Melanoma of Unknown Primary With Liver Metastasis and Widespread Vitiligo

Ahmet Gulmez1, Tamer Elkıran2

Abstract
The majority of malignant melanoma patients have a detectable primary lesion. However, only a small proportion of melanoma patients have distant metastasis and no primary lesion can be detected. Melanoma of unknown primary (MUP): it is usually detected in the lymph nodes, subcutaneous tissues, and eventually the internal organs.

MUP is more common in males than females. Generally, it is more frequently diagnosed in the fourth and fifth decades. The reason why it is more common in men than in women cannot be explained clearly. According to past genetic analysis; there were significant differences in pathogenetic mutations between cutaneous, acral, and mucosal melanomas. In the literature, a variety of visceral organ involvement has been reported in patients presenting with metastases without detecting a primary lesion in melanoma patients. These organs can be listed as follows: Brain, parotid gland, heart, mediastinum, lung, breast, liver, common bile duct, thin and thick intestine, kidney, adrenal gland, prostate, bone, bone marrow, and muscle.

In this case, we reported a patient with melanoma with liver metastasis whose primary lesion could not be detected. In addition, the patient has a history of widespread vitiligo-like skin lesions, which has been reported to have started 30 years ago.

Keywords: Malign Melanoma; Melanoma of known primary; Liver Metastases; Vitiligo

Introduction
More than 97% of the patients with melanoma present a primary site. The most common primary lesion site is skin, followed by eye and mucous membranes [1]. Rarely, melanoma is diagnosed without a clear primary site and is called MUP. The MUP was first described by Das Gupta in 1963 [2].

The majority of MUP cases are nodal (60%) and the most common sites are axilla, neck and groin regions. The remaining cases include subcutaneous tissue and various visceral regions [3]. Despite evidence of a similar or more favorable prognosis compared to melanomas with primary known; MUPs often cause more anxiety and may require different approaches [4]. In this case we presented; We talked about a patient who had liver metastasis and could not detect a primary lesion and had widespread vitiligo-like lesions.

Case Report
A 75-year-old male patient with previously known benign prostatic hypertrophy and hypertension was admitted to the hospital with abdominal pain. The patient’s abdominal examination did not reveal any finding other than common sensitivity. But; vitiligo-like lesions were observed on the hands and back of the patient. Patient; said that the existing lesions began to emerge 30 years ago and gradually increased. In addition, he stated that he did not use any treatment for skin lesions. There is no history of operation in the patient’s medical history. Abdominal ultrasonography was performed on the patient who had no sign of significant physical examination. A large number of lesions with a size of 49x47 millimeters (mm) were detected in the liver. Abdominal magnetic resonance (MR) and thorax computed tomography (CT) were performed. As a result of MRI; A large number of lesions with a diameter of 62x32 mm were detected in the liver.

In addition, several pulmonary nodules less than 1 cm (cm) were found in the lung. Endoscopy and colonoscopy were performed because of possible gastrointestinal system malignity. A mucosal pathology could not be detected in the patient’s endoscopy and colonoscopy.

Tru-cut biopsy was planned from the lesion in the liver. As a result of biopsy; S-100, Melan A, Vimentin positive; PanCK negative, histopathological diagnosis was reported as malignant melanoma. After the pathology report, skin examination of the patient was repeated by dermatologist physician in terms of primary lesion detection. In the skin examination, no lesion was considered to suggest the primary. The patient’s eye examination was performed by an ophthalmologist and no lesion was found to suggest a primary lesion in the eye. Gastrointestinal screening was previously performed by gastroenterologist and no mucosal lesion was detected. With current findings; He was accepted as MUP patient with liver metastasis with diffuse vitiligo-like lesions.

Discussion
In 2009, according to the American Joint Cancer Joint Committee (AJCC) melanoma staging system, MUP was classified as stage III disease if there was LN or subcutane involvement at the first admission and in case of visceral involvement it was classified as stage IV disease [5].

In a study performed by Oberholzer PA et al. Serum S-100 protein and positron emission tomography (PET) are recommended for basal staging in MUP patients. In the same study, S-100 protein was found to be statistically significant in patients with distant metastasis [6].

According to the dominant hypothesis for the mechanism of MUP formation, it occurs as a result of the spontaneous regression of melanoma in a known primary region. The regression theory first proposed by Smith and Stehlin in 1965 shows that primary melanoma was lost by spontaneous regression after metastasis [7].

The partial or complete spontaneous regression of melanoma from a known primary site has been well documented in the literature. Melanoma; 11%
of cases of spontaneous tumour or regression in all cancers [8–11]. Spontaneous regression of melanoma is associated with both cell mediated and humoral immune mechanisms [12].

As a result of a recent systematic review, the real incidence of MUP has been clarified. When children and adolescents are excluded from analysis; MUP was detected in 3.2% of all melanoma patients [13]. The highest incidence of MUP may be similar to cutaneous melanoma; however, it occurs in the fourth and fifth decades of life earlier than the mucosal and ocular melanoma [1,14].

MUP was most frequently diagnosed in lymph nodes (40-60% of all cases) and reported to contain axillary, cervical, inguinal and parotid lymph nodes in 52.2, 32.7, 28.3 and 2.6%, respectively [13-16]. In men, MUP is most commonly seen in axillary and cervical lymph nodes, whereas in women it is more likely to appear in lymph nodes in inguinal [13].

MUP can be combined with various clinical tables as a paraneoplastic syndrome, reported as retinopathy, systemic vasculitis, inflammatory demyelinating polyneuropathy, diffuse vitiligo-like depigmentation, and Gorham-Stout syndrome, or vanishing bone disease [17-22]. Vitiligo-like depigmentation; seems to be a widespread presentation of widespread metastatic disease. And in a previously case reported, it could be determined about 18 months before the discovery of MUP [20,23,24].

In our case; It is known that the patient’s vitiligo lesions first appeared 8 years before. These lesions began on the dorsal side of the hands first and gradually increased. In the literature, there is a case report that the primary lesion occurred on the skin 18 months after the diagnosis of MUP [25].

In another similar case report; After melanoma metastasis detected in the liver, the patient received chemotherapy and radiotherapy, 6 years after the diagnosis of MUP, the primary lesion was detected in the nasopharyngeal region [26]. In another case report, in a patient with melanoma in the small bowel, a primary lesion in the scalp was apparent after 15 years [27].

In a study of 103 MUP patients; 94% of the patients were examined by an ophthalmologist, 82% were examined by an otolaryngologist and 89% of them were examined by a gynecologist. In addition, additional gastrointestinal imaging including sigmoidoscopy and proctoscopy was performed in 92% of MUP patients [28].

In a previously reported case report; A left axillary mass occurred in a patient who had a black macula in the left axilla 17 years ago. This patient also had vitiligo-like skin lesions. However, these lesions began to occur 16 months before the axillary mass lesion occurred. The patient’s mass lesion biopsy was compatible with melanoma [23].

In the patient we have presented; After the lesion was detected in the liver, endoscopy and colonoscopy were performed. After the pathology result is compatible with melanoma; The patient underwent a detailed skin examination by the dermatologist and his ophthalmological examination was performed by the ophthalmologist. As a result of the examination, no lesion was found to suggest a primary lesion. In cases reported in the literature, the occurrence time of vitiligo-like skin lesions is expressed in months. In the patient we presented; vitiligo-like skin lesions have been present for 30 years. As a result of literature review; We could not identify an article reporting the association of vitiligo in patients with MUP with liver metastasis. For this reason; We think that it will contribute to the literature.

It is pleasing that MUP patients have a relatively better prognosis than patients with Melanoma with known primary (MKP). However, it should be kept in mind that close follow-up and treatment approaches of patients with stage 3-4 are the same for patients with MKP.

References


Author(s) information

Ahmet Gulmez [Gulmez A]*
Tamer Elkıran T [ElkıranT]*

*Department of Oncology, Inonu University Medical School, Malatya, Turkey

Corresponding Author
Ahmet Gulmez, Department of Oncology, Inonu University Medical School, Malatya, Turkey. Email: doktor.ahmetgulmez@gmail.com