

Katarzyna Kryszczyzyn-Musialik^{1, 2}, Grzegorz Słomian¹, Krzysztof Musialik³

¹Oncology Department, Provincial Specialist Hospital No. 3 in Rybnik, Poland

²Chair and Department of Medicine and Environmental Epidemiology, Medical University of Silesia in Katowice, Poland

³Trauma and Orthopaedic Department, Provincial Specialist Hospital No. 2 in Jastrzebie-Zdroj, Poland

Hodgkin's lymphoma with multifocal *Staphylococcus aureus* infection in a 29-year-old male — a case study

Address for correspondence:

Lek. Katarzyna Kryszczyzyn-Musialik
 Oddział Onkologii, Wojewódzki
 Szpital Specjalistyczny nr 3 w Rybniku
 ul. Energetyków 46, 44–200 Rybnik
 Phone: 32 429 17 60
 e-mail: kryszczyzyn@gmail.com

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ABSTRACT

Hodgkin's lymphoma (HL) is a neoplastic disease of the lymphoid tissue. It is characterised by the presence of B lymphocyte-derived monoclonal Reed-Sternberg and Hodgkin cells, which tend to create a massive inflammation reaction in lymph nodes. Lymphadenopathy is common. The prognosis depends on the clinical stage according to Ann Arbor (Cotswold's modification) classification and unfavourable prognostic factors. The ABVD chemotherapy regimen is the gold standard of treatment for patients with HL. This case report presents a patient diagnosed and treated for neck presentation of Hodgkin's lymphoma intricate sepsis and coxarthrosis because of *Staphylococcus aureus* infection. The treatment was arthrotomy. After the patient's recovery chemotherapy was continued and complete remission was achieved.

Key words: Hodgkin disease, hip joint, *Staphylococcus aureus*

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Introduction

Hodgkin's lymphoma (HL) is a malignancy of lymphoid tissue. It is characterised by the presence of B lymphocyte-derived monoclonal Reed-Sternberg cells and Hodgkin's cells, which induce a massive reaction of normal lymphocytes in the lymph nodes. Therefore, lymphadenopathy is a common clinical manifestation. In the microscopic image of affected lymph node, reactive cells predominate and cancerous cells constitute a minority — around 2% [1, 2]. The incidence of Hodgkin's lymphoma is constant, whilst the course of morbidity curve is bimodal, with two peaks at the age of 25–30 and 50–55 years [3]. In 2010, over 700 new cases were reported in Poland [3].

The prognosis in patients with HL depends on clinical stage (CS) of disease assessed according to the Ann Arbor classification and the presence of unfavourable prognostic factors [4, 5]. The ABVD chemotherapy regimen is the gold standard of the treatment for patients with HL [6]. In special cases, due to vital indications, such as: extremely

rapid disease dynamics, superior vena cava syndrome (SVCS), compression of the spinal cord, compression of the airways with dyspnoea, or ureteral closure, it may be necessary to initiate the treatment before the diagnosis is completed [5]. All issues that cause delayed diagnosis, as well as implementation and continuation of optimal therapy, reduce the patient's chances to be cured. This paper describes a case of a patient of the Oncology Department with the Haematology Subdivision of Provincial Specialist Hospital No. 3 in Rybnik — a 29-year-old man diagnosed and treated for tumours and neck phlegmon with subsequent diagnosis of HL, complicated by acute respiratory failure, purulent infections of soft tissues, and blood-borne hip arthritis with septic shock in the course of *Staphylococcus aureus* infection.

Case report

According to an interview in January 2013, a 29-year-old man noticed clinical symptoms in the

form of a neck tumour located in the middle part and then covering the left side of the neck. In March 2013, the patient visited a family doctor who ordered an antibiotic — amoxicillin with clavulanic acid administered orally. Therapy did not bring the expected improvement. The patient observed intensification of the inflammatory process with the progression of infiltration to the chest and the formation of purulent fistula. The patient was admitted to the ENT department. A neck phlegmon penetrating into the mediastinum was diagnosed and antibiotic therapy with ceftriaxone and metronidazole was introduced. In a computed tomography (CT) examination of the neck and chest, a neck abscess penetrating into the mediastinum and cervical lymphadenopathy with compression and modelling of the trachea were described. The lesions raised the suspicion of a proliferative disease of the lymphatic system with secondary purulent lesions. The patient was referred for further treatment to the chest surgery clinic, where the neck and mediastinum were drained, and antibiotic therapy was continued according to the culture (imipenem). Then a mediastinoscopy was performed with a biopsy. The histopathological report described: “*Neoplasma malignum probabiler lymphogenes*. Due to the small amount of material available for immunohistochemistry (predominant necrotic masses), its execution was abandoned, with a recommendation to carry it out in the oncological centre”. The patient was advised to continue treatment in the oncology centre, and a consultation date was agreed.

On May 24, 2013 (before the date of consultation in the oncology centre), the patient was admitted to the Hospital Emergency Department of Provincial Specialistic Hospital No. 3 in Rybnik in a severe condition with symptoms of acute respiratory failure and SVCS. The patient was intubated, and a CT scan was performed (Fig. 1, 2) in which the airway pressure was visualised. The patient was admitted to the Intensive Care Unit (ICU), where sedation and mechanical ventilation were used. Due to the pressure of tumour masses on the respiratory tract, leading to respiratory failure, a decision was made to introduce antineoplastic treatment. In the initial histopathological examination, cancer originating from the lymphatic system was diagnosed. At the time of making the decision to start treatment with vital indications, there was no more precise diagnosis. High dynamics of the disease suggested aggressive lymphoma, as in diffuse large B-cell lymphoma (DLBCL). Based on these clinical data, the patient was qualified for CHOP chemotherapy.

In ICU the patient received one cycle of CHOP rescue chemotherapy (cyclophosphamide, doxorubicin, vincristine, prednisone). Reduction in the swelling of neck tissues was achieved. The patient was disconnected

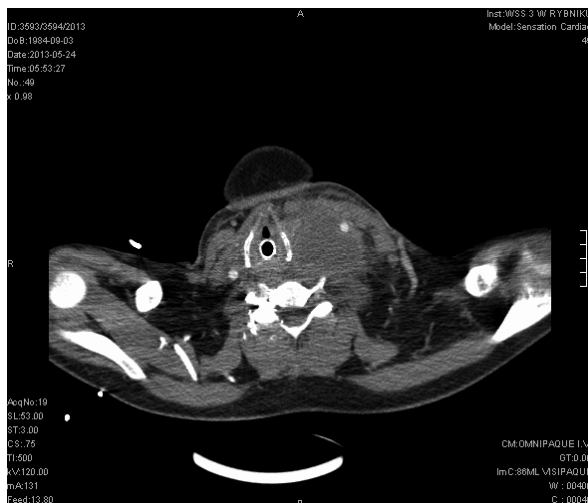


Figure 1. Computed tomography of the neck and chest before treatment. Extensive hypodense structures in the neck and mediastinum over a length of about 20 cm. The maximum cross-section of changes in the neck and mediastinum — 10 × 7.5 cm



Figure 2. Computed tomography of the neck and chest before treatment. Larynx, thyroid, and oesophagus structures are compressed and displaced towards the right side; trachea modelled, compressed, with endotracheal tube in the lumen

from the ventilator and extubated. In order to protect the airway obstruction, a tracheostomy was performed.

After improving the general condition, the patient was transferred to the Oncology Department. At admission, the patient was in good performance status according to the ECOG (Eastern Cooperative Oncology Group) scale, scoring 2. During the stay, the second CHOP cycle was administered. In order to establish the diagnosis, histopathological verification and immunohistochemical examination were ordered. After the second cycle, the patient was discharged home.

Between the cycles, the patient was hospitalised in the Department of Internal Diseases due to inflammatory infiltration of both forearms with the formation of left forearm abscess in the course of staphylococcus infection, where antibiotic therapy according to the antibiogram was continued until the symptoms resolved (ciprofloxacin was administered parenterally).

During the next, third cycle of chemotherapy a verified histopathological diagnosis was given: “Classical Hodgkin's lymphoma [CD30(+), CD15(+), MUM1(+), CD20(-), CD3(-)]. Extensive necrotic changes present in the material make it impossible to determine the subtype”. In order to determine the current clinical stage of the disease, imaging examinations were performed (Fig. 3–5), in which the reduction of infiltrative lesions was confirmed. Establishing the initial stage was very difficult because the patient started treatment in an ICU, without full diagnosis, and with no bone marrow trepanobiopsy or positron emission tomography (PET). On the basis of imaging (CT) and laboratory tests performed at the ICU, the disease clinical stage was assessed as IIB with the presence of unfavourable prognostic factors. In medical history the patient reported a decrease in body weight and recurrent fevers, so it was considered that general symptoms were also present. The patient was qualified for 6–8 cycles of ABVD chemotherapy followed by involved-field radiotherapy (IF-RT) at a dose of 20–36 Gy for residual or primary tumour [6]. ABVD chemotherapy was started. Due to the presence of additional risk factors for febrile neutropaenia (FN), such as advanced disease and poor general condition, the patient was qualified for FN primary prevention using short-acting granulocyte colony-stimulating factors (G-CSF). The patient continued chemotherapy in a good general condition, without significant complications.

On August 23, 2013, the patient was admitted for the fourth cycle of ABVD chemotherapy in severe general condition; ECOG performance status was defined as 3/4. The patient was lying due to the pain of the sacral and lumbar spine regions and lower limbs. In the physical examination the following were seen: forced abduction of lower limb, severe groin and right thigh pain, and right limb paresis with normal blood supply and innervation. The patient was suffering a lot despite intensive treatment — his pain intensity on the Numerical Rating Scale (NRS) was determined as 10. Laboratory tests revealed increased inflammation parameters (C-reactive protein [CRP] — 216.56 mg/L, erythrocyte sedimentation rate [ESR] — 110 mm/h).

A CT scan was performed in which the features of the right hip joint damage were shown (Fig. 6, 7). Based on clinical status and imaging examinations, haematogenous (blood-borne) hip arthritis was diagnosed. Broad-spectrum intravenous antibiotics were introduced: vancomycin at a dose of 1 g every 12 hours and cloxacillin 500 mg every 6 hours.



Figure 3. Computed tomography of the neck and chest before treatment. From the back the structure of infiltration reaches the paraspinal region with the width from approx. 7 cm



Figure 4. Computed tomography of the neck and chest after 2 cycles of chemotherapy. Currently, the pathological structure in the mediastinum and neck is much smaller than in the previous study



Figure 5. Computed tomography of the neck and chest after 2 cycles of chemotherapy. The largest dimensions of the lesion are 63 × 40 mm



Figure 6. Computed tomography of the chest, abdomen, and pelvis; right hip joint. Interruption of the cortical layer of the femoral head

According to the Gaechter and Stutz classification of joint inflammations, stage IV arthritis was diagnosed with infiltration and undermining of cartilage as well as radiological signs of subchondral osteolysis and erosions [7, 8] (Fig. 6, 7). According to the algorithm for the management of infectious arthritis in the case of cartilage destruction, the joint should be resected and a limp joint should be formed [7–9]. The patient was transferred to the Orthopaedic Department, where the capsule, head, and femoral neck were removed (Girdlestone procedure). *Staphylococcus aureus* was isolated by a pus culture. In the postoperative period, the patient was respiratorily insufficient with symptoms of septic shock. The patient was transferred again to the ICU, where artificial ventilation, continuous haemofiltration, intensive antibiotic therapy, and circulatory support were used. After normalisation of inflammatory parameters and creatinine concentration and improvement of his general condition the patient was transferred to the Department of Oncology, where the ABVD chemotherapy was continued. In the CT scan after the fourth ABVD cycle, a reduction in lesions meeting stable disease (SD) criteria according to RECIST (Response Evaluation Criteria in Solid Tumours) 1.1 was described. A continuation of the treatment was ordered; however, due to the suspicion of knee arthritis during the next stay, the therapy was completed at this stage. The knee joint puncture did not confirm the bacterial aetiology. The patient underwent partial oral sanitation with the extraction of affected teeth. In a PET CT examination performed after eight administration of ABVD chemotherapy (four full cycles) and two CHOP administrations, no active disease features were described.



Figure 7. Computed tomography of the chest, abdomen, and pelvis; right hip joint. Around the head of the right femur, pathological structures with densities up to 30 UH (liquid-fluid) visible between the tense capsule and the outlines of the cortical bone layer

The patient was referred to the Department of Radiotherapy. An important element of further therapy was rehabilitation, to improve the functionality of patients with so-called hanging hip and provide him with the highest level of independence. Subsequently, the patient did not report for scheduled follow-up visits. Based on the hospital records, the patient was determined to die in 2017 due to alcoholic liver failure and bleeding from oesophageal varices.

Discussion

According to the current guidelines, patients with advanced HL with clinical stage IIB and the presence of poor prognosis factors should receive 6–8 cycles of ABVD chemotherapy followed by IF-RT at 20–36 Gy for residual or primary tumour [6]. However, due to the delay of proper diagnosis and purulent lesions causing numerous and dangerous complications during the treatment the management in the presented case was significantly impeded. Delaying the proper diagnosis may not only reduce the chances of the patient being cured, but also pose an immediate threat to life, as in the case described, due to acute respiratory failure.

The time period from the collection of material for histopathological verification and immunohistochemical studies was two months. The purulent lesions with a staphylococcal aetiology occurring in the patient complicated and confused the picture of the underlying disease. After surgical treatment and targeted antibiotic therapy, they retreated and appeared in a different location. There are available in medical literature the case

reports of HL symptoms, especially the nodular sclerosis form with abscesses of various locations: abscess in the chest wall, liver, lung, spleen, axillary region, or pancreas [10–15]. The cultures of such abscesses were mostly aseptic, which indicated their non-infectious aetiology and should suggest the widening of the diagnosis. Such an unusual manifestation of the disease made diagnosis difficult, also due to the problem of obtaining material for histopathological examination; this contributed to therapeutic failures [15].

In the presented case, purulent lesions were associated with staphylococcal infection. The co-occurrence of HL and *Staphylococcus aureus* infections are rare. Immunity disorders typical for HL are associated with decreased capacity of lymphoid dendritic cells (plasmacytoid dendritic cells — s-pDCs) to produce interferon- α (IFN- α) and a reduced number of circulating CD4 + T cells [16]. These disorders mainly cause weakness of cellular immunity and contribute to systemic, opportunistic viral, fungal, protozoan, or tuberculous infections [16–22]. The spectrum of infections occurring in patients with HL is similar to other immune disorders such as acquired immunodeficiency syndrome (AIDS), glucocorticoid therapy, severe combined immunodeficiency syndrome (SCID), or Di George syndrome [16]. In the case of bacterial infections in HL, causing serious infections confirmed in a microbiological study, *Streptococcus pneumoniae* is a common aetiological factor [19]. Coexistence of *Staphylococcus aureus* infection and HL is extremely rare [23]. The only description of wrist bone osteomyelitis of staphylococcal aetiology in a patient with HL is available in the literature [23]. Bone infections with other aetiologies are also described. In presented cases of bone and marrow infections (osteomyelitis), the infection was caused by bloodstream, usually due to a wound or soft tissue damage [22–24].

According to a study by Raluca-Ana Rus, published in the “Journal of Research in Medical Sciences” in 2018, concerning infections associated with chemotherapy in patients treated for haematological malignancies, in 34.4% of HL patients infectious complications were observed, among them 21.9% were bacterial infections, 9.4% — fungal, 3.1% — viral, while in the remaining 6.3% no aetiology was established [25]. The most common bacterial infection in patients with HL observed during chemotherapy was *Clostridium difficile* infection [25].

Purulent, blood-borne hip infection in adults is very rare [8, 10, 11, 26–28]. The correct diagnosis is extremely important because of the serious consequences of the disease [26–30]. According to the literature, the risk of *Staphylococcus aureus* infection increases in cases of tissues disruption, the presence of a foreign body in tissues, or comorbidities, such as: cancer, metabolic diseases, and immunosuppressive or anticancer therapy [24, 26, 27]. The main risk factors of staphylococcal bone

infections are coexistent tissue blood supply disorders (e.g. in course of diabetes or vascular disease), high clinical stage of the cancer (e.g. HL with the presence of bone lesions — stage IV), and bone growth period when the bone is more susceptible to infection — hence osteoarthritis is more common in children. Anticancer treatment, such as chemo- and radiotherapy, is an additional risk factor [24, 25, 29, 30]. In the presented case, bone inflammation was probably blood-borne and was a consequence of changes either in the skin and soft tissues or teeth and could be associated with the chemotherapy used, as well as the presence of a malignant tumour and its advanced clinical stage.

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