 2-[F-18] fluoro-2-deoxy-D-glucose Positron Emission Tomography (FDG-PET) in patients with Wilms' tumours has not been defined as well. Preliminary reports are encouraging.

The authors of this report indicate the potential role of FDG-PET in chemotherapy efficacy assessment and in diagnosis of recurrence in patients with Wilms' tumours.

Case report

A boy was diagnosed with blastemic type of Wilms' tumour in 2003, at the age of 7. The patient underwent neoadjuvant chemotherapy and radical right nephrectomy according to SIOP protocol. The surgery confirmed stage I of the disease. Subsequent chemotherapy vincristine + actinomycin D + doxorubicin (VCR+ACT-D+DOXO) was applied due to unfavourable histology.

A follow-up CT three years later (May 2007) revealed a mass in the left lung. The patient received two cycles of cyclophosphamide + carboplatin + etoposide (CCE) chemotherapy and underwent complete (confirmed by histopathology) surgical resection of blastemic metastasis. After the surgery the boy received one cycle of iphosphamide + carboplatin + etoposide (ICE) chemotherapy and radiotherapy of the left lung and metastatic tumour site. After radiotherapy two more cycles of ICE were administered. Computed tomography (CT) performed after the treatment depicted a mass adjacent to the left lateral chest wall and was interpreted as equivocal. Anti inflammatory treatment and subsequent CT examinations did not provide information about the nature of the lesion. Consequently, in December 2007 the patient underwent left thoracotomy with surgical resection of the visualized lesion and three pleural nodules found during the surgery. No neoplastic cells were found in the resected specimen. In May 2008 a follow-up CT revealed tumour deposits in the diaphragmatic-cardiac angle and along left side of the vertebral column. Aspiration biopsy showed no suspicious cellular elements, but staphylococcus presence was confirmed. A CT examination performed one month later (June 2008) revealed progression of the lesions and was interpreted as a recurrence, and VCR+ACT-D+DOXO chemotherapy was introduced. Tomography and PET-CT examinations were performed during chemotherapy in August 2008. CT confirmed regression of the lesion whereas PET-CT revealed a consolidation of lung parenchyma at the site of previous surgery with metabolic activity of Standard Uptake Value (SUV) of $SUV_{max} = 1.1$ and a similar lesion at the basis of the left lung. These abnormalities were interpreted as probably being reparative or inflammatory, but a control examination in 3–4 months was recommended due to the histological type of the tumour. Chemotherapy was completed in November 2008 with no signs of active disease in CT examinations; therefore, PET-CT examination was not carried out. Mega-chemotherapy and autologous bone marrow transplant were considered but the mother of the patient did not agree, so "wait and watch" as an acceptable strategy was undertaken.

Four months after completion of chemotherapy (in March 2009) a follow-up CT revealed progression of the previously seen lesion in the left lung. The patient underwent surgical excision of the lesion in April 2009, confirmed as blastemic type Wilms' tumour metastasis. Due to two unsuccessful attempts to collect stem cells for autolo-

gous bone marrow (between May and October 2009) the options of allogeneic bone marrow transplant or radiotherapy were considered. Before applying mega-chemotherapy the patient was referred to PET-CT examination to assess the activity and extent of potential disease because the CT images (performed 2 and 4 months after the last surgery) were equivocal. PET-CT revealed extensive involvement of the left lung and pleura. Within three months after the examination a dramatic clinical progression was observed and the patient was referred to palliative oral chemotherapy.

Study protocol

The boy reported to our facility after 8 hours of fasting and unlimited access to plain, clear water. Glycaemia at presentation was 96 mg/dl. 5 MBq/kg bw of ^{18}F -FDG was administered intravenously with subsequent placing of the child in an uptake room. The examination was carried out on GE Discovery STE 16 SLI device. The study began 60 minutes after ^{18}F -FDG administration and consisted of CT (120 mA) examination and PET acquisition 3.5 minutes per bed. The data were reconstructed with use of iterative algorithm.

Discussion

Appropriate follow-up of patients with Wilms' tumour remains a challenge. The protocols accepted by NWTS and SIOP work well for tumours with intermediate or low risk of recurrence. There is no internationally accepted protocol for follow-up using Conventional Imaging Modalities (CIM) in "high-risk" tumours. Reliable information regarding activity and extent of the disease in a patient suspected of recurrence is of particular value as this group is characterized by high risk of distant metastases and poor outcome.

The patient described in this report underwent two PET-CT examinations. The first one was carried out during the third line therapy and interpreted as equivocal. A control PET-CT was not done because the CT examination performed at the end of the chemotherapy did not show signs of recurrence. The follow-up CT three months later revealed progression of a previously seen lesion in the left lung. Surgical resection confirmed metastasis of blastemic type Wilms' tumour. This early recurrence raises three questions:

- should PET-CT be performed regardless of CT results in therapy efficiency assessment?
- how often should we perform a follow-up CT to achieve proper tumour control?
- is PET a reliable tool for follow-up of high-risk patients?

SIOP endorses neoadjuvant chemotherapy in operable Wilms' tumours. As a consequence, chemotherapy efficacy assessment, depiction of chemotherapy resistance, and detection of possible metastases in patients with residual tumours becomes crucial. There are observations suggesting that PET-CT has a limited role in assessment after neoadjuvant chemotherapy with particularly low negative predictive value [5]. On the other hand visualization of focally increased metabolic activity (despite significant SUV reduction compared to the primary value) carries a high probability of proliferating remnant tumour or metastasis, therefore indicating unsuccessful chemotherapy. Chemotherapy outcome is associated

with clinical outcome [6–8]. The patient described in this report did not undergo a PET-CT examination at the end of chemotherapy, but an early recurrence suggests that the treatment did not eradicate the tumour cells. This could potentially have been demonstrated on a control PET-CT. There are reports indicating the ability of PET-CT to detect recurrence without visible structural lesions [5].

Computed tomography is a standard method of imaging of high-risk patients. A three-month interval seems appropriate in low- and intermediate-risk tumours. Patients from high-risk groups probably need more frequent imaging. Previous recurrence of the boy had been confirmed by two CT examinations performed four weeks apart. The authors suggest that high-risk patients should undergo monthly CT imaging for 5–6 months after completion of therapy. Such a frequent examination schedule can increase the confidence of the treating physician, but creates a problem of radiation burden. Compliance with the “As Low As Reasonably Achievable” (ALARA) rule is particularly important in children. Some authors suggest that PET-CT could be a complementary technique. There are preliminary reports confirming successful imaging of Wilms' tumour [5, 9]. In one patient, PET-CT depicted abdominal recurrence eight weeks prior to visualization of the tumour on CT [5]. Although these reports consider mostly abdominal recurrences, PET-CT seems to have potential in defining the nature of lesions observed in the chest and lungs. Differentiation of benign (inflammatory, infectious, or atelectatic) lesions from recurrence is necessary to avoid frequent imaging studies and unnecessary treatment. The results of two postoperative CT examinations in the described patient were equivocal. Despite reports indicating limited ability of PET alone to detect lung lesions [10, 11], the images revealed areas of high metabolic activity involving the left lung and pleura along the vertebral column, mediastinum, and posterior aspect of costo-diaphragmatic angle, therefore indicating recurrence with extensive involvement of the left pleura and lung. The activity and vastness of the disease depicted by PET-CT were confirmed by clinical course: within three months after the examination a dramatic progression occurred and the patient was referred to palliative oral chemotherapy. Further imaging schedules should be planned individually according to protocols and previous results.

Conclusions

Most of cited reports suffer from small numbers of patients and heterogeneity of examined populations. Despite these shortcomings several preliminary conclusions have been drawn:

PET-CT seems to be a modality capable of clarifying equivocal tomographic images in patients previously treated surgically or by radiotherapy and hence giving a reliable basis for further clinical decisions;

PET-CT should be performed at the end of treatment and four weeks after completion of therapy when CT is negative or equivocal.

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