Isolated Small Bowel Infarction Due to Aspergillosis After High Dose Chemotherapy and PBSC Tx in Patient with Hodgkin Lymphoma: Case Report

Hodgkin Lenfomalı Olguda Yüksek Doz Kemoterapi ve Periferik Kök Hücre Nakli Sonrasında Aspergilloza Bağlı İzole İnce Barsak Nekrozu

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ABSTRACT Invasive aspergillosis is an opportunistic disease that affects immunocompromised patients resulting with high mortality rates. A 54-year-old man diagnosed as non-Hodgkin's Lymphoma was treated with chemotherapy protocols and partial response achieved. Afterwards he was treated high dose chemotherapy[BEAM (BCNU, Etoposide, Ara-C ve Melphalan)] and peripheral blood stem cell transplantation (PBSCT). The patient had abdominal pain and distention 14 days after stem cell transplantation. Surgical exploration of the abdomen was performed and intestinal necrosis was diagnosed. Resection and anastomosis was done. Pathology showed transmural necrosis of intestine due to microthrombosis caused by aspergillosis. Intestinal aspergillosis should be kept in mind when an immunocompromised patient suffers from severe abdominal pain, distention and rapid clinical detoriation with fever.

Key Words: Chemotherapy, adjuvant; lymphoma; aspergillosis; intestine, small; ischemia

ÖZET İnvazif aspergilloz yüksek mortalite oranlarıyla immünsüprese hastaları etkileyen fırsatçı bir enfeksiyondur. 54 yaşında non-Hodgkin lenfoma tanılı erkek hastaya uygulanan kemoterapilere kısmi cevap elde edildi. Bunun üzerine yüksek doz kemoterapi [BEAM (BCNU, Etoposit, Ara-C ve Melfalan)] ve otolog periferik kök hücre nakli (OPKHN) tedavisi uygulandı. Periferik kök hücre naklinden 14 gün sonra hastada karın ağrısı ve abdominal distansiyon gelişti. İntraabdominal cerrahi eksplorasyon yapıldı ve ince barsak nekrozu gözlendi. İnce barsak rezeksiyonu ve anastomoz gerçekleştirildi. İnce barsak rezeksiyon materyalinin patolojik incelemesinde aspergilloz plaklarının infiltrasyonuna bağlı transmural ve mukozal infarktlar saptandı. Ateşle birlikte şiddetli karın ağrısı, distansiyon ve hızlı genel durum bozukluğu tablosundaki immünsüprese hastalarda intestinal aspergilloz düşünülmelidir.

Anahtar Kelimeler: Adjuvan kemoterapi; lenfoma; aspergiloziz; ince barsak; iskemi

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Deep fungal infections that originate from opportunistic mycoses are feared complications with high mortality rates after high dose of chemotherapy and stem cell transplantation.[1] *Aspergillus* species are usually susceptible to be disseminated in immunocompromised individuals.[2-4] The process may progress to life-threatening point if rescue therapy delays. Primary intestinal invasive aspergillosis is extremely rare and highly lethal opportunistic infection despite new effective drugs and usually involves immunocompromised patients. It is rapidly progressive and diagnose is

difficult for invasive intestinal aspergillosis. Abdominal pain, galactomannan antigenemia and isolation of Aspergillus in the intestine are important for the diagnosis of invasive aspergillosis.[3,5,6]

CASE REPORT

A 54-year-old man with symptoms of high fever and weakness was diagnosed as possible B cell malignant lymphoma after fine needle biopsy from the mass in the right upper lung. Excisional axillary lymph node biopsy was performed to confirm diagnosis and pathology showed lymphocyte rich type Hodgkin's Lymphoma. He was treated with 6 cycles of ABVD (Doxorubicin, Bleomycin, Vinblastine, Dacarbazine). The final diagnosis was considered B cell non-Hodgkin's Lymphoma because the improvement was not enough and he was treated with 8 cycles of R-CHOP(Rituximab, Cyclophosphamide, Doxorubicin, Vincristin, Prednisone) chemotherapy.

PET- CT scan obtained after treatment showed a partially response and the patient received high dose of chemotherapy (BEAM(BCNU, Etoposide, Ara-C, Melphalan)) and peripheral blood stem cell transplantation(PBSCT).

Intravenous combined antibiotherapy with amicasin, imipenem and teicoplanin was given because fever developed on the second day of autologous peripheral stem cell transplantation . It was started amphothericine-B administration despite intravenous antibiotherapy on the twelfth day of transplantation. Leukocyte engraftment was achieved after ten days of transplantation.

The patient suffered of abdominal pain and distention with no gas and stool passage at day fourteen after transplantation. His mental status rapidly confused and was consulted with surgery. Abdominal ultrasound showed thickening of the intestinal wall without peristalsis and fluid accumulation particularly in the left lower quadrant. Laparoscopic exploration was performed and necrotic bowel loops were seen in the proximal part of intestine. Procedure was converted to open exploration and 70-cm long necrotic segment of the terminal jejunum was removed and ileo-jejunal anastomosis was performed.

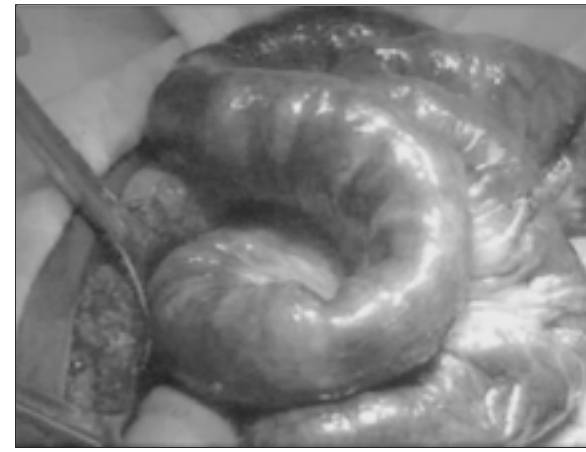

FIGURE 1: Small bowel necrosis with thickened and purple wall.

During the operation it was observed that the mesenteric vascular circulation was intact, indicating that the small bowel wall necrosis was due to occlusion in microvascular circulation. Macroscopic inspection of the bowel showed large mucosal ulcerations and necrotic areas and histopathologic examination revealed transmural necrosis and disseminated hemorrhagic areas (Figure 1) (Figure 2a). In Hemotoxyline Eosine stained slides, branching hyphae were detected invading intestinal arterioles. It was realized that fungi were morphology of *Aspergillus* hyphae using histochemical method of GMS (Grocott's Methenamine Silver) (Figure 2b).

The patient developed sepsis post-operatively and could not be weaned from ventilatory support.

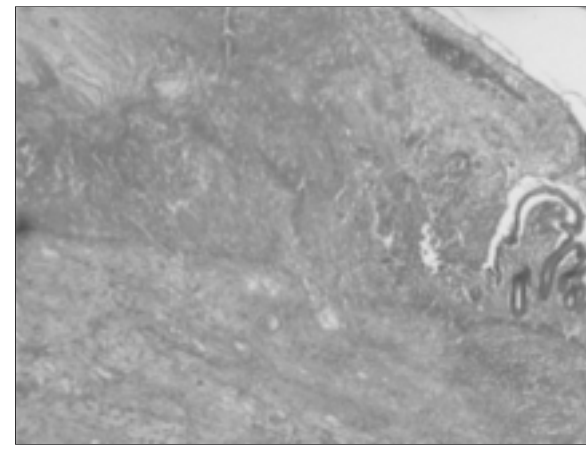

FIGURE 2a: Ulceration, active chronic inflammation, transmural necrosis (Hemotoksilen eosin*50).

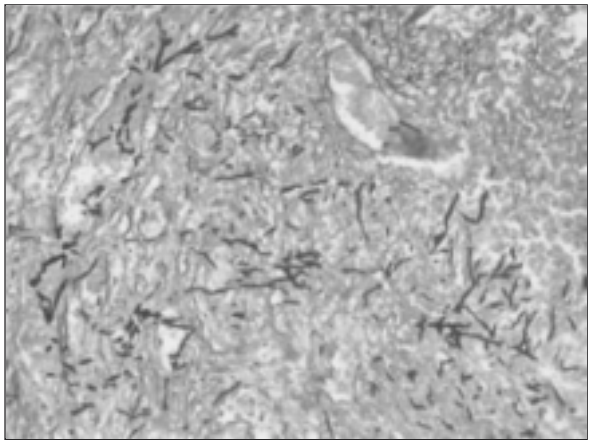

FIGURE 2b: Aspergillus hyphae showing the development of bundle (Grocott's Methenamine Silver; magnification*100).

His condition gradually deteriorated despite liposomal amphotericin B treatment and pressor agents. Ventilatory support was continued but the patient died 12 days after the operation.

DISCUSSION

Reports of invasive aspergillosis cases have increased in recent years possibly resulting from more effective but more toxic chemotherapy regiments.[7] Small bowel infarction due to aspergillosis is associated with high mortality rates more than 80%.[8,9]

Early diagnosis of invasive intestinal aspergillosis is difficult in the period of chemotherapies as the clinical symptoms are usually vague and nonspecific.[4] The presence of primary intestinal aspergillosis should be considered in patients receiving high dose of chemotherapy with symptoms of persistent fever and abdominal pain.

Histopathologic examination of specimen is essential to for the diagnosis of intestinal aspergillosis.[4] Computerized tomography and ultrasound may contribute to diagnosis. Bronchoalveolar lavage fluid should be tested for Aspergillus because intestinal invasive aspergillosis may be the part of a disseminated disease with lung involvement.[10] Surgery is inevitable in cases with bowel obstruction, peritonitis or bowel infarction. Typically bowel has thickened and purple wall with areas of necrosis may be observed when invaded by Aspergillus. Resection and immediate anastomosis of bowel is performed in favorable cases. It is seen grey necrotic debris covering mucosa removable when the bowel specimen opened.

Mortality rates of invasive aspergillosis remain high despite of early diagnosis.[7,11] One should be careful for invasive aspergillosis in neutropenic patients with fever, abdominal pain and bowel obstruction. Aspergillus antigenemia should be detected and other aspergillus localizations should be evaluated as to start early treatment. It needs to search until diagnosis of fungus.

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