

A CASE OF SARCOIDOSIS IN REGIONAL LYMPH NODES MIMICKING METASTASIS IN A PATIENT WITH MULTICENTRIC INTRAEPITELIAL NEOPLASIA OF LOWER GENITAL TRACT AND ANUS

ALT GENİTAL SİSTEM VE ANÜSTE MULTİSENTRİK İNTRAEPİTELYEL NEOPLAZİSİ OLAN BİR OLGUDA METASTAZI TAKLİT EDEN SARKOİDOZA BAĞLI BÖLGESEL LENF NODU TUTULUMU

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ÖZET

Sarkoidoz; sistemik, etiyojisi bilinmeyen, akciğer ve akciğer-dışı bulgularla seyreden nonkazeifiye granülatöz bir hastalıktır (1). Literatürde, kanser hastalarında yeni başlangıçlı sarkoidoz ve sarkoidoz hastalarında yeni başlangıçlı kanser olguları birkaç kez bildirilmiş olmasına rağmen, kanser ve sarkoidoz eşzamanlı tanısı belgeleyen raporlar oldukça nadirdir (2). Bu takdimde, in situ servikal ve anal karsinomu olan multisentrik ve multifokal vulvar intraepitelyal neoplazi ile sarkoidoza bağlı ancak metastaz izlenimi veren büyümüş bölgesel lenf nodu tutulumu mevcut 61 yaşında bir olgu sunulmuştur.

Anahtar Kelimeler: Human Papilloma Virüs; Multisentrisite; Sarkoidoz; Vulva Kanseri.

ABSTRACT

Sarcoidosis is a systemic, noncaseating granulomatous disease of unknown etiology with pulmonary and extrapulmonary manifestations(1). Although new onset of sarcoidosis in cancer patients and new cancer onset in sarcoidosis patients have been reported several times, reports documenting simultaneous diagnosis of cancer and sarcoidosis have only rarely been published(2). Here, we report a 61-year-old case diagnosed with multicentric multifocal vulvar intraepithelial neoplasia presented with cervical and anal carcinoma in situ and enlarged regional lymph nodes due to sarcoidosis, but not metastasis.

Key Words: Human Papillomavirus; Multicentricity; Sarcoidosis; Vulvar Carcinoma.

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INTRODUCTION

Sarcoidosis is a chronic, multisystemic disease characterized by the formation of noncaseating granulomas, commonly affecting the lungs and lymphatic system (2). Although the relationship between sarcoidosis and malignancy is controversial, studies favors the possible etiologic linkage between these two diseases(3). On the other hand, sarcoidosis may mimic cancer metastasis by enlarging lymph nodes or extrapulmonary manifestations(4).

CASE REPORT

A 61-year-old woman, gravida 3, para 2 presented to our institution with vulvar pruritis. In examination, multiple vulvar and anal condylomatous lesion were observed. In addition to vulvar and anal biopsy, co-test has been done. Result of co-test showed low grade intraepithelial lesion and HPV 16 (+). Colposcopic examination has been done and biopsies have been collected from acedowhite positive and Schiller negative areas. Pathologic examination revealed condylomatous lesions and areas suspected to examine in terms of Warty VIN. On the basis of the pathology result; conization, simple vulvectomy and anal condylom excision had been performed. The result of histopathological examination was vulvar carcinoma insitu (high grade vulvar intraepithelial neoplasia – VIN III) with negative margin, cervical carcinoma in situ (high grade cervical intraepithelial neoplasia – CIN III) with endocervical glandular involvement in addition to positive margin and high grade anal intraepithelial neoplasia (AIN – III). An abdomen computed tomography scan showed normal findings except a few millimetric lymph nodes including mesenteric and paraaortic lymph nodes. Liver and renal function tests, electrolytes, serum tumor markers and a complete blood count were all normal. But serum calcium was 9,67 mg/dl, laktat dehydrogenase was 217 U/L and ALP was 110 U/L. Complementary surgery had planned and preoperatively, this case was speculated to be cervical cancer. At the exploration of the surgical area, enlarged paraaortic lymph nodes had been seen and considered as metastatic involvement of cervical malignancy. Frozen section of a paraaortic lymph node were examined and revealed noncaseating granulomas. Radical hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, appendectomy and pelvic lymphadenectomy were performed. Histopathological examination revealed cervical carcinoma in situ (high grade cervical intraepithelial neoplasia – CIN III) with negative margin, atrophic endometrium and ovaries and granulomatous lymphadenitis in lymph nodes including paraaortic(n=1), iliac(n=12) and obturator(n=8) regions. Fibrous obliteration was revealed in appendix. Omentum and periton biopsies was also described as hemoragic fibroadipose tissues without malignancy. There were no evidence of metastasis was found. Histochemical examination with ehrlich ziehl neelsen staining to exclude tuberculosis test was performed, and the result was negative. Transbronchial biopsy was performed and revealed well-demarcated noncaseating epithelioid granulomas. On the basis of histological and clinical findings, the patient was diagnosed with sarcoidosis. The patient received methotrexate therapy. At the 1-year follow-up, lymph node swelling due to sarcoidosis was stable, and there was no malignancy associated finding, regarding lower genital tract.

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DISCUSSION

A review of revelant literature suggest that the relationship between sarcoidosis and malignancy is controversial. There are hypothesis that explain malignancy in patients with sarcoidosis. The first setting relates to the sarcoidosis-lymphoma syndrome, which refers to the development of lymphoma at least 1 to 2 years after the diagnosis of sarcoidosis. The second setting consists of patients with sarcoidosis who develop solid tumors and oncologic patients in whom sarcoidosis subsequently appears; in addition to melanoma and nonmelanoma skin cancer, the neoplasms most commonly associated involve the cervix, liver, lung, testicles, and uterus. The third setting of malignancy-related sarcoidosis occurs when sarcoidosis presents as a paraneoplastic syndrome for the associated cancer, specifically when the discovery of cancer within 1 year of the diagnosis of sarcoidosis(3). But these are the hypothesis regarding the new onset of malignancy in patients with sarcoidosis; reports documenting coexistence of cancer and sarcoidosis is definitely rare(2,4). Malignancy can also be associated with the occurrence of sarcoid reactions that typically are restricted to the regional lymph nodes or the visceral organ of tumor origin; or can only be limited to the skin unless findings from other organs meet the criteria for sarcoidosis (2, 3, 4).

According to the classification system introduced by International Society for the Study of Vulvar Diseases (ISSVD), the diagnostic category of VIN1 has been canceled, and described as condyloma and/or HPV effects. The term VIN has been defined the histologic lesions previously classified as VIN 2-3 and differentiated VIN(5). The most common VIN type is usual type including basaloid, warty and mixed lesions generally related to HPV 16 infection and tends to be multifocal. In

addition, multicentricity (lesions in cervix, vagina and/or anus), that can be explained with 'HPV field effect', often presented in cases with uVIN(5). The presented case is also a good example to show the multicentric neoplasia in lower genital tract and anus associated with HPV. It should always be kept in mind that examination of perineum, perianal areas and also cervix and vagina is mandatory in cases with vulvar intraepithelial neoplasia to rule out multicentricity.

There is an increased frequency of solid tumors in patients with sarcoidosis and also new onset of sarcoidosis has been conducted in oncologic patients(3). But cases of sarcoidosis diagnosed simultaneously with preinvasive/invasive lesions are definitely rare. In a study, four cases affected by gynecological malignancies including serous papillary ovarian adenocarcinoma, cervical adenosquamous carcinoma, endometrioid endometrial carcinoma and ovarian clear cell carcinoma coinciding with granulomatous necrotizing lymphadenitis has been reported(4). A case of sarcoidosis diagnosed simultaneously with endometrial cancer was reported in 2015 that mimicking advanced cancer (2).

The widely accepted hypothesis about possible relationship between malignancy and solid tumors is that the dysregulation of the T-cell system may be related to malignancy in patients with sarcoidosis (6). Another possibility is that the chronic inflammatory process in sarcoidosis may promote the development of malignancy as conducted for systemic lupus erythematosus and inflammatory myopathies(7).

In cancer patients, sarcoidosis may mimic advanced-stage cancer, potentially leading to inappropriate management of the cancer (4). Enlarged lymph nodes in sarcoid patients are smaller than 2 cm unlike lymphoma, detected nearly 30% patients and widely revealed in porta hepatis, paraaortic region and celiac axis. In our case, lymph nodes involvement were prominent in iliac and obturator region not like general but like the case presented by Gorkem et al(8).

Preoperative diagnosis of sarcoidosis is currently almost impossible because imaging technologies are not sufficient to make the distinction between cancer

metastasis and sarcoidosis, yet. Frozen can be used to inform decisions on appropriate treatment. Above all, a pathological diagnosis should be obtained to differentiate sarcoidosis and cancer metastasis. In addition, the findings of noncaseating granulomas are not enough for establishing a diagnosis of sarcoidosis; therefore, additional examinations for sarcoidosis are necessary for accurate diagnosis (1,2).

Although no definite causal relationship has been yet identified, until more definitive data are available, sarcoid patients who develop new lesions or adenopathy and cancer patients with diffuse lymph nodal involvement should be considered for histologic examination to rule out coexistence of sarcoidosis and malignancy.

REFERENCES

1. Judson MA. The clinical features of sarcoidosis: A comprehensive review. *Clin Rev Allergy Immunol* 2015;49(1):63-78
2. Tamauchia S, Shimomura Y, and Hayakawab H. Endometrial cancer with sarcoidosis in regional lymph nodes: A Case Report. *Case Rep Oncol.* 2015; 8(3): 409–15.
3. Cohen PR, Kurzrock R. Sarcoidosis and malignancy. *Clinics in Dermatology* 2007; 25(3):326-33.
4. Mapelli P (1), Mangili G, Picchio M, et al. Sarcoidosis mimicking metastatic gynecological malignancies: A diagnostic and therapeutic challenge ? *Rev Esp Med Nucl Imagen Mol.* 2013; 32(5):314-7
5. Preti M, Igidbashian S, Costa S, et al. VIN usual type from past to future. *Ecancermedicallscience* 2015;29(9):501-14
6. Miyara M, Amoura Z, Parizot C, et al. The immune paradox of sarcoidosis and regulatory T cells. *J Exp Med* 2006;203:359-70
7. Ungprasert P, Leaphorn N, Hosiriluck N, Chaiwatcharayut W, Ammannagari N, Raddatz DA. Clinical features of inflammatory myopathies and their association with malignancy: a systematic review in Asian population. *ISRN Rheumatol* 2013;2013:509254
8. Gorkem U, Gungor T, Bas Y, Togrul C. Abdominal sarcoidosis may mimic peritoneal carcinomatosis. *Case Rep Obstet Gynecol*, Volume 2015, Article ID: 363945, 4 pages doi:10.1155/2015/263945