CORRESPONDENCE

Molecular Imaging in Oncology Using Positron Emission Tomography (PET)

by Prof. Dr. med. Thorsten Derlin, Prof. Dr. med. Viktor Grünwald, Prof. Dr. rer. nat. Jörg Steinbach, Dr. rer. nat. Hans-Jürgen Wester, and Prof. Dr. rer. nat. Tobias L. Ross in issue 11/2018

Some Necessary Additional Points

The authors provided an excellent review of the options for using positron emission tomography in combination with computed tomography (PET/CT) (1).

The authors wrote: "The HD15 study conducted by the German Hodgkin Study Group (GHSG) investigated whether radiotherapy could be restricted to patients with PET-positive residual findings following the completion of chemotherapy. Even without subsequent radiotherapy, patients with PET-negative residual lymphomas had a similar prognosis to patients that achieved complete remission on CT."

Some additional comments are needed in this context. The HD15 Study (2) investigated patients with advanced cancers, whose prognosis is notably worse and whose default treatment is six to eight courses of polychemotherapy (BEACOPP). The patients who still have PET-positive residual findings after completing this treatment have a significantly worse progression-free survival period compared with PET-negative patients (86.2% versus 92.6% after four years), which justifies the use of radiotherapy.

For all other stages, the standard therapy is consolidating radiotherapy after chemotherapy, which, in accordance with the results of the HD10 and HD11 studies of the GHSG, is administered to the most restricted irradiation field and at the lowest possible dose without endangering the success of the treatment. Studies that waived radiotherapy in favor of intensified chemotherapy—such as the UK RAPID trial (3, 4)—observed substantially more disease progression after such experimental methods, which prompted early termination of the respective study arms.

The most recent studies of the GSHG (HD16–17) evaluated again the importance of PET in the early stages for the purpose of treatment stratification, by not providing for subsequent radiotherapy in the respective experimental arm in PET negative findings after completed chemotherapy (2*ABVD or 2*BEACOPP escalated/2*ABVD). Forgoing radiotherapy is admissible only in clinical trials or at advanced stages (in analogy to the HD15 Study). DOI: 10.3238/arztebl.2018.0417a

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Conflict of interest statement
The authors declare that no conflict of interest exists.

In Reply:

We thank Oertel and Eich for their response to our article, which—in a somewhat loose connection to the subject—provides an overview of the role of radiotherapy in Hodgkin's lymphoma (HL), which we support with regard to central issues raised.

As they correctly cited, we explicitly mentioned the context of the GHSG's HD15 Study, which showed that in advanced stages after standard polychemotherapy (BEACOPPescalated), risk can be successfully stratified by using PET. In PET-negative patients, radiotherapy can be omitted, and the same applies for patients with PET-positive residual findings <2.5 cm (1). In this example, re-staging by using PET shows its potential for an individualized treatment adapted to the prognosis, among others with the aim of avoiding late toxicity, which is of particular relevance in mediastinal irradiation, which can, for example, include the development of secondary malignancies or early coronary heart disease (2).

As far as the UK RAPID Trial is concerned, progression-free three-year survival and overall survival after three cycles of ABVD and with negative findings on PET was 90.8% ad 99.0%, or 94.6% and 97.1% after radiotherapy. The authors concluded that patients with early stage HL and negative PET findings had a very good prognosis after three cycles of ABVD, with or without consolidating radiotherapy (3). The relative significance of a 4% difference in the recurrence rate after three years vis-à-vis the (late) toxicity of additional therapy is the subject of discussion in the context of this study.

The most recently conducted therapy optimization studies of the GHSG (HD16–17) also evaluated the importance of PET for the purpose of treatment

stratification in the early and intermediate stages, as well as the question of whether in this disease context, radiotherapy can be omitted for selected patients. We fully agree that until these studies have been analyzed, radiotherapy remains the clinical care standard in these stages.

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CLINICAL SNAPSHOT

12 Vertebral-Body Fractures and Simultaneous Skin Changes

A 57-year-old woman had developed a pruritic, brownish-red, maculopapular rash on her legs at age 40 (positive Darier's sign) that persisted thereafter, with variable intensity. A physician had suspected urticaria pigmentosa at the time, but no treatment was recommended. At age 51, she had sustained a femoral neck fracture and four vertebral body fractures, without any antecedent trauma and without any known risk factors. Osteoporosis was diagnosed and treated with strontium ranelate. At age 57, the patient had fractures of all vertebral bodies from T6 to L5 and a threefold elevation of the serum tryptase level. Laboratory findings, skin and bone marrow biopsy fulfilled the criteria for systemic mastocytosis (major: multifocal mast-cell infiltrates, minor: fusiform mast cells, expression of CD25 and CD2, KIT mutation, serum tryptase level). The patient was initially treated with zoledronate 4 mg every six months. At one year, no further compression fractures were seen.

Systemic mastocytosis can cause cytokine-mediated stimulation of osteoclasts, leading to osteoporosis. Osteoporosis of unclear origin (in a young patient without any known risk factors) should be thoroughly evaluated, and systemic mastocytosis should be considered in the differential diagnosis.

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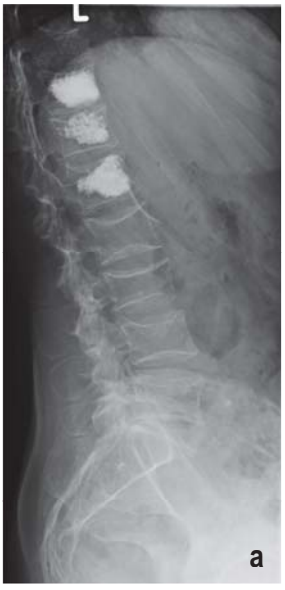

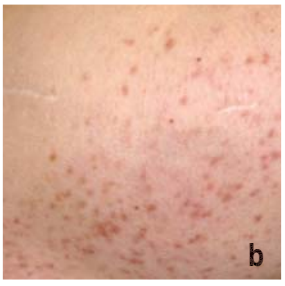

a) Lateral lumbar spine x-ray: there are osteoporotic fractures of all vertebral bodies from T10 to L5 (superior endplate impression fractures, concave fractures of both endplates, wedge fractures). Bone cement has been introduced into T11, T12, and L1 by vertebroplasty.
b) Red-brownish maculopapular efflorescences along the thighs. Skin changes were augmented by rubbing (positive Darier's sign). These findings fit to urticaria pigmentosa. The scars were related to a fracture of the femoral neck 6 years earlier.