Transthoracic ultrasonography for the follow-up of a chronic lymphocytic leukemia patient with chemotherapy-induced immunosuppression prior to allogeneic stem cell transplantation. A case report

Ioana Frinc^{1,2}, Delia Dima^{1,3}, Mariana Chitic¹, Cristian Berce¹, Ioana Berindan-Neagoe^{4,5}, Tiberiu Tat⁶, Alina Tanase^{3,7}, Ciprian Tomuleasa^{1,2,3,4}, Anca Bojan^{1,2}

¹Department of Hematology, Ion Chiricuta Oncology Institute, Cluj-Napoca, ²Department of Hematology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, ³Working Party of the Romanian Society for Bone Marrow Transplantation, ⁴Research Center for Functional Genomics, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, ⁵Department of Genetics, Ion Chiricuta Oncology Institute, Cluj-Napoca, ⁶Department of Anesthesiology-Intensive Care, Ion Chiricuta Oncology Institute, Cluj-Napoca, ⁷Department of Stem Cell Transplantation, Fundeni Clinical Institute, Bucharest, Romania

Abstract

In the last years, significant progress has been made in the clinical follow-up of leukemia patients who are especially prone to various infections because of the specific immunosuppressive state following chemotherapy. The follow-up of such patients is of special interest and is based on modern imaging protocols especially computer tomography (CT). Still, CT may not always be effective in the diagnosing of respiratory infections. We report a chronic lymphocytic leukemia patient in which the pleuro-pulmonary complications were successfully diagnosed and followed up using transthoracic ultrasonography.

Keywords: transthoracic ultrasonography; immunocompromised patient; follow-up

Introduction

The diagnostics of pleuropulmonary complications in immunocompromised patients is based on the clinical examination, chest X-rays, computer tomography (CT), and specific laboratory tests. All these methods have a low specificity, with a high rate of false positive tests [1]. Transthoracic ultrasonography (TTUS) is a new, valuable, sensitive and efficient diagnostic method for pleuropulmonary complications and a good alternative for CT

examination. Due to no risk of irradiation and accessibility, the ultrasound examination can be performed on a daily basis. Recent recommendations from both the European and American Societies of Hematology suggest the reduction of excessive, repeated, sometimes useless irradiation for hematological patients [2,3].

Case report

A 58-year old man was diagnosed with chronic lymphocytic leukemia (CLL) stage IV Rai, and complete clinical remission was obtained under chemotherapy. After 1.5 years the disease relapsed and a new cycle of immunochemotherapy was administered. In context of a bilateral bronchiectasias and severe hypogammaglobulinemia secondary to rituximab two days after the end of the second cycle of the treatment, the patient presented with persistent fever, altered general status, and marked asthenia. Clinical examination revealed a low grade fever, facial itchy

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Corresponding author: Ciprian Tomuleasa, M.D.

Department of Hematology, "Ion Chiricuta"
Oncology Institute

73, 21 Decembrie 1918 Boulevard,

400124, Cluj-Napoca, Romania

Phone +40741337480

E-mail: ciprian.tomuleasa@umfcluj.ro

Fig 1. a) Thoracic computer tomography revealing a nodule of 0.2 cm² surface area, under the right pleura; b) Trans-thoracic ultrasonography, longitudinal scan of the 3rd intercostal space showing two small areas of condensation located in the left parasternal subpleural area; bilateral basal pulmonary interstitial edema with “frosted” appearance; c) Trans-thoracic ultrasonography, transversal scan, that shows one lesion located in the right axillary region based on the anterior axillary line, but with reduced ultrasound detection; bilateral basal pulmonary interstitial edema with “frosted” appearance

squamous skin lesions, left palpebral ptosis, low body mass index, and diminished bilateral vesicular murmur. Laboratory data showed lymphocytosis (Ly=6800/mm³) and an important inflammatory syndrome. Empiric antibiotic treatment was initiated (third generation cephalosporines, quinolones and antifungal medication). After 3 days of treatment the patient's condition was stationary. Serial blood cultures, urine culture and galactomannan test were negative and procalcitonin was in the normal range. The therapeutic support was increased with the administration of imipenem and teicoplanin, with antifungal treatment (Voriconazole). Highly increased C-reactive protein (CRP) persisted despite the aggressive treatment, with a maximum value of 25.82mg/dl. Due to severe hypogammaglobulinemia and resistant febrile status intravenous immunoglobulins were administered.

The CT examination (AURA 2002) revealed numerous nodular images in the right latero-posterior cervical area, the left latero-tracheal space, the right pulmonary hillus, as well as lumbo-aortic and aorto-intercaval areas, up to 12-15 mm (fig 1a). There was also a hepatosplenomegaly up to 19 cm. TTUS (Toshiba Aplio 500, 6-12 MHz linear transducer) found 2 additional small lesions in the left parasternal area, located under pleura, up to 1 cm in diameter. Bilateral basal pulmonary interstitial edema was detected with frosted glass appearance (fig 1b, 1c). When comparing TTUS with CT, the physician could identify pleural effusion and additional parenchymal condensation using US, whereas these changes could not be identified using a CT.

The patient's clinical status improved with the new treatment. Follow-up was carried out using both thoracic CT and TTUS. For the follow up, there was no difference between the two follow-up protocols. Afterwards, the patient was transferred for allogeneic stem cell transplanta-

tion. The patient recovered after the transplant and now is in complete remission.

Discussions

Early onset pulmonary infections can be missed or underdiagnosed by classic CT examination given that CT scan cannot detect lesions smaller than 1 cm and less than 100 ml of pleural effusion. Recent studies suggest that TTUS has a higher specificity in comparison with CT for the diagnosis of pleuro-pulmonary pathology [4,5]. There have been very few cases published so far in which TTUS was compared to CT and the total number of patients enrolled in the studies is not high enough to prove this without any doubt [6-8]. Still, preliminary data suggest that TTUS brings a new perspective into the follow-up management of such patients, as also it did in our case [9,10].

Respiratory distress in the immunocompromised patients is a leading indication for performing critical care US, that includes thoracic, abdominal, and vascular US. This procedure is usually performed and interpreted by the attending physician (in our case the hematologist) and by the attending intensivist, in order to establish in due time a proper diagnosis and further guide the therapeutic management. TTUS allows the identification of both findings, may it be pleural effusion and/or parenchymal condensation, and artifacts such as lung sliding, lung point, A-line or B-line [11,12]. One of the limitations of TTUS remains the absence of a standardized quantification of B-lines.

According to the guidelines for invasive fungal infections for hematologic malignancies and hematopoietic stem cell transplantation [13], a patient diagnosed with a hematologic malignancy and who is eligible to undergo hematopoietic cell transplant, as in our case, is at an increased risk for invasive fungal infection as a result of im-

munosuppression or organ damage stemming from their underlying disease, its treatment, or both. The gold standard for clinical follow-up is CT. Typical findings of fungal infections are lung nodules larger than 1 cm lung masses and the signs associated with these nodules and masses: the ground glass opacities that surround the nodule (halo sign), the focal area of ground glass opacities that is surrounded by a ring of consolidation (reversed halo sign), the central hypodensity of a nodule, and the collection of air in a crescent shape that might separate the wall of the cavity from the inner mass [14-16]. All of these elements of diagnosis (major criteria for the diagnosis of a probable invasive fungal pneumonia) were not identified in our patient.

A joint consensus defines the follow-up protocols for the immunocompromised patient. Thus, the follow-up protocols are defined as “proven”, “probable”, and “possible” [17]. In our case, TTUS has yet to be proven to be at least an interesting alternative diagnostic option, along with the CT, in a significant cohort of immunocompromised patients for the early diagnosis of disseminated infections, but may represent a probable or at least a possible method of follow-up for such cases, that should be investigated more thoroughly in the near future. For the hematological immunocompromised patients, at a high increased risk of disseminated infections and with possible rapid fatal outcome, an accurate and rapid diagnosis is mandatory. TTUS may provide the method to achieve the accurate and fact diagnosis, whereas CT may be reserved for patients that have undergone an allogeneic stem cell transplantation and for whom prone and expiratory imaging are needed, such as in patients suspected of having air-trapping (bronchiolitis obliterans or graft-versus-host disease) or early fibrosis. In our case TTUS examination proved to be superior in terms of specificity compared with CT.

Up till now, the TTUS is used on a routine basis only in a few European centers, specialized in thoracic ultrasound.

In conclusion, TTUS is an important imaging technique that can be used on a regular basis in the follow up of immunocompromised patients with pleuro-pulmonary complications. In our case TTUS examination proved to be superior in terms of specificity compared with CT.

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