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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

^{18}F-fluorodeoxyglucose positron emission tomography / computed tomography in primary Ewing sarcoma of the lung

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SUMMARY

Introduction Ewing sarcoma is rare in medical practice, and evaluating positron emission tomography / computed tomography (PET/CT) imaging of soft tissue Ewing sarcoma is a challenge. Primary Ewing sarcoma of the lung is an infrequent diagnosis.

Case outline A 22-year-old female patient was sent for PET/CT examination to the Center for Nuclear Medicine with Positron Emission Tomography, of the University Medical Center of Serbia, with a referral diagnosis of primary Ewing sarcoma of the right lung. In parallel to tumor visualization, the PET/CT imaging showed a radiological entity named "kissing sign," due to an enlarged beaver tail liver.

Conclusion According to the concept of functional mimicry and tissue specificity of molecular markers, a better understanding of the molecular mechanisms of soft tissue Ewing sarcoma is the challenge. These observations can be the platform for further investigation of new therapeutic regimens.

Keywords: Ewing sarcoma of the lung; ^{18}F-FDG PET/CT; kissing sign of the liver and spleen; the beaver tail liver; Tartrate-resistant acid phosphatase

INTRODUCTION

Ewing sarcoma belongs to the group of primitive neuroectodermal tumors originating from a neuroendocrine cell in bone or soft tissue [1]. As reported by Haas et al. [1], this kind of tumor often occurs in patients under 25 years of age, but has the congenital presentation of extraosseous Ewing sarcoma, although it is exceedingly rare. Multiple loci of soft tissue Ewing sarcomas develop at multiple localization: lungs [2–6], liver [7], and extremely rarely, primary Ewing sarcoma occurs in female genital organs, in the uterus [8].

According to the positron emission tomography / computed tomography (PET/CT) imaging, this study described an extremely rare visualization of tumor mass of Ewing sarcoma clinically confirmed as primarily localized in the right lung.

CASE REPORT

The present study refers to a 22-year-old female patient admitted for PET/CT examination at the Center for Nuclear Medicine with Positron Emission Tomography, University Medical Center of Serbia, diagnosed with Ewing sarcoma of the right lung three years ago. Upper right lobectomy and chemotherapy were performed. There are multiple focal partially confluent secondary tissue changes in the right hemithorax.

Before the diagnostic examination, the patient signed her informal consent for the ^{18}F-FDG PET/CT study.

After the patient's fasting six hours before the PET/CT study, and the median cubital vein cannulation, injection dose of 225 MBq ^{18}F-FDG was applied, followed by a 85-minute data acquisition. ^{18}F-FDG PET/CT examination on a 64-slice hybrid PET/CT scanner (Biograph; Siemens Medical Solutions USA, Inc., Malvern, PA, USA). A three-dimensional PET scan (three minutes per bed position acquisitions) and low-dose non-enhanced CT scan was acquired from the base of the skull to the mid-thigh. Multidetector CT was acquired with 120 kV and with automatic, real-time dose modulation amperage (CareDose4D [Siemens Healthare GmbH, Erlangen, Germany], with the baseline being 45 mA) (slice thickness of 5 mm, the pitch of 1.5, and a rotation time of 0.5 seconds). CT, PET (attenuation-corrected), and combined PET/CT images were displayed for analysis on a single Multimodality Workplace (Siemens Healthcare GmbH).

The PET/CT study shows the condition after upper right lobectomy, elevated anterior part right hemidiaphragm (Figures 1, 2B). In the middle and lower lobe of the right lung, multiple single and fused, nodular, and soft tissue changes of variable size are observed, partly continuously with the mediastinal, costal, and diaphragmatic pleura, which inhomogeneous intensively uptake ^{18}F-FDG (SUVmax 11) with zones of absent accumulation corresponding

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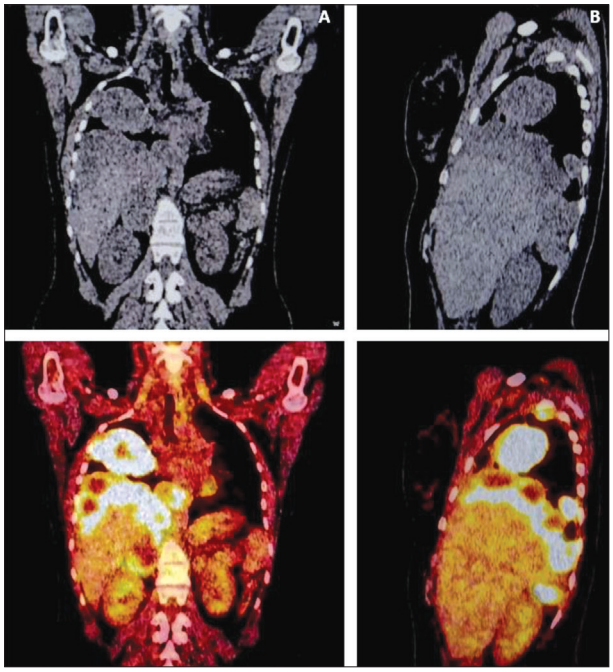


Figure 1. A – coronal; B – sagittal computed tomography, fused positron emission tomography/computed tomography images of elevated anterior part right hemidiaphragm after upper-right lobectomy

to [18]F-FDG zones of necrosis or hemorrhage (Figures 1, 2, and 3). There is an enhanced [18]F-FDG accumulation in activated brown adipose tissue in supraclavicular regions (Figure 2A).

Liver enlarged diameter of 13 × 22 × 22 cm (Figures 1B, and 3B) contacting the left lobe of the liver and spleen, a radiological finding known as the "kissing sign" of the liver and spleen has appeared (Figure 3), which is due to morphological variation of the beaver tail liver.

DISCUSSION

Dharmalingam et al. [3], state that "Primary Ewing sarcoma of the lung is anecdotally rare, with few cases reported in the literature" until 2020. The "Ewing family of tumors" includes other tissue types, such as soft tissue origin classified as extraosseous Ewing sarcoma or primitive neuroendocrine origin [2]. Because of the rarity of extraosseous Ewing sarcomas, the therapeutic approach is the same as for osseous ones [7].

The patient in this study showed no signs of reducing tumor mass despite chemotherapy. The present study indicates the radiological finding of the "kissing sign," which may exist because of the morphological variety of the left liver lobe. The enlarged liver in this patient showed the morphological type of beaver tail liver. Radiological finding known as the "kissing sign" of the liver and spleen in this specific case is a consequence of contact of the left lobe of the beaver tail liver and spleen.

Ewing sarcomas, both bone and soft-tissue varieties, are aggressive neoplasms. In one-quarter of patients, there are clinically evident metastases at presentation. The primary therapeutic approach for Ewing sarcoma is systemic

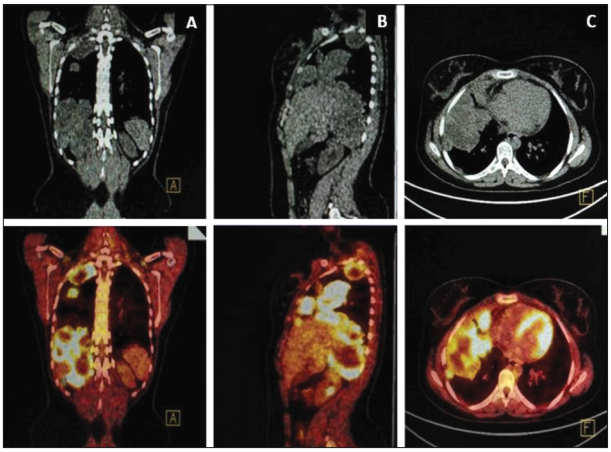


Figure 2. A – coronal; B – sagittal; C – axial computed tomography, fused positron emission tomography/computed tomography images (mediastinal window) of multiple single and fused nodular and soft tissue changes of variable size in the middle and lower lobe of the right lung, partly continuously with the mediastinal, costal and diaphragmatic pleura, which bind [18]F-fluorodeoxyglucose inhomogeneous intensely, with zones of absent [18]F-fluorodeoxyglucose accumulation corresponding to zones of necrosis or hemorrhage

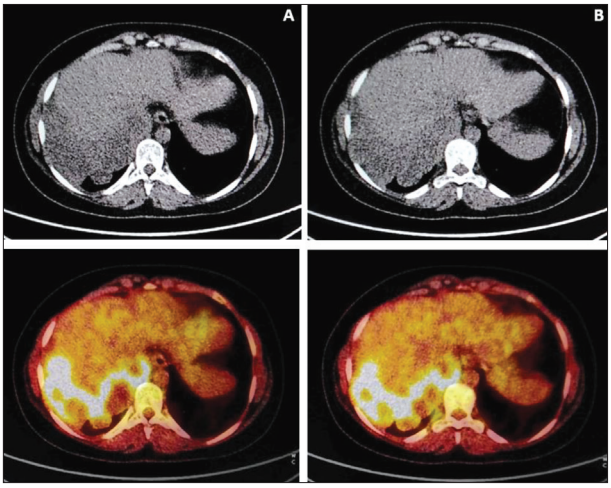


Figure 3. A, B – axial computed tomography, fused positron emission tomography/computed tomography images "kissing sign" liver and spleen

treatment [9]. Relapse is systemic mainly, followed by combined and local relapse. The five-year post-relapse survival rate is 15–25% [9].

Understanding the molecular biology of these tumors and novel treatment approaches are the challenges.

The facts of Ewing sarcomas as a systemic illness evoke the thesis on functional mimicry and tissue specificity of the acid phosphatase family of enzymes. Acid phosphatases are a family of enzymes with different structural, catalytic, and immunological properties, tissue distribution, and subcellular location [10]. There are five isoenzymes of acid phosphatase. The tartaric acid inhibits isoenzymes 1–4, but isoenzyme 5 is resistant to the inhibition [11]. The functional relationship between the lysosomal acid phosphatase (tartrate sensitive) and tartrate-resistant acid phosphatase is unknown.

Isoenzyme 5 is called the tartrate-resistant acid phosphatases (TRAP). Human TRAP is a member of a

widely-distributed and structurally highly-conserved group of iron-containing proteins [12]. The alveolar macrophages and osteoclasts exert TRAP enzyme activity [13]. TRAPs are expressed in bone-resorbing osteoclasts (5b form), alveolar macrophages (5a form), or can be markers of inflammation [14]. The functional importance of TRAP is the involvement in bone resorption and iron homeostasis (transport, metabolism) [15]. The TRAP exerts a homology to uteroferrin, a purple acid phosphatase family [16].

According to GeneCards®: The Human Gene Database (https://www.genecards.org), tartrate-resistant acid phosphatase has marked expression in bone, stomach, colon, liver, kidney, lung, pancreas, and prostate. The same organs/tissues, including bone and lung, are referred to in the scientific literature as loci for primary Ewing sarcoma of soft tissue [7, 17–21]. As TRAP has a promotive effect on cancer cell elongation, proliferation, migration, and invasion [22], we can propose that TRAP inhibitors may be possible therapeutic agents. According to Boorsma et al. [23], the Au(III) compound AubipyOMe is the most potent inhibitor of TRAP activity. The formula of Au(III) compound AubipyOMe can be a step forward for Fullerene-based delivery systems in the body as a new therapeutic approach for (extra)osseous Ewing sarcomas [24].

Although Ewing sarcoma of soft tissues, including lungs, is rare, the unfavorable outcome is a challenge in understanding the molecular mechanisms of the pathogenesis of soft tissue Ewing sarcoma. There is an urgent need to test high technology and nanomaterials as potential therapeutic tools in this type of cancer.

The present study showed a rare clinical condition related to primary Ewing sarcoma of the lung using ^{18}F-FDG PET-CT. This method is convenient in staging, restaging, and assessing therapy response in patients with Ewing sarcoma. As a diagnostic (pretreatment) tool, ^{18}F-FDG PET-CT of patients with Ewing sarcoma improves the detection of metastases compared to conventional imaging [25]. According to Hack et al. [26], PET/CT metrics in soft tissue and bone-originated sarcomas could not be the same. The maximum standardized uptake value is a better prognostic factor for soft tissue Ewing sarcomas, but tumor volume, rather than FDG PET activity, is more informative in evaluating bone Ewing sarcoma [26].

Conflict of interest: None to declare.

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[18]Ф-флуородеоксиглукозна позитронска емисиона томографија / компјутеризована томографија у примарном Јуинговом саркому плућа

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САЖЕТАК

Увод Јуингов сарком није чест у клиничкој пракси. Углавном захвата скелетне структуре, док је изузетно ретка појава Јуинговог саркома са примарном локализацијом у меким ткивима. Појава примарног Јуинговог саркома плућа је реткост и представља дијагностички и терапијски изазов.

Приказ болесника Болесница (22 године старости) са дијагнозом примарног Јуинговог саркома десног плућног крила упућена је на испитивање позитронском емисионом томографијом / компјутеризованом томографијом у Центар за нуклеарну медицину са позитронском емисионом томографијом Универзитетског клиничког центра Србије. Извршена је лобектомија горњег десног плућног лобуса две године раније и примењена је хемиотерапија. [18]Ф-флуородеоксиглукозна позитронска емисиона томографија је приказала мултипле фокалне, делимично конфлуентне секундарне ткивне депозите у десном хемитораксу. Уочен је радиолошки феномен „знака пољупца" слезине и увећане јетре са анатомском варијацијом левог лобуса јетре која се описује као феномен дабровог репа.

Закључак Пратећи до сада објављене публикације које се односе на ванскелетну примарну локализацију Јуинговог саркома плућа, приметно је да се овај тумор јавља углавном у ванкоштаним ткивима у којима је изражена експресија киселе фосфатазе резистентне на тартарат. Сходно концепту функционалне мимикрије и ткивне специфичности, ова сазнања чине платформу за истраживање нових дијагностичких и терапијских приступа код Јуинговог саркома нескелетног порекла.

Кључне речи: Јуингов сарком плућа; [18]Ф-флуородеоксиглукозна позитронска емисиона томографија / компјутеризована томографија; знак пољупца слезине и јетре; знак дабровог репа; кисела фосфатаза резистентна на тартарат