



Hypothermia in Hodgkin's disease: unexpected state; case report and review of the literature

Hodgkin hastalığında hipotermi: Beklenmedik bir durum;
olgu sunumu ve literatür incelemesi

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Hypothermia and hypotension is a rare phenomenon having uncertain etiology. We reported a case of stage IIIB Hodgkin's disease who developed hypothermia after naproxen sodium administration, initially presenting with hyperthermia. In this case, the reduction of pyrogens production after naproxen sodium administration, appears to be the most probable physiopathologic hypotheses. Hypothermia may correlate with worse prognosis. According to the outcomes of published cases in literature, we suspect that the hypothermia and hypotension may be an unidentified syndrome in Hodgkin's disease.

Key words: Hypothermia; hypotension; naproxen sodium; Hodgkin's disease.

Hipotermi ve hipotansiyon, etyolojisi bilinmeyen nadir bir fenomendir. Bu yazıda, hipertermi ile kendini gösteren, naproksen sodyum uygulaması sonrasında hipotermi gelişen evre IIIB Hodgkin hastalıklı bir olgu sunuldu. Bu olguda; naproksen uygulaması sonrası pirojenlerin üretimini azalması, en muhtemel fizyopatolojik hipotez olarak gözükmetedir. Hipotermi daha kötü prognozla ilişkilendirilebilir. Literatürdeki sonuçlara göre, biz hipotermi ve hipotansiyonun Hodgkin hastalığında henüz tanımlanmamış bir sendrom olabileceğini düşünüyoruz.

Anahtar sözcükler: Hipotermi; hipotansiyon; naproksen sodyum; Hodgkin hastalığı.

Hypothermia is a rare clinical manifestation, commonly resulting from chemotherapy, laparotomy, and antipyretic administration in Hodgkin's disease. In literature, this clinical manifestation has been reported from several case reports.^[1-16] Herein we presented a case of stage IIIB Hodgkin's disease, complicating with hypothermia and hypotension after naproxen sodium administration.

CASE REPORT

A 38-year-old man entered the hospital in November, 2008, for evaluation of painless cervical and axillary lymphadenopathies. Also he had night

sweats and 10 kg weight loss in 3 months. Physical examination demonstrated the normal findings except lymphadenopathies. Computed tomography (CT) scan showed cervical, axillary and paraaortic adenopathy. Excisional biopsy diagnosed lymphocyte depletion Hodgkin's disease. Hodgkin's disease in patients with stage IIIB, and treatment was started. He achieved a complete remission after six courses of ABVD (doxorubicine 25 mg/m², bleomycin 10 mg/m², vincristine 1.4 mg/m², dacarbazine 375 mg/m²). Then, two months later, he relapsed with B-symptoms and hyperthermia (40.2 °C). In addition, physical examination was normal

except multiple thyroid nodules. Involvement of mediastinal lymph nodes, paraaortic lymph nodes and bones were showed by Positron Emission Tomography (PET/CT) scan. Involvement of bone marrow was confirmed by biopsy. The Laboratory tests showed that; white blood count 4.800 K μ /L, with 69.6% neutrophils, 18.5% lymphocytes, 5.5% monocytes, 3.5% eosinophils and 2.9% basophiles. Hemoglobuline 13.8 g/dl, platelets 176.000 K μ /L. He was treated empirically with multiples antibiotics for hyperthermia. Blood and urines cultures were negative for bacteria and fungi. HBV DNA levels were 1.800 IU/ml. His thyroid functions tests were normal (thyroxin or triiodothyronin, thyroid- stimulation hormone, anti-tiroglobuline antibody). Thyroid fine needle biopsy was multinodular goiter. Second line chemotherapy consisting in dexametazon 40 mg, cisplatin 100 mg/m² and cytarabine 2 gr/m² was started. After the infusion of chemotherapy, hyperthermia remained unchanged during two days. Naproxen sodium (Apranax[®]), known non-steroidal anti-inflammatory drug, was applied orally for hyperthermia. Hypothermia (34 °C) was developed in this patient on the day that followed. Hypotension and bradycardia were attended to hypothermia. Magnetic resonance (MR) was employed to the verification cerebral involvement. MR scan was normal. His temperature returned normal spontaneously within 3 days. Three weeks later, in the second application, naproxen sodium induced hypothermia followed by hyperthermia was repeated. Like before hypothermia was returned normal spontaneously. He was refractory to chemotherapy and died from progressive Hodgkin's disease within 6 months.

DISCUSSION

This present case was reported as 15th case of the association of Hodgkin's disease and hypothermia^[1-11] We noted the case of a patient presenting with hyperthermia secondary to Hodgkin's disease who subsequently developed hypothermia after naproxen sodium administration. Nine of these patients developed hypothermia after chemotherapy, two patients after paracetamol and naproxen sodium administration, one patient after laparotomy/prednisone. Hypothermia was developed prior

to therapy in two patients.^[1,11] Eleven of these 14 patients had hyperthermia, in the other cases, no information was available. Hypotension with hypothermia was observed in 7 cases. Involvement of the liver was reported in 7 cases (two case probably) and hepatic disorders (hepatitis B) were reported in one case (present case). Involvement of bone marrow including present case was reported in 3 cases.^[4,9] Hypothermia and hypoglycemia was reported in one case. Hypothermia did not relapse in all cases except the present case. Six of 14 cases died in the early period after hypothermia.^[4,9,10] Duration of hypothermia ranged between 3-10 days.

Hypothermia in Hodgkin's disease is rare and etiology of hypothermia is uncertain. Hypothalamic functions affected by the involvement of the brain were showed.^[2] Hypothermia was described with different cancers infiltrating the brain. Primary and metastatic brain tumors may cause hypothermia.^[4,12-15]

Autonomic neuropathy was suggested to define the role of the autonomic nervous system by the authors.^[5,9] Another view is that the different drugs are associated with hypothermia. Vinblastine and vincristine have a potential to create neurological toxicity as a dose-dependent, but relation of vinca alkaloids with hypothermia has not been shown yet. 9 cases received a treatment which consisted of vinca alkaloid. 3 cases received a treatment which consisted of cisplatin. Phenothiazine, salicylate, paracetamol and naproxen sodium could be considered with hypothermia.^[3]

Pyrogens are produced by Hodgkin lymphoid tissues.^[16] In addition, down-regulation may be occurred in the thermoreceptors because of an increase the pyrogens. After chemotherapy or administration naproxen sodium, a reduction in the production of these pyrogens could lead to decreased body temperature.^[10] Kupffer's cells are another source of pyrogens.^[4,10] Therefore, hepatic infiltration by Hodgkin or hepatic disorders could be important and it could cause hypothermia documented in 6 cases.

CONCLUSION

In this case, reduction of pyrogens caused to

hypothermia after naproxen sodium administration appears the most probable physiopathologic hypotheses. Hypothermia may be an indicator of tumor burden as well as measurable lesions. Hypothermia and hypotension may be an unidentified syndrome in Hodgkin's disease yet. In as much as some of the cases died in the early period after hypothermia according to literature, more aggressive approach may be considered to the treatment of these patients like dose-dense schedule. Although hypothermia and hypotension are seen rarely in literature, blood pressure and body temperature should be monitored both pre-treatment and post-treatment.

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