Case Report

Transient increase in lactate dehydrogenase after granulocyte colony-stimulating factor administration during chemotherapy in a patient with advanced seminoma

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Abbreviations & Acronyms
AFP = α-fetoprotein
BEP = bleomycin, etoposide and cisplatin
CT = computed tomography
G-CSF = granulocyte colony-stimulating factor
HCG = human chorionic gonadotropin
LDH = lactate dehydrogenase
TNM = tumor-node-metastasis
VIP = etoposide, ifosfamide and cisplatin
WBC = white blood cell count

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Received 18 August 2018; accepted 9 November 2018. Online publication 13 December 2018

Introduction: Granulocyte colony-stimulating factor is often reported to induce increases in lactate dehydrogenase, complicating the evaluation of treatment effects on germ cell tumors.
Case presentation: A 30-year-old patient was diagnosed with left testicular seminoma showing enlarged para-aortic lymph nodes and a retroperitoneal tumor. Serum levels of lactate dehydrogenase were elevated. Three cycles of bleomycin, etoposide, and cisplatin were administered. After chemotherapy, computed tomography showed marked reduction in the metastatic sites. However, serum lactate dehydrogenase levels increased transiently at the end of each course of chemotherapy. In consideration of the residual tumors, one cycle of another chemotherapy was added. Five months after final chemotherapy, lactate dehydrogenase remained within normal limits with no evidence of tumor recurrence.
Conclusion: In our case, transient elevation of lactate dehydrogenase was considered relevant to granulocyte colony-stimulating factor use. Examination of lactate dehydrogenase isoenzymes may be helpful to estimate the cause of serum lactate dehydrogenase elevation.

Key words: granulocyte colony-stimulating factor, isoenzymes, lactate dehydrogenases, seminoma, testicular germ cell tumor.

Keynote message

- G-CSF is often reported to induce serum LDH rising, which makes it difficult to evaluate treatment effects of germ cell tumors.
- We describe the case of a 30-year-old patient diagnosed as pure seminoma that serum LDH behavior did not correlate with efficacy of chemotherapy.
- In our case, transient elevation of LDH was considered to have relevance to G-CSF use, and it is thought that examination of LDH isoenzymes is helpful to estimate the cause of serum LDH elevation.

Introduction

G-CSF used for leukopenia following chemotherapy is often reported to induce increases in serum LDH. LDH is also one of the serum tumor markers for germ cell tumor, and non-malignant elevations in LDH complicate the evaluation of treatment effects. Some reports said that LDH isoenzyme analysis may contribute to distinguish between malignant and non-malignant cause. Here, we present the case of a male patient diagnosed as seminoma that serum LDH behavior did not correlate with efficacy of chemotherapy.

Case presentation

A 30-year-old man visited a hospital with a left testicular mass. He had no past medical history except asthma. CT revealed enlarged para-aortic lymph nodes and a retroperitoneal tumor (diameter, 45 mm) (Fig. 1). Serum concentrations of LDH and β-HCG were elevated (317 IU/L and 0.5 ng/mL, respectively), while AFP was within normal limits (1 ng/mL). Total HCG was not measured at this institution and the preoperative value was thus unknown.

Left radical orchiectomy was performed and pathological examination showed pure seminoma. The TNM classification was pT1N1M1aS1 and the International Germ Cell Consensus Classification risk category suggested a good prognosis. The patient was referred to our institution to receive adjuvant chemotherapy after surgery. Serum LDH was 382 IU/L at his first visit. He was administered three cycles of BEP (bleomycin at 30 mg on days 1, 9, and 16, etoposide at 100 mg/m^2 on days 1–5, cisplatin at 20 mg/m^2 on days 1–5). Although serum LDH and β-HCG levels normalized immediately after the first course of BEP, serum LDH levels increased transiently at the end of each course of chemotherapy, and correlations were evident between LDH elevation and G-CSF use (Fig. 2). After three cycles of BEP, CT showed resolution of the swelling in para-aortic lymph nodes and marked reduction in the size of the retroperitoneal mass (Fig. 1). We examined LDH isoenzymes during the third cycle of BEP (Fig. 3). The percentages of LDH-3 and LDH-4 were increased after G-CSF use, returning to the normal pattern of isoenzyme ratios when total LDH normalized. This phenomenon suggests that the transient increase in serum LDH was attributed to G-CSF administration. However, these test results were not available at the end of the third cycle and the possibility of residual tumors could not be completely ruled out. In consideration of the possible of viable tumors, one cycle of VIP (ifosfamide at 1.2 g/m^2 on days 1–5, cisplatin at 20 mg/m^2 on days 1–5, and etoposide at 75 mg/m^2 on days 1–5) was added. Five months after final chemotherapy, LDH remains within normal limits and no evidence of tumor recurrence has been identified.

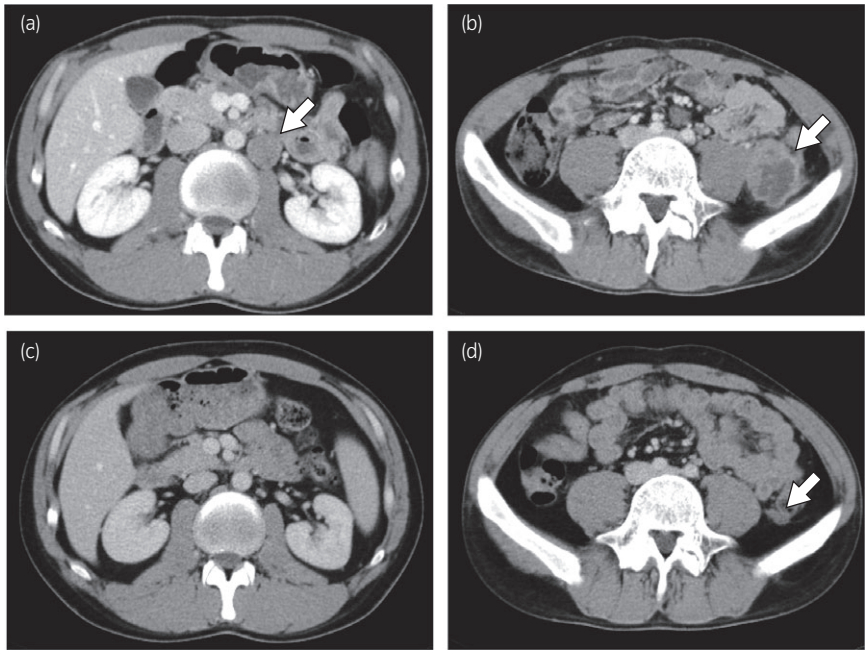

Fig. 1 CT shows enlarged para-aortic lymph node (a, arrow) and retroperitoneal tumor (b, arrow). After three cycles of BEP, there were marked reduction in para-aortic lymph node (c). The retroperitoneal tumor was reduced to 20 mm in diameter (d, arrow).

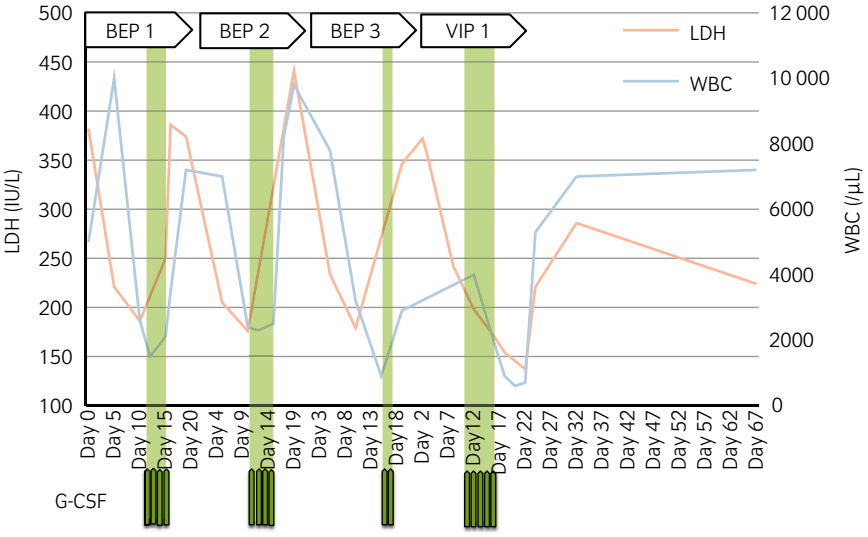

Fig. 2 The serum LDH was transiently increased after G-CSF administration in the middle of each course of chemotherapy.

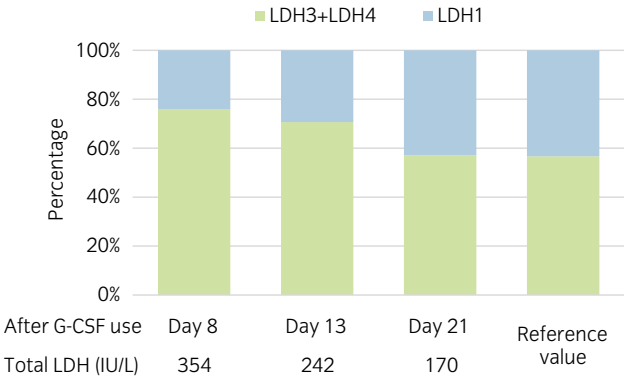

Fig. 3 LDH isoenzyme ratios were transiently changed during the third cycle of BEP. The percentages of LDH-3 and LDH-4 were increased after G-CSF use and returned to the normal pattern of isoenzyme ratios when total LDH normalized.

Discussion

Administration of three cycles of BEP has been the standard regimen in patients with good prognosis according to the International Germ Cell Consensus Classification and clinical stage IIIa seminoma, with approximately 90% of cases showing complete response.[1,2] Clinical assessment of response to first-line chemotherapy is made by imaging studies and evaluation of serum tumor markers. Patients with residual tumor mass smaller than 3 cm and negative serum tumor markers can be observed safely.[3] In this case, however, although the swollen para-aortic lymph nodes and the retroperitoneal mass were markedly reduced in size after first-line chemotherapy, serum LDH levels increased transiently and assessment of the existence of residual malignancy proved difficult.

Serum LDH is not a specific marker for germ cell tumor during chemotherapy. Non-malignant conditions that can raise serum LDH include drug-induced liver injury, interstitial pneumonia, and use of G-CSF.[4] Serum LDH is often reported to increase after G-CSF administration during chemotherapy for lung or breast cancer.[5,6] However, few reports have described G-CSF for germ cell tumor.[7] G-CSF induces rapid production and consumption of neutrophils, and releases LDH originating from neutrophils. In our case, grade 4 neutropenia occurred in each cycle of chemotherapy and G-CSF was used to prevent severe infection. Liver enzymes did not increase and chest CT yielded normal results. This LDH increase was reproducible and G-CSF and LDH could be considered correlated. G-CSF was thus considered as the cause of the increase in serum LDH. However, accurate determination of the cause of LDH increases is difficult.

Some reports have stated that LDH isoenzyme analysis may help to distinguish between malignant and non-malignant causes.[5] Five LDH isoenzymes are known, with four patterns of combination for these isoenzymes. The predominant LDH isoenzymes from immature neutrophils are LDH-2, LDH-3 and LDH-4. Increases in LDH-1 are known to suggest myocardial infarction and the presence of germ cell tumor.[8] Levels of LDH-3 and LDH-4 reportedly become significantly higher than those of other LDH isoenzymes after G-CSF administration.[7] This phenomenon was also shown in our case (Fig. 3), and LDH isoenzymes helped to diagnose the cause of the LDH bounce. However, data on LDH isoenzymes were not available at the end of the third cycle and the possibility of residual tumors could not be completely ruled out. We should have examined LDH isoenzymes at least during the second cycle of BEP.

In conclusion, we encountered a case of seminoma in which serum LDH increases during BEP therapy were difficult to evaluate. Elevation of serum LDH might be induced by G-CSF administration and examination of LDH isoenzymes appears helpful to estimate the causes of serum LDH elevation and decide therapeutic strategies.

Conflict of interest

The authors declare no conflict of interest.

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