ACUTE RENAL FAILURE IN A PATIENT WITH DIFFUSE LARGE B-CELL LYMPHOMA: CASE REPORT

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Abstract: Introduction: Renal parenchymal involvement is common in systemic lymphomas. In almost all cases, renal involvement appears to be a secondary process, either by direct extension from a retroperitoneal mass or via haematogenous spread in the setting of disseminated disease. Secondary renal involvement in systemic lymphomas is generally presented as multiple masses, but also as a solitary nodule. Acute renal failure by a lymphoma infiltration of the kidney is extremely rare. Primary renal non-Hodgkin’s lymphoma is even more uncommon and it is a debated issue because of the absence of lymphoid tissue in normal kidneys.

Case presentation: We report on the case of a 62-year old woman, who had melena, abdominal pain, malaise and fever. She was hospitalized at the Nephrology Clinic due to severe anemia and signs of acute renal failure. The peripheral blood smear showed the presence of dysplastic erythroblasts and hypo-granular neutrophils. Ultrasound was performed, which showed enlarged kidneys with signs of urinary obstruction of the first degree, with swollen, hypoechoic parenchyma. After not responding to the conducted treatment, the patient died from heart failure. An autopsy was performed and Non-Hodgkin’s, diffuse large B-cell lymphoma infiltrating multiple parenchymal organs was determined as the main cause of death.

Conclusion: Diffuse large B-cell lymphoma with multiple organ affection and secondary renal involvement, presented as an acute renal failure is a rare case. We report on this case to update the literature concerning this topic and highlight the importance of renal biopsy in the diagnostics.

Key words: non-Hodgkin’s lymphoma, primary, secondary, acute renal failure, biopsy.
Introduction

The genitourinary system is often affected by the extranodal spread of lymphoma, being the second most commonly affected anatomic entity next to the haematopoietic and reticulo-endothelial organs [1]. The kidneys are most commonly involved. Reports from autopsy series of patients who have succumbed to the disease describe foci of lymphoma in the kidneys in approximately one third of cases [1, 2]. Primary renal lymphoma (PRL) is a comparatively rare entity, because this organ is free of lymphoid tissue [3–5]. Primary renal lymphoma comprises only 0.7% of extra nodal lymphomas [6]. PRLs are commonly seen in middle-aged people and those with immunodeficiency and EBV infections [7, 8]. Renal involvement commonly occurs in patients with non-Hodgkin’s lymphoma, the majority of which are of intermediate or high grade, dominantly having a B-cell origin. However, acute renal failure (ARF) by a lymphomatous infiltration of the kidney is extremely rare and usually occurs due to bilateral infiltration [3, 15] which urges the patient to seek medical attention.

Case

A 62-year-old female was admitted to the Nephrology Clinic with signs of severe anaemia, acute renal failure and high blood levels of glucose. Three days prior to admission, the patient had generalized abdominal pain, malaise, fever (38°C) and one black stool. The cardiological examination excluded acute coronary suffering. The laboratory tests showed high levels of degradation products: Blood urea 38 mg/dl, Creatinine 494 µmol/l, LDH 1063 U/l; severe anaemia: Erythrocytes 2.1, Haemoglobin 60 mg/dl, Haematocrite 0.20, Leukocytes 19 (Neutrophils 77.6%, Lymphocytes 19.9%), Platelets 52, K. 6.1 mmol/l, Na 135 mmol/l, Ca 2.1 mmol/l, CRP 90, total proteins 45 of which albumins 18 and globulins 27, glucose 30, D-Dimmer 4500, AST 25, ALT 22. The urine analysis showed pH 5, with specific weight of 1015, and qualitative presence of proteins. An 24 hour urine analysis showed presence of proteins in the urine 1.5 g/l. The patient had been treated for high blood pressure for 5 years. After admission, because of the suspected ARF, ultrasound of the abdomen was performed. The ultrasound showed enlarged kidneys, with the dimensions of the right one 15.1 × 7.3 cm and of the left 15 × 8.3 cm, with signs of urinary obstruction of first degree and with swollen, hypo-echogenic parenchyma. The ultrasound did not show signs of enlarged lymph nodes in the abdomen and the performed chest ray did not show enlarged lymph nodes in the thoracic cavity. Also, there were no palpable lymph nodes on physical examination. The peripheral blood smear showed the presence of dysplastic erythroblasts and hypo-granular neutrophils with no presence of atypical lymphoid cells considering the later pathohistologic diagnosis. Due to the markedly elevated levels of blood
urea and creatinine, a conservative treatment for ARF with stimulation of diuresis was applied, which was followed by a dialysis because the patient did not respond to the previous one. Also, because of the high glucose levels a treatment with insulin for the newly discovered diabetes mellitus was applied. Multiple erythrocyte and platelet transfusions were given for correction of the severe anaemia. The conducted treatment did not improve the condition and the patient died from heart failure. After the lethal outcome, an autopsy was performed. At the autopsy, infiltrates of variable size and shape were found in the thyroid gland, lungs, liver, spleen, pancreas, stomach, bone marrow, myocardium, lymph nodes, both above and below the diaphragm, as well as multiple lesions in the small intestine. The thyroid gland was asymmetrically enlarged with dimensions of the right lobe $6.5 \times 3.5 \times 3$ cm and a weight of 25 g, whereas the left lobe weighed 15 g. Beside the infiltrates, changes characteristic of goitre were also present.

The kidneys were enlarged (right – 670 g, left – 700 g), with diffuse, confluent zones of necrosis and bleeding, hardly recognizable tissue architecture and the cortex hardly distinguishable from the medulla. Histological examination of the kidneys showed interstitial space heavily infiltrated by a mononuclear substrate distracting the renal histomorphology. The infiltrate was mainly concentrated in the medullar part of the kidneys, sparing the glomeruli, whose capillaries showed slight congestion and discrete hypercellularity, whereas the surrounding tubules were atrophic, with a notable focal presence of casts (Fig. 1).

Figure 1 – Diffuse dense interstitial lymphomatous infiltration. Note the tubular compression and atrophy with presence of casts. (hematoxylin & eosin; large figure, × 40; insert, × 100)
With immunohistochemical analyses of the tissue samples from the kidneys and other organs, a diffuse large B-cell lymphoma, immunoblastic variant, was diagnosed. The vast majority of the infiltrating cells (> 90%) were positive for CD20 (Fig. 2), CD79 and Bcl-2 (Fig. 3). Interestingly, Bel-6 which is characteristic of diffuse large B-cell lymphomas, was negative. The mitotic index Ki67 was high, above 80%.

The conclusion from the autopsy was that the cause of death was advanced (stage IV) diffuse large B-cell lymphoma, that led to multiple organ failure and finally to cardio-respiratory insufficiency as a direct cause of death (bearing in mind the findings of myocardial infiltrates, one of which was located in the interventricular septum).
**Discussion**

Diffuse large B-cell lymphoma is relatively common, making up to 25–30% of all lymphomas with a slightly male prevalence. It can affect any age group but occurs mostly in older people (commonly seen in the seventh decade) [9]. The genitourinary system is often affected by the extranodal spread of lymphoma, being the second most commonly affected anatomic entity next to the haematopoietic and reticulo-endothelial organs [1]. The kidneys are most commonly involved. In autopsy series secondary renal involvement in systemic lymphomas is reported to be in up to 30–60% of patients [10]. Reports from autopsy series of patients who have succumbed to the disease describe foci of lymphoma in the kidneys in approximately one third of cases [1, 2]. In one series of 322 autopsies, lymphoma involved the kidneys in 37.6% of cases but the urinary bladder and testes in only 8.4% and 5.9% of cases, respectively [2]. Renal lymphoma has a wide variety of manifestations including multiple lesions, a solitary lesion, direct extension from retroperitoneal adenopathy, preferential involvement of the perinephric space and diffuse infiltration of one or both kidneys. Despite the relatively high prevalence of renal involvement, imaging studies demonstrate renal abnormalities in only 3–8% of patients undergoing routine evaluation for staging [11, 12]. This apparent discrepancy between the pathology literature and the radiology literature can be explained by several factors: renal lymphoma is often poorly documented, since the disease is often clinically silent and renal biopsy is rarely indicated to confirm the diagnosis in the context of systemic disease. In ultrasound, lymphomatous masses are typically hypoechogenic and homogenous and even exhibit some degree of enhanced through transmission, thereby mimicking a cystic mass [13]. This correlates to the ultrasound findings in our patient, but regarding the fact that biopsy had not been performed, we call upon the importance of it in the diagnostic process and final outcome. Renal involvement usually occurs late in the course of the disease and is clinically often silent. Occasionally, as in our case, patients present with nonspecific signs and symptoms including flank and abdominal pain, malaise, weight loss or haematuria, or even signs of upper GI bleeding as a result of generalized dissemination [14]. Acute renal failure (ARF) by a lymphomatous infiltration of the kidney is extremely rare and usually occurs due to bilateral infiltration [3, 15]. The absence of other causes of ARF together with enlarged and slightly obstructed kidneys on renal ultrasound strongly suggested an infiltrative process in our patient. Pathophysiological characteristics of ARF in patients with kidney involvement by lymphoma are believed to be caused by tubular compression and atrophy or obstruction by light chain precipitation and impairment of renal parenchymal blood flow [16]. The massive interstitial lymphomatous infiltration, tubular compression and atrophy noted in our patient might have been the cause of ARF. As expected, conservative therapy with hydration, in our patient, did not result in an improvement of renal function.
Secondary renal lymphomas are 30 times more common than primary. The primary renal lymphoma is a rather rare entity and is a debated issue, especially among pathologists due to the absence of lymphoid tissue in the normal kidney [3–5]. There is a proposal that lymphoid tissue in the renal capsule may be the origin of lesions, or chronic inflammation may be the cause [8]. Although there is no evidence that chronic inflammation usually induces PRL, in our studies of renal biopsies with glomerular lesions we have found foci of reactive infiltrates of lymphocytes with B cell phenotype [17]. Whether these inflammatory lesions are precursors of malignancy remains to be further discussed and/or proven. Some pathologists tend to think that primary renal lymphoma is a disseminated malignancy, because in 10% to 20% of cases lymphomas affect both kidneys [4]. Some criteria are proposed for the confirmation of a PRL diagnosis: presence of a renal mass, absence of lymph node invasion and other visceral invasion at the time of diagnosis, absence of myelosuppresion and of leukaemic blood picture [8]. It is also stressed that PRL is highly aggressive and rapidly invades systemic lymphatic tissue.

In summary, we report on a patient with ARF due to kidney infiltration by a diffuse large B-cell non-Hodgkin’s lymphoma. Also, we underline the importance of renal biopsy in obtaining a correct diagnosis, selecting the appropriate therapy and improving the final outcome.

REFERENCES


Резиме

АКУТНА БУБРЕЖНА ИНСУФИЦИЕНЦИЈА КАЈ ПАЦИЕНТ СО ДИФУЗЕН КРУПНО-КЛЕТОЧЕН БЛИМФОМ: ПРЕЗЕНТАЦИЈА НА СЛУЧАЈ

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Вовед: Зафаќање на бубрежинот паренхим е честа појава кај системските лимфоми. Речиси во сите примери реналната афекција е секундарна, било со директно ширење на процесот од ретроперитонеумот или хематогено во услови на
дисеминирана болест. Секундарната ренална афекција при системските лимфоми најчесто се манифестира со присуство на мултипни маси, но може да биде и во формата на единечен јазол. Акутна бубрежна инсуфициенција заради лимфоматозна инфилтрација е исключително ретка појава. Примарните non-Hodgkin-ови бубрежни лимфоми се уште поретки и се предмет на дискусија, заради отсувството на лимфно ткиво во нормалните бubreзи.

Презенијација на случај: Презентираме случај на 62-годишна пациентка со следнава симптоматологија: мелена, абдоминална болка, премаленост и висока температура. Пациентката била хоспитализирана на Клиниката за Нефрологија заради изразена анемија и знаци на акутна бубрежна инсуфициенција. Периферната крвна размаска покажа присуство на диспластични еритробласти и хипогрануларни неутрофили. Ултразвучниот преглед покажа зголемени бubreзи со знаци на опструкција од лесен степен и едематозен, хипохоген бубрежен паренхим. И покрај спроведениот третман, пациентката егзитираше заради срцев застој. На извршениата аутопсија како главна причина за смртта, беше докажан дифузен (non-Hodgkin-ов) крупно-клеточен Б лимфом, со мултипна органска афекција.

Заклучок: Мултипна органска афекција од страна на дифузен крупно-клеточен Б лимфом со секундарно ренално зафаќање, клинички презентирано со знаци на акутна бубрежна инсуфициенција, е редок случај. Го презентираме овој случај со цел да ја дополнниме литературата во однос на оваа тема и да ја потенцираме улогата на реналната биопсија како дијагностичка алатка.

Клучни зборови: non-Hodgkin-ов лимфом, примарен, секундарен, акутна бубрежна инсуфициенција, биопсија.

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