Case Report

Cutaneous Extramedullary Plasmacytoma with Multiple Nodular Skin Lesions with an unexpected involvement of lip
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Abstract
Extramedullary Plasmacytoma of the skin is a rare condition especially appears with multiple skin nodules localised on chest, back, and abdomen. Here, we report a case of 47-year-old man with known extramedullary plasmacytoma who had a cervical mass initially. The patient developed cutaneous lesions on the lip, scalp, chest wall and leg in the course of the disease. Lip was an unusual involvement site in an unusual disease, cutaneous plasmacytoma. His bone marrow biopsy showed no myeloma infiltration. The histopathological diagnosis was IgGκ extramedullary plasmacytoma. Chemotherapy and radiotherapy was applied but treatment response was not good overall. Radiotherapy was effective in reducing tumor bulk and the pain associated with the lesions. However, the patient died five months later due to the systemic myeloma infiltration.

Keywords: Cutaneous; Chemotherapy; Extramedullary; Leukemia; Plasmacytoma; Radiotherapy.


Introduction
Extramedullary plasmacytoma (EP) is a plasma cell tumor that involves soft tissues, without any signs of systemic spread of multiple myeloma (MM).\(^1\) EP of the skin is an uncommon condition which is mostly seen as a direct extension from a bony focus and rarely found as initial manifestation of the disease without evidence of coexisting MM. As in EP, specific skin involvement in patients with other types of malignant plasma cell tumors, multiple myeloma, solitary and multifocal bone plasmacytoma and plasma cell leukemia) is uncommon. Chest, back, and abdomen are the most frequently involved areas in EP.\(^2\) Here we report a rare case of 47-year-old man with extramedullary plasmacytoma and multiple cutaneous involvements. The clinicopathologic features, prognostic factors and treatment modalities of this rare disease with its unusual involvement of cutaneous plasmacytoma of lip is being discussed.

Case Report
A 47-year-old man was referred to our hospital with complaint of pain and muscle weakness on his neck and left arm. He had multiple painless, red and waxy nodular skin lesions on his lip, scalp, chest, back, and leg changing in size from one to 60 mm. The lesion appeared on lip was nodular, reddish and 2 x 2 cm in size (Fig 1a). The morphological appearance of other lesions was similar (Fig 1b &c). He had no history of allergic reactions, infectious, or inflammatory disease. He had a medical history of EP fourteen months before the referral. Initial presentation of the patient was neck pain. On his cervical magnetic resonance imaging, a 6x6x4 cm solitary tumor lying paravertebrally between foramen magnum and third cervical vertebra, was detected. Positron Emition-Computerized Tomography also revealed high pathological uptake on the tumor and other parts of the body showed no pathological uptake. Systemic evaluation was normal and bone marrow biopsy was negative for myeloma infiltration.

The immunohistopathologic confirmation of the biopsy from the lesion revealed kappa light chain monotype plasmoblastic high grade neoplastic infiltrate. On the laboratory findings Ig-G was high. The diagnosis was immunoglobulin g-kappa (IgGκ) extramedullary plasmacytoma. Histopathologically the tumor was composed of a relatuity uniform population of large cells with scant cytoplasm, a vesicular nucleus with fine reticular chromatin and one or more large nucleolus. Necrosis and frequent mitotic figures were present (Fig 1d). The neoplastic cells were strongly positive for CD138 (Fig 1e) and CD79a with a light chain restriction and were negative for CD20, CD56, and Epstein-Barr virus–encoded RNA (EBER).
The patient had been referred to surgery department for surgical procedure. After the evaluation the mass was found to be inoperable. Due to the severe neck pain, the patient has been referred to a radiation oncology department and received palliative radiotherapy to the tumor. Radiation therapy was prescribed as 2Gy per fraction per day to a total dose of 50Gy encompassing the visible lesion on MRI on linear accelerator machine. His pain was decreased but not disappeared after the end of the radiotherapy. Then the patient was referred to hematology department and received VAD (vincristine, doxorubicin, and dexamethasone) chemotherapy.

After two cycles of chemotherapy, the neck pain was returned and a new pain and weakness appeared on his left arm. The patient underwent cervical MRI and a tumor lying between second and seventh vertebra (on his left neck and left axilla) was detected. At the same time cutaneous lesions appeared on his chest wall, leg, face and scalp. Due to the symptom progression, the patient was referred to our clinic for palliative radiotherapy. Also a biopsy from nodular lesion on the chest wall was taken and the histopathological diagnosis was same with the initial biopsy specimen. The cutaneous lesions were papillary / nodular and in red, pinkish or yellow colour. Also there was a lesion on the lip in same appearance with other lesions. There was no ulceration and necrosis. There was no pain associated with the cutaneous lesions.

We prescribed an external beam radiation dose of 39Gy (3Gy/day, 5 days/week) on linear accelerator machine with 3-D conformal radiation encompassing gross tumor volume according to the CT images applied for radiation planning (Fig 1f). After the end of the radiotherapy his pain was decreased, but the cutaneous lesions were enlarged and multiplied, and a pain appeared on larger lesions. Therefore another palliative irradiation was planned for the most symptomatic and large lesions located on his chest and leg. At the same time, due to the rapid progression of the cutaneous lesions patient received one cycle of chemotherapy, again. The lesions were regressed during radiotherapy but the patient discontinued the treatment course, because of the systemic progression of the disease. The patient died five months after the first skin lesions developed.

Discussion
Primary cutaneous plasmacytoma (CP) is a rare condition with relatively limited data. As well as cutaneous involvement in patients without the diagnosis of MM is rare. Cutaneous involvement by malignant plasma cell tumors defined as CP may appear in any area of the skin whether primary or metastatic. Clinically, cutaneous lesions are solitary or multiple (up to 50) reddish to purple nodules or plaques with no predilection site. However, It has been shown that chest, back, and abdomen are the most frequently involved areas. Face, scalp, neck, and extremities are later most seen localisations. Scrotum, eyelid, tongue and perianal area, are rarest localisation of CP reported in the literature. According to the literature lip is relatively an unusual site affected by CP, appeared in our case.

The pathophysiology is unknown how myeloma cells attack skin. In a case report, it has been shown that lymphocyte function–associated antigens and intercellular adhesion molecules may have contributed to this pattern of growth through endothelial cells. In a report, alterations in natural killer (NK) cell activity have been implicated as a factor in the malignant plasma cells spreading to the skin. The third hypothetic pathophysiology in CP is ectaxis (the migration of circulating cells into tissues with an appropriate microenvironment) which has been suggested for lymphoid cells in lymphoid neoplasms. Also in myelomatous cells, the same pathophysiologic pathway can be valid in cutaneous metastatic process.

The sizes and shapes of the cutaneous lesions can vary. They can appear as papules or cutaneous lesions with firm consistency, smooth surface, and a red or violaceous color. Lesions are sometimes very large in size, and may be in the form of nodule or plaques and ulceration of the nodules is rarely detected. Usually the lesions range in diameter from 1 to 5 cm. Also the cutaneous lesions appeared as papillary and mostly nodular in our patient without ulceration. There are several treatment strategies in CP, such as thalidomide, bortezomib, dexamethasone and radiotherapy. All of them have effective disease control, has been reported in the literature.

Cutaneous involvement has been developed on the same time with the second
paravertebral EMP in our patient. Because of the rapid progression of cutaneous lesions patient received both chemotherapy and palliative radiation therapy, concomittantly. The palliative effect of radiotherapy was well on EMP and on CP, too. The cutaneous lesions were being to disappear while radiation therapy was continuing. But radiation therapy was terminated early due to the rapidly systemic dissemination of the disease.

Figure 1: The clinical picture showing cutaneous plasmacytoma on lip (a), on chest wall (b) and on scalp (c). The photomicrograph showing monomorphic plasmablastic cytologic features (Hematoxylin-eosin, ×400) (d) and cells expressing immunopositivity for CD138 (x400) (e). The computerized tomographic image of extramedullary plasmacytoma located on left neck (f).

Cutaneous plasmacytoma generally appears in the late course of the disease. Some authors have argued that, cutaneous involvement occurs when the total body tumor cell mass is large. The skin lesions developed fifteen months after the first EP diagnosis and the lesions were multiplied while the disease was recrudescing in the patient. The IgG subtype is the most reported subtype to be associated with skin involvement. Consistent with the literature, the diagnosis of our patient was IgGκ extramedullary plasmacytoma. The survival is generally short in patients with CP, because most of the patients have extensive tumor burden, and on account of this, patients have poor prognosis. Most of the patients die 12 months after the diagnosis of CP. However better prognosis and an indolent course of the disease is reported in solitary CP.

Five months after the first skin lesions developed, the patient died from disseminated disease. Consistently with the literature, the prognosis was poor and the
survival was short after multiple skin involvements developed. On palliative meaning, radiation treatment was effective in reducing tumor bulk and the pain associated with the lesions.

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