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Lipidized Dermatofibroma: The Clinical and Demographic Characteristics of Twelve Cases

Lipidize Dermatofibrom: On İki Olgunun Klinik ve Demografik Özellikleri

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ABSTRACT Objective: Lipidized dermatofibroma is a rare and lesser-known variant of dermatofibromas. This study aimed to reveal the clinical and demographic features of lipidized dermatofibromas. **Material and Methods:** Histopathologically confirmed twelve cases of lipidized dermatofibroma were included in the study and retrospectively evaluated. Clinical and demographic characteristics such as patients' age, sex, location and duration of lesions, lesion size and serum total cholesterol and triglyceride values of the patients were evaluated from their medical records. **Results:** The ages of the patients ranged from 36 to 65 years, with a mean of 51 years. The size of the lesion varied between 1.5 cm and 4 cm. All lesions were located on the lower extremities with 75% being below the knee. Seven lesions were tumoral. Some of the exophytic lesions were yellow in color macroscopically and the others were recorded to be yellow in color during biopsy. Eighty percent of the cases had a high serum level of either cholesterol or triglyceride or both. **Conclusion:** Lipidized dermatofibromas occur at a later age than classic dermatofibromas. They are larger than classic dermatofibromas and they may be identical to giant dermatofibromas. Larger dermatofibromas tend to be lipidized and localized in the lower extremity. Since this situation necessitates histopathological validation, diagnosed lipidized dermatofibromas are usually located on the lower extremities. The yellow areas observed in a dermatofibroma may be an indication of lipidized form. The lipidization can be related to the high cholesterol levels of the patients.

Keywords: Ankle; histiocytoma, benign fibrous; dermatofibroma

ÖZET Amaç: Lipidize dermatofibrom, dermatofibromların nadir ve az bilinen bir varyantıdır. Çalışmanın amacı, lipidize dermatofibromların klinik ve demografik özelliklerini tanımlamaktır. **Gereç ve Yöntemler:** Histopatolojik olarak tanısı doğrulanmış 12 lipidize dermatofibrom olgusu çalışmaya dâhil edildi ve retrospektif olarak değerlendirildi. Hastaların yaşı, cinsiyeti gibi demografik özellikleri ile birlikte lezyonların yeri, süresi, boyutu ve hastaların serum total kolesterol ve trigliserid seviyeleri medikal kayıtlarından değerlendirildi. **Bulgular:** Hastaların yaşı 36-65 arasında değişiyordu, ortalama yaş 51 idi. Lezyon boyutu 1.5-4 cm arasında değişmekteydi. Lezyonların %75'i diz altında olmak üzere tüm lezyonlar alt ekstremiteye lokalizeydi. Lezyonların 7'si tümöral lezyon şeklindeydi. Ekzofitik lezyonların bazıları makroskobik olarak sarı renkteydi, diğer lezyonların ise biyopsi esnasında sarı renkte oldukları gözlendi. Hastaların %80'inde, serum kolesterol veya trigliserid düzeyleri veya her ikisi birlikte yüksek saptandı. **Sonuç:** Lipidize dermatofibromlar klasik dermatofibromlara göre daha geç yaşlarda ortaya çıkar. Klasik dermatofibromlara göre daha büyüktür ve dev dermatofibromlarla özdeş olabilir. Daha büyük dermatofibromlar lipidize olmaya ve alt ekstremitede lokalize olmaya eğilimlidir. Bu tür durumlarda histopatolojik doğrulama gerektiğinden, tanı alan lipidize dermatofibromlar genellikle alt ekstremiteye lokalizedir. Bir dermatofibromda gözlenen sarı alanlar lipidize formun bir göstergesi olabilir. Lipidizasyon hastaların yüksek kolesterol seviyeleriyle ilişkili olabilir.

Anahtar Kelimeler: Ayak bileği; histiyositom, benign fibröz; dermatofibrom

Dermatofibromas, also known as fibrous histiocytomas, are one of the most frequent mesenchymal neoplasms of the skin. They are most commonly seen in middle-aged women and the lower extremities, but they may also occur at any age in both sexes and any area of the body. They present as red-brown, slowly-growing, round and hard nodules of 0.5-1 cm in diameter.[1]

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Several clinicopathologic variants of dermatofibroma have been reported to lead to diagnostic difficulties. Typical histologic features of classic dermatofibromas are found at least in a focal region.[2] Apart from classic dermatofibromas, aneurysmal, cellular, palisading, hemosiderotic, epithelioid, atypical, clear cell, granular cell, lichenoid, myxoid, signet-ring cell, balloon cell, and lipidized variants have also been reported.[2,3] Knowledge of these variants is important to avoid misdiagnosis of possible aggressive lesions and preventing false treatment.

Lipidized dermatofibromas comprise 2.1% of all dermatofibroma cases; they are a rare and lesser-known variant.[2] To date, the clinical data reported from a few case series of lipidized dermatofibroma are limited and controversial. Lipidization has been accepted as an incidental finding without clinical significance. In this paper, a retrospective case series is presented to describe the clinical features of lipidized dermatofibromas.

MATERIAL AND METHODS

In this study, patients diagnosed with lipidized fibrous histiocytoma between 2014 and 2019 were retrospectively evaluated. Written informed consent was obtained from all patients included in the study when the diagnosis was confirmed with histopathology results. This study was conducted at İstanbul Training and Research Hospital and Sultan Abdulhamid Han Training and Research Hospital, Department of Dermatology, and was approved by Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (approval number: HNEAK-KAEK 2019/117). The study was actualized according to the rules expressed in the Declaration of Helsinki. All patients included in the study had a histopathologically confirmed diagnosis. The characteristic features of lipidized dermatofibroma, together with classic dermatofibroma features, made a histopathological diagnosis. The clinical and demographic characteristics such as patients' age, sex, location of lesions, duration of lesions, and lesion size, and the total cholesterol and triglyceride levels of patients were obtained from their medical records. Patients with serum cholesterol higher than or equal to 200 mg/dL or serum triglyceride higher than or equal to 150 mg/dL were considered to have hyperlipidemia. The laboratory results were obtained from the internal medicine and cardiology polyclinic records.

The SPSS program v. 21.0 was used for the statistical evaluation of the data obtained from the study. Continuous data are expressed as mean and standard deviation and categorical data as number and percentages.

RESULTS

Twelve patients (four males and eight females) were included in the study. The average age of the patients was 51 (range: 36-65) years. The average lesion size was 2.5 (range: 1.5-4) cm. The duration of the lesions was two to 15 years (Table 1). The reason for referral to the hospital was an asymptomatic mass in all patients and bleeding in one patient.

All of the lesions were located in the lower extremities. Seventy-five percent of the lesions were found below the knees and 41% on the ankles. The lesions presented clinically as firm, round or oval exophytic nodules, tumors or infiltrated plaques. Seven lesions was tumoral (Table 1). The color of the lesions were pink, brown and purplish. The center of some tumoral and nodular lesions were lighter and had a distinct yellowish color (Figure 1). In tumoral lesions undergoing incisional or shave biopsy, the content of almost all lesions was found to have a yellow elastic structure (Figure 2a, Figure 2b).

There were brown discolorations around the lesions; some were very visible and prominent, whereas others were very faint and hardly noticeable (Figure 1). Two of the tumoral lesions had ulceration (Figure 1i, Figure 1l) and a plaque lesion had a collarette scale (Figure 1d).

Classic dermatofibroma, xanthogranuloma, leiomyosarcoma, Kaposi's sarcoma, tuberous xanthoma, granular cell tumor, prurigo nodularis, aneurysmal dermatofibroma, Bowen's disease, dermatofibrosarcoma protuberans and amelanotic malignant melanoma were considered in the differential diagnosis of the lesions. Clear cell acanthoma was also considered in the differential diagnosis of the plaque lesion with a collarette scale. Squamous cell carcinoma, eccrine porocarcinoma and B-cell lym-

TABLE 1: The clinical and demographic characteristics and laboratory results of patients with lipidized dermatofibromas.

	Age	Sex	Location	Duration of lesion	Size	Lesion type	Total cholesterol (mg/dL)	Triglyceride (mg/dL)	Differential diagnosis	Follow-up
1	51	F	Right cruris	3 years	1.5 cm	Exophytic nodule	-	-	Xanthogranuloma, dermatofibroma	No recurrence
2	65	F	Right thigh	7 years	4 cm	Tumor	143	148	Leiomyosarcoma, dermatofibroma	No follow-up
3	50	F	Right ankle	3 years	3 cm	Tumor	317	293	Kaposi's sarcoma, dermatofibroma	No recurrence
4	42	F	Left cruris	4 years	1.5 cm	Infiltrated scaly plaque	233	188	Clear cell acanthoma, Bowen's disease	No recurrence
5	43	M	Left ankle	6 years	3 cm	Tumor	298	190	Tuberous xanthoma, ankle-type dermatofibroma	No recurrence
6	47	M	Left thigh	15 years	3 cm	Tumor	-	-	Aneurismal dermatofibroma, granular cell tumor	No recurrence
7	52	F	Left ankle	10 years	3 cm	Exophytic nodule	250	234	Dermatofibrosarcoma protuberans, amelanotic malignant melanoma, dermatofibroma	No recurrence
8	53	M	Left thigh	3 years	2 cm	Infiltrated plaque	182	205	Dermatofibroma	No follow-up
9	62	F	Right ankle	8 years	3 cm	Ulcerated tumor	190	143	Squamous cell carcinoma, Kaposi's sarcoma, B-cell lymphoma, eccrine porocarcinoma	No recurrence
10	36	F	Left cruris	2 years	2 cm	Tumor	287	205	Prurigo nodularis, dermatofibroma	No follow-up
11	50	F	Right cruris	2 years	1.5 cm	Nodule	249	247	Dermatofibroma	No follow-up
12	62	M	Left ankle	2 years	2.5 cm	Ulcerated tumor	260	102	Squamous cell carcinoma, malignant melanoma, eccrine porocarcinoma	No follow-up

phoma, leg type, were also included in the differential diagnosis of hemorrhagic tumoral lesions containing ulceration (Table 1).

Some of the lesions were completely excised after histopathologic confirmation by punch biopsy and others were excised without histopathologic confirmation. All of the lesions showed significant hyalinized collagen and a fibrohistiocytic tumor composed of different proportions of cells with large, lipidized, foamy cytoplasm localized in the dermis. Polygonal, oval or satellite-shaped foamy cells had large nuclei, prominent nucleoli, and vacuolated cytoplasm (Figure 2d). Spindle cell proliferation with a storiform pattern reflecting classic dermatofibroma was also focally observed.

Immunohistochemical staining revealed positive results for factor XIIIa and CD68 and negative results for CD34. The aneurysmal areas were also observed in the histopathology of one tumoral lesion. There was no recurrence in the follow-up of seven patients after total excision. The follow-up period ranged from four months to four years. Rest of the patients did not attend the follow-up sessions.

One of the tumoral lesions was examined with dermoscopy prior to biopsy. In the dermoscopy of the clinically purplish ulcerated tumoral lesion, a yellowish unstructured area was observed on the periphery of the ulcerated hemorrhagic crust at the center (Figure 2c).

For 10 of the 12 patients included in the study, the laboratory records within the last year were available. Six of these 10 patients had high blood levels of both total cholesterol (upper limit 200 mg/dL) and triglyceride (upper limit 150 mg/dL). One patient had high total cholesterol alone and another patient had high triglyceride alone (Table 1). In other words, 80% of the patients had a high blood level of at least one of the two parameters. Only two patients had normal cholesterol and triglyceride levels.

DISCUSSION

Previous studies concerning lipidized dermatofibromas focused on the clinical and histopathologic features and dermoscopy of the lesions. However, data on clinical features is limited and controversial due to the rarity of the reports on this entity.[4,5]

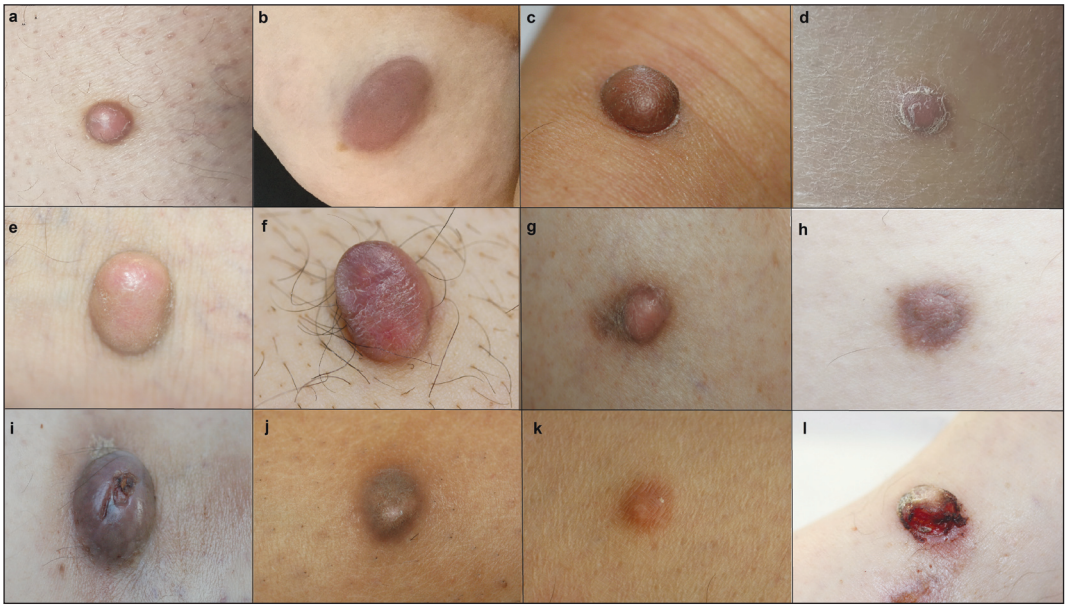

FIGURE 1: Macroscopic photographs of 12 lipidized dermatofibromas. All but two **(d and h)** lesions appeared as exophytic nodules and tumors. A yellowish discoloration was observed in the middle of some lesions *(a, c, e, g, and j)*. Two lesions had ulceration **(i and l).** A lesion had a peripheral scale **(d).**

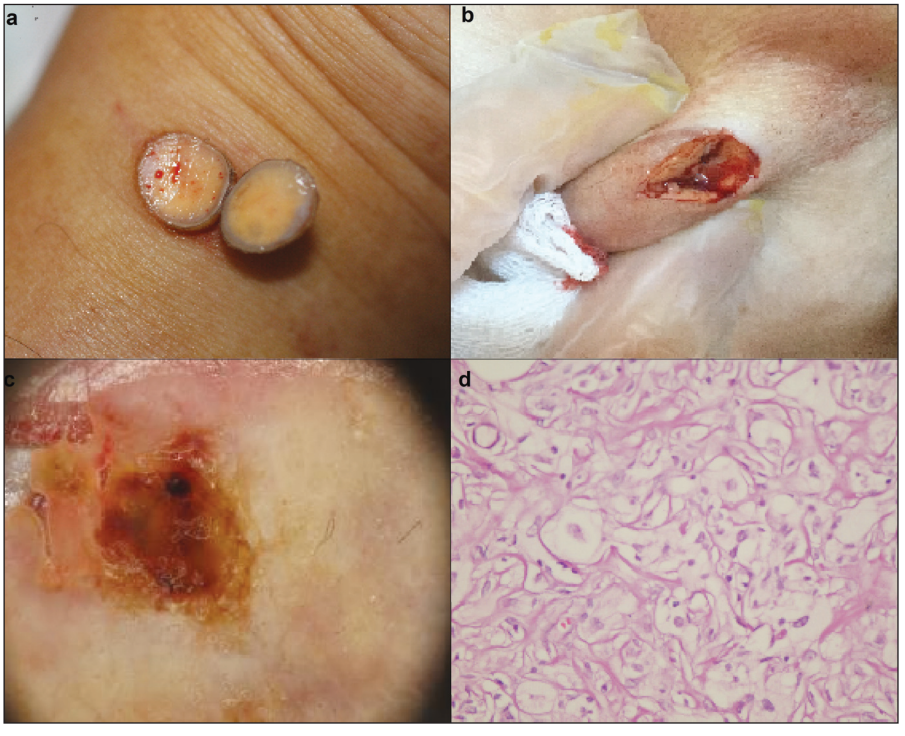

FIGURE 2: It is seen in the pictures that all lesions had elastic yellow content during shave **(a)** and incisional **(b)** biopsy. In the dermoscopic examination of the lesion in Figure 1i; wide, yellowish and unstructured area **(c)** around the middle crusted and ulcerated region is remarkable. Histopathologic examination shows polygonal foamy cells with large nuclei, marked nucleoli, and abundant vacuolized cytoplasm, surrounded by hyalinized collagen in the dermis (H&E ×200) **(d).**

The lipidized dermatofibromas in our series developed at slightly later ages (mean 51 years) than classic dermatofibromas reported in other case series.[4,5] Wagamon et al. found no significant difference between classic and lipidized dermatofibromas in terms of age.[6] In contrast to Iwata et al., Wagamon et

al. reported a male majority; in the current study, the lipidized dermatofibromas were more commonly seen in women, similar to classic dermatofibromas (female/male: 2/1).[4] This is consistent with the results of Zaballos et al. who noted a higher number of female patients with this condition.[5]

Lipidized dermatofibromas generally present at a larger size than classic dermatofibromas. Although classic dermatofibromas are usually smaller than 2 cm, their lipidized types were reported to reach 8 cm.[4] In our study, we found the mean size of the lesions as 2.5 cm, with the largest lesion being 4 cm, accordant with previous studies.

Due to observing the majority of lesions below the knee, Iwata et al. suggested an alternative term for these lesions: 'ankle-type dermatofibroma'.[4] However two further studies did not agree with this nomenclature, and defended that lipidized dermatofibromas had a similar distribution to nonlipidized dermatofibromas.[5,6] In our study, the lesions were located in the lower extremities and the majority of the lesions were below the knee, around the ankle. The most common site of involvement of classic dermatofibromas is the lower extremities, but they can also be seen in other parts of the body. However, lesions which are clinically and dermoscopically compatible with dermatofibromas and that reveal a "dimple" sign may not always be examined histopathologically in clinical practice. In contrast, when the characteristics of a lesion appear to differ from those of classic dermatofibromas or when they present as a nodule or tumor, histopathologic verification is required.

Giant dermatofibromas, which are clinically and histopathologically similar to lipidized dermatofibromas have been reported in the literature. Their size, clinical appearance and location are similar to those of lipidized dermatofibromas. They are named as giant dermatofibromas due to their large size and lipidization is a histopathologic finding. Half of all giant dermatofibromas reported to date have been shown to have lipidized features with foamy cells.[7,8]

Exophytic and tumoral lesions located outside the lower extremities have never been reported. In our study, the lesions had tumoral and nodular features in all but two cases. In the study of Iwata et al., the lesions were tumoral and all were located in the lower extremities.[4]

In accordance with our prediction, the dermatofibromas located in the lower extremities had a higher tendency to be exophytic and tumoral. These can be identical to the giant dermatofibromas reported in the literature. Furthermore, as their size grows, the tendency to lipidization increases. The lower extremity is an area open to trauma. Trauma can cause trauma-associated vascular leakage and phagocytosis by dermal macrophages of lipoproteins, and dermatofibromas located in this area may have a tendency to being larger due to this lipidization.[9] A histopathologic examination should be done for these lesions because they show different characteristics to classic dermatofibromas. This may also be the reason why these entities were mostly located below the knee in the study of Iwata et al. and our study. Lipidized dermatofibromas may be diagnosed less frequently in other parts of the body because they are less likely to be exophytic and their histopathologic verification is rarer. Therefore, we consider that 'ankle-type dermatofibroma' is not an appropriate term to replace lipidized dermatofibromas.

Lipidized dermatofibromas appear as slowly-growing exophytic nodules or tumoral lesions that remain symptomatic unless there is secondary ulceration.[4] In this study, all but two lesions had these characteristics. The yellow color on dermatologic examination may give a clue for the identification of lipidized dermatofibromas. This had been previously reported in some patients and some lesions in our series attracted attention due to the yellowish color. Furthermore, even if the lesions were not initially seen as having a yellow color, the yellow color was detected in the lesion section during the biopsy. Such a case can be suspected for the diagnosis of lipidized dermatofibromas. Zaballos et al. emphasized that the presence of a homogeneous yellowish area covering the whole or one part of the lesion on dermoscopy could be significant for the diagnosis of lipidized dermatofibromas.[5] This specification was also seen in one of our patients. This clinical and dermoscopic yellowish color corresponds to lipid-loaded foamy histiocytes in histopathology.

In the differential diagnosis of lipidized dermatofibromas, malignant and benign lesions such as xanthogranuloma, epidermal cyst, atypical melanocytic lesions, vascular tumors, basal cell carcinoma, adnexal tumors, and dermatofibrosarcoma protuberans have been reported.[5] In addition to these, our differential diagnosis also included leiomyosarcoma, granular cell tumor, aneurysmal fibrous histiocytoma, Kaposi's sarcoma, malignant melanoma, B-cell lymphoma, and prurigo nodularis. Squamous cell carcinoma and eccrine porocarcinoma were also among the differential diagnoses in ulcerated and hemorrhagic tumoral lesions. Furthermore, clear cell acanthoma and Bowen's disease were considered before the biopsy in an infiltrated scaly plaque lesion on the cruris. It is also important to distinguish lipidized dermatofibroma from malignant skin lesions, which require a different treatment approach. Prognosis is excellent in lipidized dermatofibromas and previous studies did not report recurrence after total excision.[4] Similarly, we observed no recurrence in patients' follow-up in our series after total excision.

The blood lipid levels of the patients were investigated to search for the causes of lipidization in lipidized dermatofibromas. Wagamon et al. compared blood lipid levels in patients with lipidized and non-lipidized dermatofibromas but found no statistically significant difference between these patients. The authors suggested that lipidization was an incidental finding related to the dystrophic process. However, their results may be misleading because their control group comprised the patients whose lipid values were frequently measured and the patients who used statins were included in the group with high cholesterol levels.[6]

In our study the rate of the patients with high lipid levels was found as 80%. This result is higher than the rates of both lipidized and non-lipidized dermatofibroma cases in a previous series (70% and 59%, respectively).[6] Therefore, we consider that lipidization of dermatofibromas may be due to high blood lipid levels. However, further studies with large case series are needed to ascertain whether lipidization is caused by high blood cholesterol or the dystrophic process.

The limitations of our study are its retrospective design and lack of a control group comprising classic, nonlipidized dermatofibromas. Furthermore, the blood lipid values of two patients could not be obtained. Also a biopsy is not performed on each patient who is clinically suspected to have dermatofibroma. This may result in overlooking some lipidized cases among patients presenting with the clinical signs of classic dermatofibromas and may lead to an underreporting of lipidized cases. Moreover, the presence of lesions in the form of nodules and tumors, and their intensive localization below the knee can be explained by the necessity for histopathologic examinations in such lesions, which may lead to detecting a relatively higher incidence of tumoral lesions and lesions that are localized below the knee.

CONCLUSION

Lipidized dermatofibromas present at later ages than classic dermatofibromas. They are also larger than classic dermatofibromas and may be identical to the giant dermatofibromas described in the literature. Dermatofibromas, which have a greater diameter than classic dermatofibromas, tend to be localized in the lower extremities and to be lipidized. Given that this situation requires a histopathologic examination, lipidized dermatofibromas that could be diagnosed are usually localized in a lower limb. When located in other parts of the body, these entities may be overlooked because they exhibit the typical characteristics of classic dermatofibromas. The yellow area observed clinically, dermoscopically or during biopsy may give a clue for lipidized dermatofibromas. However, the definitive diagnosis is made through histopathologic examination. Distinguishing lipidized dermatofibromas from malignant skin tumors is important in determining the appropriate treatment. Although high blood cholesterol levels could explain lipidization, further studies including a larger number of patients are needed to elucidate this issue.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authorship Contributions

Idea/Concept: *Tuğba Falay Gür;* ***Design:*** *Tuğba Falay Gür, Ezgi Özkur;* ***Control/Supervision:*** *Ayşe Esra Koku Aksu, Mehmet Salih Gürel;* ***Data Collection and/or Processing:*** *Tuğba Falay Gür, Sevil Savaş Erdoğan;* ***Analysis and/or Interpretation:*** *Cem Leblebici, Ayşe Esra Koku Aksu;* ***Literature Review:*** *Ezgi Özkur, Sevil Savaş Erdoğan;* ***Writing the Article:*** *Tuğba Falay Gür, Sevil Savaş Erdoğan;* ***Critical Review:*** *Ayşe Esra Koku Aksu, Mehmet Salih Gürel;* ***References and Fundings:*** *Ayşe Esra Koku Aksu, Mehmet Salih Gürel;* ***Materials:*** *Cem Leblebici.*

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