Bölüm 23

PLAZMA HÜCRELİ LÖSEMİ TANI VE TEDAVİSİNDE YENİLİKLER

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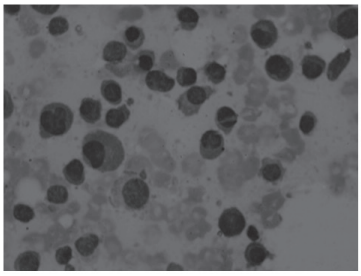
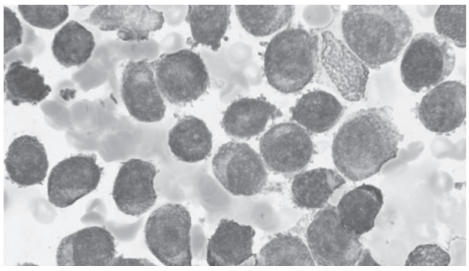
GİRİŞ

Plazma hücre diskrazileri arasında plazma hücreli lösemiler (PHL), en agresif kliniğe sahip ve kötü prognozlu hastalık grubu olarak anılmaktadır. Periferik kan yaymasında olgun veya olgunlaşmamış plazma hücrelerinin (PH) artmış sayıda görülmesi PHL tanısını düşündürür (resim 1.)



Resim1.*



Resim 2. *

İlk PHL vakası 1906'da Gluzinski ve Reichenstein tarafından tanımlanmıştır (Gluzinski & Reichenstein. 1906). Kırk yedi yaşında anemi, splenomegali, sırt ağrısı ve kaburgasında palpe edilen bir kitle ile başvuran bir hastanın periferik yaymasında 2-3 nükleouslu immatur plazma hücreleri görülmüştür. Arsenik içeren bir bileşik ile tedavi edilmeye başlandıktan sonra kitlenin boyutunda belirgin küçülme, ağrı şiddetinde azalma olmasına rağmen, 6 ay sonra ilk pnömoni atağında hasta ex olmuştur. Hastalığın günümüz tanı kriterlerinin temelleri ise

1970'de Robert Kyle ve arkadaşları tarafından ortaya konmuştur (Kyle, Maldonado & Bayrd. 1970).

Klasik bilgi olarak; monoklonal gammapati saptanan hastalarda, perifer kanda dolaşan klonal plazma hücre oranın %20 nin üzerinde ve/veya mutlak plazma hücre sayısının 2x109/L olması tanısaldır (Jimenes-Zepeda & Dominguez 2006).

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Sonuç olarak PHL nadir görülen fakat agresif doğası nedeni ile mortalitesi yüksek seyreden bir plazma hücre hastalığıdır. Son yıllarda miyelom tedavisi ile birlikte klinik pratiğimize kazandırılan yeni ajanlar hastalar hastalığın prognozunda olumlu gelişmelere neden olmuştur. Fakat mevcut tedavilere rağmen hızlı nüks eden, kür sağlanamayan bu hastalıkta kök hücre nakli yerini korumaktadır. Özellikle genç, vericisi bulunan PHL hastalarında allojenik nakil sonrasında yeni ajanlarla kombine edilmiş idame tedavisi, mevcut bilgiler ışığında uygulanabilecek en optimal tedavi seçeneği gibi görünmektedir.

KAYNAKLAR

Gluzinski A, Reichenstein M. Myeloma und leucaemia lymphatica plasmocellularis Wien Klin Wochenschr. 1906;12:336-39.

Kyle RA, Maldonado JE, Bayrd ED. Plasma cell leukemia: report on 17 cases. Arch Intern Med. 1974;133:813-18.

Jiménez-Zepeda VH, Domínguez VJ. Plasma cell leukemia: a rare condition. Ann Hematol. 2006;85:263-7

Avet-Loiseau H, Daviet A, Brigaudeau C, et al. Cytogenetic, interphase, and multicolor fluorescence in situ hybridization analyses in primary plasma cell leukemia: a study of 40 patients at diagnosis, on behalf of the Intergroupe Francophone du Myelome and the Groupe Francais de Cytog en etique Hematolo. Blood. 2001;97:822–825.

Mohite S, Baladandayuthapani V, Thomas SK, et al. Circulating plasma cells by routine complete blood count identify patients with similar outcome as plasma cell leukemia. Blood. 2013;122:5356.

An G, Qin X, Acharya C, et al. Multiple myeloma patients with low proportion of circulating plasma cells had similar survival with primary plasma cell leukemia patients. Ann Hematol. 2015;94:257–64.

Shtalrid M, Shvidel L, Vorst E. Polyclonal reactive peripheral blood plasmacytosis mimicking plasma cell leukemia in a patient with Staphylococcal sepsis. Leuk Lymphoma. 2003; 44:379–80.

Touzeau C, Pellat-Deceunynck C, Gastinne T, et al. Reactive plasmacytoses can mimick plasma cell leukemia: therapeutical implications. Leuk Lymphoma. 2007; 48:207–8.

Tiedemann RE, Gonzalez-Paz N, Kyle RA, et al. Genetic aberrations and survival in plasma cell leukemia. Leukemia. 2008;22:1044-52.

Ramsingh G, Mehan P, Luo J, et al. Primary plasma cell leukemia: a Surveillance, Epidemiology, and End Results database analysis between 1973 and 2004. Cancer. 2009;115:5734–39.

Dimopoulos MA, Palumbo A, Delasalle KB, Alexanian R. Primary plasma cell leukaemia. Br J Haematol. 1994;88:754–59.

García-Sanz R, Orfão A, González M, et al. Primary plasma cell leukemia: clinical, immunophenotypic, DNA ploidy, and cytogenetic characteristics. Blood. 1999;93:1032–37.

Noel P, Kyle RA. Plasma cell leukemia: an evaluation of response to therapy. Am J Med. 1987;83:1062–68.

Liedtke M, Medeiros BC. Plasma cell leukemia: concepts and management. Expert Rev Hematol. 2010;3:543–49.

Sant M, Allemani C, Tereanu C, et al. Incidence of hematologic malignancies in Europe by

morphologic subtype: results of the HAEMACARE project. Blood. 2010;116:3724–34.

Yamamoto JF, Goodman MT. Patterns of leukemia incidence in the United States by subtype and demographic characteristics, 1997-2002. Cancer Causes Control. 2008; 19:379–90.

Musto P, Simeon V, Todoerti K, et al. Primary plasma cell leukemia: Identity card 2016. Curr Treat Options Oncol 2016;17:19.

Blade J, Kyle RA. Nonsecretory myeloma, immunoglobulin D myeloma, and plasma cell leukemia. Hematol Oncol Clin North Am. 1999; 13:1259–72.

Buskard NA, Boyes DA, Grossman L. Plasma cell leukemia following treatment with radiotherapy and melphalan. Can Med Assoc J. 1977 Oct 8;117(7):788-89.

Candoni A, Tiribelli M, Fanin R. Plasma cell leukemia occurring in a patient with thrombocythemia treated with hydroxyurea and busulphan. Leuk Lymphoma. 2004;45:821-4.

Maral S, Bakanay SM, Yikilmaz AS, Dilek I. Development of plasma cell leukemia in a patient with chronic myeloid leukemia while on treatment with imatinib mesylate. J Cancer Res Ther. 2018;14:1431-33

Clayberger C, Wright A, Medeiros LJ, et al. Absence of cell surface LFA-1 as a mechanism of escape from immunosurveillance. Lancet. 1987; 2:533-36.

Kraj M, Kope c-Szlęzak J, Pogło d R, et al. Flow cytometric immunophenotypic characteristics of 36 cases of plasma cell leukemia. Leuk Res. 2011;35:169–76.

Vande Broek I, Leleu X, Schots R, et al. Clinical significance of chemokine receptor (CCR1, CCR2 and CXCR4) expression in human myeloma cells: the association with disease activity and survival. Haematologica. 2006;91:200–6.

van de Donk NWCJ, Lokhorst HM, Anderson KC, et al. How I treat plasma cell leukemia. Blood. 2012;120: 2376–89.

Turhal N, Henehan MD, Kaplan KL. Multiple myeloma: a patient with unusual features including intracranial and meningeal involvement, testicular involvement, organomegaly, and plasma cell leukemia. Am J Hematol. 1998;57:51-6.

Iseki T,Iwasa S,Okuda K et al. IgA-lambda plasma cell leukemia with gum infiltration and pleural effusion. Rinsho Ketsueki. 1987 ;28:428-33.

Klug S, Höltermann F, Fritsch H. IgG-lambda-type multiple myeloma with plasma-cell pericardial effusion and terminal plasma-cell leukemia. Dtsch Med Wochenschr. 1992;117:900-4.

Vela-Ojeda J, Garcia-Ruiz Esparza MA, Rosas-Cabral A, et al. Intermediate doses of melphalan and dexamethasone are better than vin- cristine, adriamycin, and dexamethasone (VAD) and polychemotherapy for the treatment of primary plasma cell leukemia. Ann Hematol. 2002; 81:362-367.

Costello R, Sainty D, Bouabdallah R, et al. Primary plasma cell leukaemia: a report of 18 cases. Leuk Res. 2001;25:103-7.

Pagano L, Valentini CG, De Stefano V, et al. Primary plasma cell leukemia: a retrospective multi- center study of 73 patients. Ann Oncol. 2011; 22:1628-35.

Colovic M, Jankovic G, Suvajdzic N, et al. Thirty patients with primary plasma cell leukemia: a single center experience. Med Oncol. 2008;25:154-60.

Woodruff RK, Malpas JS, Paxton AM, et al. Plasma cell leukemia (PCL): a report on 15 patients. Blood. 1978;52:839-45.

Avet-Loiseau H, Roussel M, Campion L, et al. Cytogenetic and therapeutic characterization of primary plasma cell leukemia: the IFM experience. Leukemia. 2012;26:158-59.

Chang H, Qi X, Yeung J, et al. Genetic aberrations including chromo- some 1 abnormalities and clinical features of plasma cell leukemia. Leuk Res. 2009;33:259-262.

Chiecchio L, Dagrada GP, White HE, et al. Frequent up-regulation of MYC in plasma cell leukemia. Genes Chromosomes Cancer. 2009;48:624-36.

Musto P, D'Auria F, Petrucci MT, et al. Final results of a Phase II study evaluating lenalidomide in combination with low-dose dexamethasone as first-line therapy for primary plasma cell leukemia. Blood (ASH Annual Meeting Abstracts). 2011;118:2925.

Xu W, Li JY, Fan L, et al. Molecular cytogenetic aberrations in 21 Chinese patients with plasma cell leukemia. Int J Lab Hematol. 2009;31: 338-43.

Chang H, Yeung J, Xu W, et al. Significant increase of CKS1B amplification from monoclonal gammopathy of undetermined significance to multiple myeloma and plasma cell leukaemia as demonstrated by interphase fluorescence in situ hybridisation. Br J Haematol. 2006;134: 613-15.

Gutiérrez NC, Hernández JM, García JL, et al. Differences in genetic changes between multiple myeloma and plasma cell leukemia demonstrated by comparative genomic hybridization. Leukemia. 2001; 15:840-45.

Pérez-Andrés M, Almeida J, Martín-Ayuso M, et al. Clonal plasma cells from monoclonal gammopathy of undetermined significance, multiple myeloma and plasma cell leukemia show different expression profiles of molecules involved in the interaction with the immunological bone marrow microenvironment. Leukemia. 2005;19:449-55.

Avet-Loiseau H, Attal M, Moreau P, et al. Genetic abnormalities and survival in multiple myeloma: the experience of the Intergroupe Francophone du Myelome. Blood. 2007;109:3489-95.

Fonseca R, Blood EA, Oken MM, et al. Myeloma and the t(11;14)(q13;q32); evidence for a biologically defined unique subset of patients. Blood. 2002;99:3735-41.

Usmani SZ, Nair B, Qu P, et al. Primary plasma cell leukemia: clinical and laboratory presentation, gene-expression profiling and clinical outcome with Total Therapy protocols. Leukemia. 2012;26:2398–405.

Cifola I, Lionetti M, Pinatel E, et al. Whole-exome sequencing of primary plasma cell leukemia discloses heterogeneous mutational patterns. Oncotarget. 2015;6:17543–58.

Lionetti M, Barbieri M, Todoerti K, et al. Molecular spectrum of BRAF, NRAS and KRAS gene mutations in plasma cell dyscrasias: implication for MEK-ERK pathway activation. Oncotarget. 2015;15:24205–17.

Lionetti M, Musto P, Di Martino MT, et al. Biological and clinical relevance of miRNA expression signatures in primary plasma cell leukemia. Clin Cancer Res. 2013;19:3130–42.

Jelinek T, Kryukov F, Rihova L, et al. Plasma cell leukemia: from biology to treatment. Eur J Haematol. 2015;95:16–26.

Fernandez de Larrea C, Kyle RA,Durie BGM,et al. Plasma cell leukemia: consensus statement on diagnostic requirements, response criteria and treatment recommendations by the International Myeloma Working Group. Leukemia. 2013;27:780–91.

Pellat-Deceunynck C, Barill e S, Jego G, et al. The absence of CD56 (NCAM) on malignant plasma cells is a hallmark of plasma cell leukemia and of a special subset of multiple myeloma. Leukemia. 1998;12:1977–82.

Guo J, Su J, He Q, et al. The prognostic impact of multiparameter flow cytometry immunophenotyping and cytogenetic aberrancies in patients with multiple myeloma. Hematology. 2016;21:152–61.

Murray ME, Gavile CM, Nair JR, et al. CD28-mediated prosurvival signaling induces

chemotherapeutic resistance in multiple myeloma. Blood. 2014;123: 3770–79.
Gonsalves W.I., Rajkumar S.V., Go R.S. Trends in survival of patients with primary plasma cell leukemia: a population-based analysis. Blood. 2014;124:907–12.
Musto P, Pietrantuono G, Guariglia R, et al. Salvage therapy with lenalidomide and dexamethasone in relapsed primary plasma cell leukemia. Leuk Res. 2008;32:1637–1638.
Guglielmelli T, Merlini R, Giugliano E, et al. Lenalidomide, melphalan, and prednisone association is an effective salvage therapy in relapsed plasma cell leukaemia. J Oncol. 2009;2009:867380.
Lebovic D, Zhang L, Alsina M, et al. Clinical outcomes of patients with plasma cell leukemia in the era of novel therapies and hematopoietic stem cell transplantation strategies: a single-institution experience. Clin Lymphoma Myeloma Leuk. 2011;11:507–11.
Royer B, Minvielle S, Diouf M, et al. Bortezomib, Doxorubicin, Cyclophosphamide, Dexamethasone induction followed by stem cell transplantation for primary plasma cell leukemia: a prospective phase II study of the intergroupe francophone du myelome. J Clin Oncol. 2016;34:2125–32.
Jaskiewicz AD, Herrington JD, Wong L. Tumor lysis syndrome after bortezomib therapy for plasma cell leukemia. Pharmacotherapy. 2005;25:1820–25.
Petrucci MT, Martini V, Levi A, et al. Thalidomide does not modify the prognosis of plasma cell leukemia patients: experience of a single center. Leuk Lymphoma. 2007;48:180–82.
Johnston RE, Abdalla SH. Thalidomide in low doses is effective for the treatment of resistant or relapsed multiple myeloma and for plasma cell leukaemia. Leuk Lymphoma. 2002;43:351–54.
Bauduer F. Efficacy of thalidomide in the treatment of VAD-refractory plasma cell leukaemia appearing after autologous stem cell transplantation for multiple myeloma. Br J Haematol. 2002;117:996–97
Musto P, Simeon V, Martorelli MC, et al. Lenalidomide and low-dose dexamethasone for newly diagnosed primary plasma cell leukemia. Leukemia. 2014;28: 222–25.
Olivieri A, Attolico I, Cimminiello M, et al. Lenalidomide can induce graft versus leu- kemia effect in primary plasma cell leukemia: a case report. Leuk Res. 2009;33:191–3.
Mele G, Coppi MR, Guaragna G, et al. Response to pomalidomide plus fixed low-dose dexamethasone in a case of secondary plasma cell leukaemia. Leuk Res. 2016;40:30–2.
Yamashita Y, Tamura S,Oiwa T et al. Successful Intrathecal Chemotherapy Combined with Radiotherapy Followed by Pomalidomide and Low-Dose Dexamethasone Maintenance Therapy for a Primary Plasma Cell Leukemia Patient.Hematol Rep.2017:9;6986
Katodritou E, Terpos E, Kelaidi C, et al. Treatment with bortezomib-based regimens improves overall response and predicts for survival in patients with primary or secondary plasma cell leukemia: analysis of the Greek myeloma study group. Am J Hematol. 2014;89:145–50.
Reece DE, Phillips M, Chen CI, et al. Induction therapy with Cyclophosphamide, Bortezomib, and Dexamethasone (CyBorD) for primary plasma cell leukemia (pPCL). Blood. 2013;122:abstract 5378
Jimenez-Zepeda VH, Reece DE, Trudel S, et al. Lenalidomide (Revlimid), Bortezomib (Velcade) and Dexamethasone for the treatment of secondary plasma cell leukemia. Leuk Lymphoma. 2015;56:232–35.
McElwain TJPR. High-dose intravenous melphalan for plasma cell leukaemia and mye-

loma. Lancet. 1983;2:822–24.
Drake MB, Iacobelli S, van Biezen A, et al. Primary plasma cell leukemia and autologous stem cell transplantation. Haematologica. 2010;95:804–9.
Mahindra A, Kalaycio ME, Vela-Ojeda J, et al. Hematopoietic cell transplantation for primary plasma cell leukemia: results from the Center for International Blood and Marrow Transplant Research. Leukemia. 2012;26:1091–97.
Morris C, Iacobelli S, Gahrton G, et al. Has allogeneic transplantation a role in the management of plasma cell leukaemia? a study on behalf of the myeloma subcomittee of the chronic leukaemia working party of the EBMT. Blood. 2011;118:Abstract 2008.