


Case Report

Rare case of Richter syndrome with testicular involvement successfully obtained good prognosis with rapid operation and immunochemotherapy

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Abbreviations & Acronyms

CLL = chronic lymphocytic leukemia
 CT = computed tomography
 DLBCL = diffuse large B-cell lymphoma
 HE = hematoxylin and eosin
 LDH = lactate dehydrogenase
 MRI = magnetic resonance imaging
 PET = positron emission tomography
 RS = Richter syndrome
 SLL = small lymphocytic lymphoma
 WHO = World Health Organization

Introduction: Richter syndrome refers to the transformation from chronic lymphocytic leukemia to assaultive lymphoma, often a diffuse large B-cell lymphoma, and has a greatly poor prognosis. Richter syndrome is characterized by rapidly growing lymphadenopathy but rarely presents with extra-nodal involvement, common sites being the digestive tract, lungs, kidneys, and central nervous system. However, Richter syndrome with testicular involvement is extremely rare.

Case presentation: Herein we report a very scare case of a male at the age of 72 with Richter syndrome and testicular involvement, diagnosed by the investigation of bilateral scrotal swellings. The patient had attained disease-free survival for over a year with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone, and the intrathecal administration of chemotherapeutic agents after diagnosis by immediate orchiectomy.

Conclusion: An early pathological diagnosis by immediate orchiectomy and the early initiation of induction immunochemotherapy may be good prognostic factors in Richter syndrome involving the testes.

Key words: CLL/SLL, diffuse large B-cell lymphoma, Richter syndrome, testicular germ cell tumor.

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Keynote message

We report a case of RS with testicular involvement and the clinical characteristics of a germ cell tumor. Immediate orchiectomy for an early histopathological diagnosis may result in a good response to induction treatment.

Introduction

RS, first described by Richter in 1928,¹ and the WHO Classification of Hematopoietic Tumors in 2008² defines RS as the development of an assaultive lymphoma in a patient with a previous or concomitant diagnosis of CLL/SLL. Common knowledge of this tumor entity among urologists is very confined because RS rarely presents extra-nodal involvement including digestive tract, and is extremely rare in urological organs.^{3–5} Herein we describe one case of RS with testicular involvement found by asymptomatic scrotal swellings.

Case presentation

A 72-year-old Asian male was consulted to our hospital with sudden scrotal swelling but no additional symptoms. His past history included low risk CLL in revised Rai stage 0 without any treatment 16 years ago. On physical examination, his left scrotum was slightly swollen,

whereas his right scrotum had marked swelling and a detectable hard mass. Blood examination showed high levels of white blood cell (27 840 μ L: normal range 3300–8600) and LDH (341 U/L: normal range 124–222); however, other abnormalities including for the testicular tumor markers, serum alpha fetoprotein and human chorionic gonadotropin, were not evident. Enhanced CT showed a round, bilateral testicular tumors (right side 72 \times 58 mm and left side 22 \times 18 mm) with homogeneous iso-enhancement relative to normal testis, and 8-mm-sized para-aortic masses. These

masses were slightly and gradually enhanced in dynamic contrast-enhanced CT without any suspicious lesions of visceral metastases noted except the surrounding lesions of the para-aorta (Fig. 1a,b). MRI revealed a low intensity on T2-weighted images compared to those of normal testis and a low intensity on an apparent diffusion coefficients map (Fig. 1c,d). The clinical diagnosis was bilateral testicular tumors including malignant lymphoma, and after informed consent, an immediate bilateral orchietomy was performed. The tumor was solitary, and rounded shape, with the cut surface of that showing

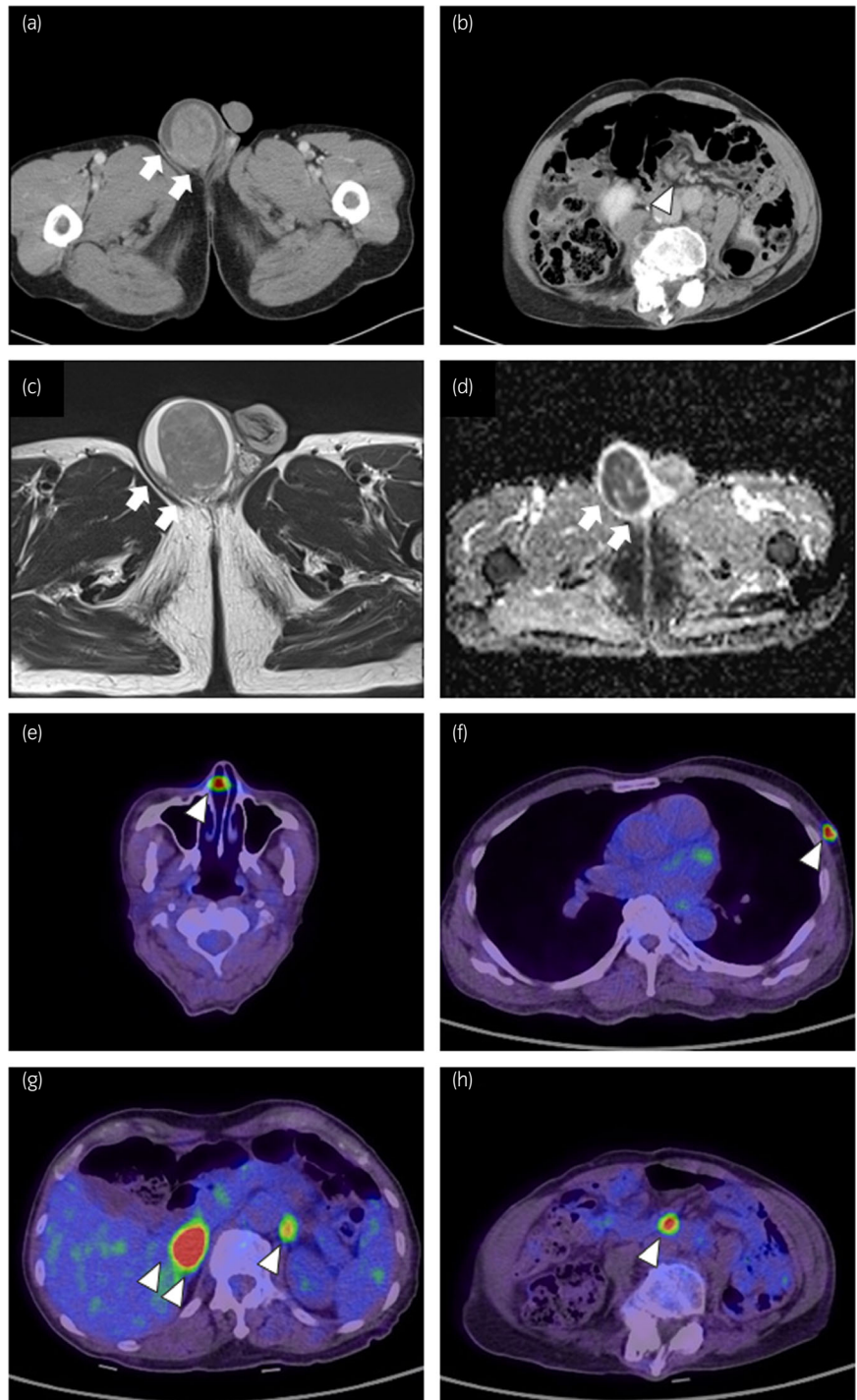


Fig. 1 (a–d) Abdominal enhanced CT (a,b), T2-weighted MRI (c), apparent diffusion coefficients MRI (d) of a 70-mm sized right testicular tumor (white arrows) and a suspicious para-aortic metastasis (white arrowheads). PET–CT revealed multiple hot lesions (e–h) undetected in CT. A mass occurred in lesions of the nasal septum (e), left axillae (f), bilateral adrenal glands (g), and near the para-aorta (h).

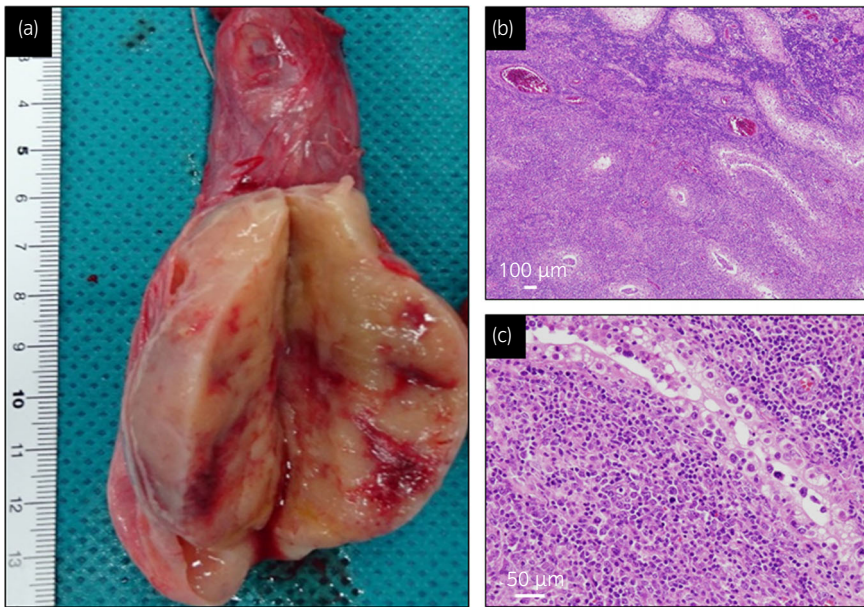


Fig. 2 (a) Macroscopic finding of a right orchietomy specimen. (b,c) HE staining of the tumor specimen.

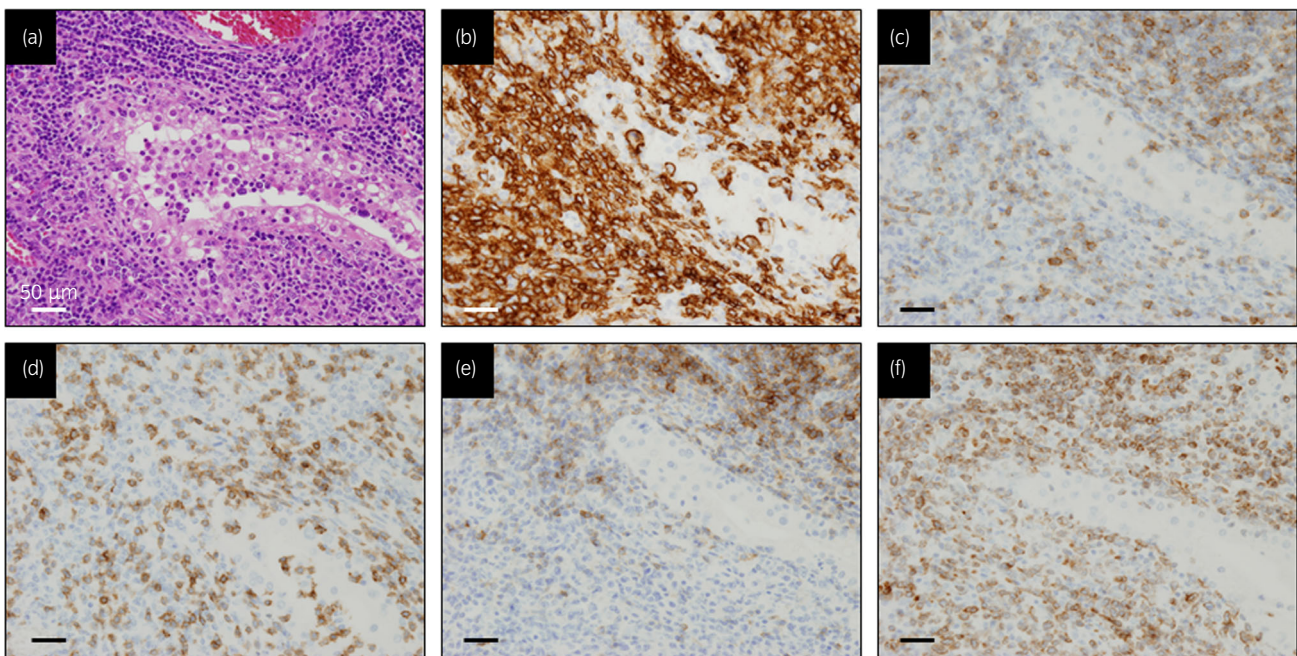


Fig. 3 (a) HE staining of the tumor specimen. (b–f) Immunohistochemical analysis revealed that a lesion with large neoplastic B lymphocytes was immunoreactive for CD20 (b), and negative for CD5 (c), CD3 (d), and CD23 (e). Atypical small rounded cells around large neoplastic B lymphocytes were immunoreactive for CD20, CD5, CD23, and Bcl-2 (f), and negative for CD3.

a yellowish color (Fig. 2a). Pathological finding revealed that the tumor consisted of blastemal cells, each with an atypical small round shape, and scant cytoplasm. These cells morphologically composed of confluent sheets of large neoplastic B lymphocytes resembling either centroblasts or immunoblasts (Figs 2b,c,3a). The tumor lesion of large neoplastic B lymphocytes was immunoreactive for CD20 (Fig. 3b), and negative for CD5 (Fig. 3c), CD3 (Fig. 3d), and CD23 (Fig. 3e). Atypical small round cells around large neoplastic B lymphocytes were immunoreactive for CD20, CD5, CD23, and Bcl2

(Fig. 3f), and negative for CD3. These histopathological findings were consistent with a DLBCL variant, a transformation of CLL, with the final diagnosis being RS. PET-CT revealed the presence of positive lesions in the nasal septum, a tiny subcutaneous tumor in front of the left chest, and bilateral adrenal glands that could not be detected on CT (Fig. 1e–h). Therefore, the patient immediately underwent an induction combination of rituximab with cyclophosphamide, doxorubicin, vincristine, prednisone immunochemotherapy, and the intrathecal administration of chemotherapeutic agents,

including methotrexate, cytarabine, and prednisone. After four cycles of the regimen, the patient showed a complete response in an imaging study. Totally, eight cycles of chemotherapy was performed, and the patient was monitored on an outpatient basis. He was successfully in remission for 14 months after the end of immunochemotherapy.

Discussion

The WHO Classification defines two distinct pathologic variants of RS: a DLBCL variant, which is the most often, and a rare Hodgkin lymphoma variant. RS occurs in 2–8% of patients with CLL/SLL, and the prognosis of the disease is generally poor.² Only rarely, RS presents with extra-nodal involvement including in the digestive tract, lung, pleura, bone, skin, oropharynx, and central nervous system.^{3–5} As typified by our patient, testicular involvement is extremely rare, and in the literature, only two case reports have been found.⁶

Generally, previous reports about RS described how the presence of one or more clinical symptoms including fever without the sign of infection, rapid, and inconsistent expansion of localized lymph nodes, were only about 50% specific for the diagnosis of RS, and how CLL patients suspected of disease onset should be monitored.⁴ Specific laboratory markers for RS are lacking; however, about 80% of patients showed twice the upper limit of normal for serum LDH levels,⁷ unlike our patient. In addition, discriminating between testicular germ cell tumors and DLBCL occurring in the testes by imaging study is very difficult. However, in this case, pathological findings in immediate orchiectomy revealed the CD20 positive and CD5 negative neoplastic cells surrounding CD20 positive and CD5 positive small rounded cells were clearly detected as described in Figure 3, and these rapidly caused final diagnosis as RS.

Numerous therapies can induce a response, however, with regard to chemoresistance, patients with RS show an assaultive clinical phenotype. Parikh *et al.* reported that in an analysis using a Mayo Clinic CLL database, the median overall survival of RS was only 2.1 years, but a range of 0.1–12.0 years suggested considerable variability.⁷ Treatment strategies mainly combine intensive immunochemotherapy, with or without transplantation of stem cell.⁸ The optimal timing of the start of induction treatment after a diagnosis is not fully understood. In this case, in accordance with treatment for testicular germ cell tumors, an immediate orchiectomy was preferred and performed. As a result, an early diagnosis was obtained, and induction treatment was started as soon as possible. Consequently, 1-year progression-free survival was obtained as in a previously reported case.

Even with data from the very few cases studied, a patient with CLL showing signs of extra-nodal involvement of the

scrotum should be suspected of having RS. Confirmation by immediate orchiectomy for an early histopathological diagnosis may lead to a good response to induction treatment. However, further investigation of this rare disease is needed.

Conclusion

We report here a case of RS with testicular involvement, and with clinical characteristics resembling those of a germ cell tumor, who showed 1-year recurrence-free survival after immediate orchiectomy and induction treatment.

Conflict of interest

The authors declare no conflict of interest.

Declarations

This article was approved by the Nagoya City East Medical Center Institutional Review Board. The approval number was 18-04-372.

Consent

A copy of the written informed consent is available for review by the Editor-in Chief of this journal. And written informed consent was obtained from the patient for publication of this article and accompanying images.

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