Giant Conjunctival Melanoma with Breast Cancer and Chronic Lymphocytic Leukemia: A Case Report and Mini-Review of the Literature

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ABSTRACT Our aim is to present a case with rapidly progressing conjunctival malign melanoma who was taking treatment for invasive ductal breast cancer and chronic lymphocytic leukemia. 83-year-old male patient with chronic lymphocytic leukemia and breast cancer was presented with a rapidly growing hyperpigmented mass on his upper left eyelid. Slit-lamp examination showed a hyperpigmented mass in the upper tarsal conjunctiva and diffuse hyperpigmentation in the lower tarsal conjunctiva of the left eye. The patient was diagnosed as conjunctival melanoma with rapid progression. We performed exenteration surgery and removed all suspicious tissues. Histopathology report revealed nodular type malign melanoma. Rapidly growing conjunctival melanomas which co-exist with multiple malignancies require more frequent follow-ups and early treatment.

Keywords: Melanoma; breast neoplasms, male; leukemia, lymphocytic, chronic, b-cell; conjunctival neoplasms; conjunctival diseases


Anahtar Kelimeler: Melanom; meme neoplazileri, erkek; lösemi, lenfositik, kronik, b hücreli; konjonktival neopaziler; konjonktival hastalıkları

Well-known risk factors for conjunctival malignant melanomas (CM) are hyperpigmented nevus, family history, ultraviolet (UV) light exposure, genetic syndromes like familial melanoma syndrome, xeroderma pigmentosum, Hodgkin’s lymphoma and hereditary retinoblastoma. However, there is still limited data about risk factors because of its the low incidence.1–6 Primary acquired melanosis causes 75% of CM, while existing nevus is responsible for 20% and 5% of CM occurs as de novo.7–9 It account for 0.25% of all melanomas, 2% of extraocular tumours and 5% of ocular region melanomas.10,11 It mostly develops on bulbar conjunctiva (60-92%) due to the direct UV and it usually has typical pigmentation, however some of them may be amelanotic (15–19%) which can be difficult to differ-
entiate from ocular surface squamous tumours and lymphoma.\textsuperscript{7,8} Significant increase in the incidence of conjunctival melanoma was observed in the age group over 60 years and among white men.\textsuperscript{12}

Conjunctival melanomas are usually diagnosed by well obtained history, careful physical examination and slit-lamp microscopy. History and physical examination should include age, symptoms, sun exposure, development and growth rate of the lesion, cancer history, inspection of eyelids and neighbouring tissues, ocular surface examination, lymph node palpation. Pigmentation on the tarsal conjunctiva should increase the suspicion of CM.\textsuperscript{13}

In this paper, we present a case with rapidly progressing conjunctival malignant melanoma who was taking treatment for invasive ductal breast cancer and chronic lymphocytic leukemia (CLL). Increased incidence of malignant melanoma and breast cancer in CLL patients is well established in the literature, however, to best of our knowledge, this is the first case with co- incidental CM, CLL and breast cancer. There is limited information regarding the treatment of these cases in the literature. These secondary cancers are thought to occur because of the immune suppression in CLL patients. We aimed to draw attention to the aggressive course and the need of immediate treatment for these cases.

\section*{CASE REPORT}

A 83-year-old caucasian male admitted to hospital with 2x2 cm sized mass on the nipple of left breast. Breast ultrasonography showed 2x3 cm mass on the areola of the left breast with left and right axillary lymph node metastasis. Laboratory tests revealed hemoglobin level of 11.9 g/dl, white blood cell count of 14 500 cells/µl (neutrophils, 38\% [normal range: [NR]:34-71]; lymphocytes, 62\% [NR:19.3-51.7]; monocytes, 2.1\% [NR:4.4-12.5]), platelet count of 356 103 cells/µl (NR: 182-369), lactate dehydrogenase (LDH) level of 250 units/l (NR: 125-247), erythrocyte sedimentation rate (ESR) of 45 mm/h (NR: 1-20). Excisional biopsy was performed for breast mass and pathologic evaluation was reported as invasive ductal carcinoma, estrogen 95\% positive, progesterone 70\% positive and HER 3 +++ positive. Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) was performed for the staging of breast cancer. 18F-FDG PET/CT revealed the involvement of mediastinal lymph nodes and bilateral axillary lymph nodes, and hypermetabolic mass in the left breast. Owing to higher lymphocyte rate in complete blood count and common lymph nodes involvement in 18F-FDG PET/CT scan, a flow cytometry analysis from peripheral blood sample was performed. CD5 was 93\% and patient was diagnosed with CLL. CLL was staged as II according to Ann Arbor staging system. Chemotherapy for CLL was not administered thanks to absence of B symptoms, anemia, hemolytic anemia, thrombocytopenia. Chemotherapy was administered for breast cancer as trastuzumab 6 mg/m\textsuperscript{2}, carboplatine (AUC6), and docetaxel 75 mg/m\textsuperscript{2} intravenously (IV) per three weeks for three cycles, then oral tamoxifen 10 mg per day was started. Patient did not want to be operated for breast cancer and he was followed only with hormone therapy. While the patient was taking hormone therapy, he admitted to ophthalmology department of Gaziantep University with a rapidly growing, painless mass on the upper left eyelid. Best corrected visual acuities (BCVAs) were 5/10 and 2/10 in the right and left eyes, respectively. Slit-lamp examination showed nuclear scleros in the right eye, hyperpigmented mass in the upper tarsal conjunctiva and diffuse hyperpigmentation in the lower tarsal conjunctiva of the left eye (Figure 1A). Fundus examination, fundus fluorescein angiography and optical coherence tomography were normal in both eyes. We sent the patient for orbital magnetic resonance imaging (MRI). When the patient has returned with his MRI results two weeks later, the mass had grown and covered the whole interpalpebral fissure (Figure 1B). Orbital MRI revealed a 17x9 mm mass on the anterior of left globe which extends to lateral rectus muscle (Figure 1C). We performed exenteration surgery and removed all suspicious tissues. Histopathology report revealed nodular type malignant melanoma (Figure 1E-F). Patient was referred to oncology department for further treatment. An in-
formed consent was obtained from the patient for reporting his medical data.

**DISCUSSION**

Conjunctival melanomas arise from melanocytes settled in the basal layer of the epithelium of the conjunctival membrane which is a vulnerable area on account of direct exposure to sun radiation unlike the other mucous membranes. A large retrospective study evaluated the 84,836 cases with cutaneous and non-cutaneous malign melanoma during 9 years. Accordingly, the rate of cutaneous, ocular, mucosal, and unknown primaries site melanomas were 91.2%, 5.2%, 1.3%, and 2.2%, respectively. Ocular melanomas were the second most frequent type of the malign melanomas and 85.0% of all were uveal, 4.8% were conjunctival melanomas. Several clinical factors are associated with high mortality, including advanced stage, tumor size, extrabulbar location, caruncular location and invasion of adjacent tissues, nodular or acral lentiginous histology, increased age, male gender, and lower income features. The most common symptoms are pigmented spot or lump, and irritation on conjunctiva, our case applied with a round, hyperpigmented, giant mass which is different from other presentations in the literature.

Primary treatment modalities are wide local excision in the case of patient which is suitable for resection with adjuvant therapy, including cryotherapy, brachytherapy, and topical mitomycin C. Despite the effective treatment options for the conjunctival malign melanoma, high local recurrence rate is still the most important problem for the management of the disease. It is a rare ophthalmologic pathology with high mortality risk which may infiltrate neighbouring tissues and spread systemically via lymphatic and hematogenous pathways, and can show recurrence despite treatment. It may spread extensively in 1% of the patients and this invasion usually occurs via lymphatic pathways. Orbital exenteration as the primary therapy is used for advanced conjunctival melanoma as in our case. Although survival benefit with early exenteration was not shown, owing to course of locally advanced tumor with multiple recurrences, unfortunately exenteration remains as the primary treatment approach in this area and was performed still in about one third of cases.

Previous studies showed that patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) have increased risk of developing a secondary cancer and an increased frequency of certain cancer types. Possible responsible pathogenesis are administered chemotherapy and radiotherapy, and underlying immune dysfunction. Untreated 2,028 patients with CLL/SLL were analysed to determine the co-incidence the other malignancies rates. Accordingly, 16% of all had a history of other cancers at diagnosis and 11.2%
developed other malignancies during the follow-up and treatment period. Rate of breast cancer coincidence with CLL/SLL was 9% and it was 9% for malign melanoma.28 Lam et al. showed that melanoma risk after CLL/SLL was significantly increased among patients who received infused fluorouracil-containing chemotherapy with or without rituximab (hazard ratio [HR], 1.92; 95% CI, 1.09-3.40, HR, 2.92; 95% CI, 1.42-6.01, respectively).29 All mentioned studies above were evaluated malign melanoma of skin cancer unlike our patient, ocular melanoma. Also our case did not take immunosuppressive treatment for CLL, he only received tamoxifen for breast cancer. Presented case is the first case in the literature with ocular melanoma which co-existed with CLL and breast cancer.

In conclusion, local excision, chemotherapy or brachytherapy are the treatment options for early detected conjunctival malign melanomas. We had to perform exenteration in our case because of the rapidly growing lesion and the risk of metastasis. Rapidly growing conjunctival melanomas which co-exists with multiple malignancies require frequent follow-ups and early treatment.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions


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