

Case Report

Metastatic Crohn's disease accompanying granulomatous vasculitis and lymphangitis in the vulva

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Abstract: Metastatic Crohn's disease (CD) is an extremely rare extragastrointestinal manifestation of CD, and is characterized histopathologically by the presence of non-caseating granulomatous inflammation. Granulomatous vasculitis and lymphangitis have rarely been documented in metastatic CD. Herein, we report the first documented case of metastatic CD accompanied by both granulomatous vasculitis and lymphangitis in the vulva. A 35-year-old Japanese female with CD presented with multiple small nodules in her vulva. Biopsy was performed under a clinical diagnosis of genital warts. A histopathological study revealed marked lymphangiectasia in the papillary dermis. Within the dilated lymphatics, lymphocytes and aggregates of macrophages were present, which are typical features of granulomatous lymphangitis. Tiny non-caseating granulomas and granulomatous vasculitis were also observed. Accordingly, a diagnosis of metastatic CD accompanied by both granulomatous vasculitis and lymphangitis was made. The occurrence of cutaneous lesions in patients with CD is well known. Albeit extremely rare, lymphangiectasia has been reported in the vulva of CD patients that clinically mimicked viral warts, as in the present case. The diagnosis of metastatic CD in the present case was not difficult because characteristic histopathological features were present, and a clinical history of CD was available. However, a few cases of genital swelling associated with granulomatous inflammation prior to a diagnosis of gastrointestinal CD have been documented. Therefore, granulomatous vasculitis and lymphangitis in the external genitals should be considered as potential indication of metastatic CD even in cases without a history of gastrointestinal CD.

Keywords: Metastatic Crohn's disease, granulomatous vasculitis, granulomatous lymphangitis, vulva

Introduction

Crohn's disease (CD) is a chronic inflammatory disorder that can involve the gastrointestinal tract from the oral mucosa to the perianal tissue. Metastatic CD is an extremely rare extragastrointestinal manifestation of CD, first described by Parks *et al.* in 1965 [1, 2]. This condition is characterized by the presence of non-caseating granulomatous inflammation far from the gastrointestinal tract [1, 2]. The skin is the most common location of metastatic CD, and this disease clinically presents as solitary or multiple nodules, plaques, ulcers, or lichenoid lesions [2, 3]. Metastatic CD most frequently involves the legs, followed by vulva, penis, and face [2, 3]. The characteristic histopathological feature of metastatic CD is the presence of sarcoidal type granulomas with foreign body and Langhans giant cells [2, 3]. Granulomatous

vasculitis and lymphangitis have rarely been documented in metastatic CD [2, 4, 5]. Herein, we report the first documented case of metastatic CD accompanied by both granulomatous vasculitis and lymphangitis in the vulva, and review the histopathological characteristics of this disease.

Case report

A 35-year-old Japanese female with CD presented with multiple small nodular lesions in her vulva, which had been noticed several years earlier. She had been diagnosed as CD at the age of 24 years, and an ileocecal resection was performed for fistula when she was 26 years old. A perianal abscess had also been present for several years. No connection was present between vulval lesions and the perianal abscess.

Metastatic Crohn's disease

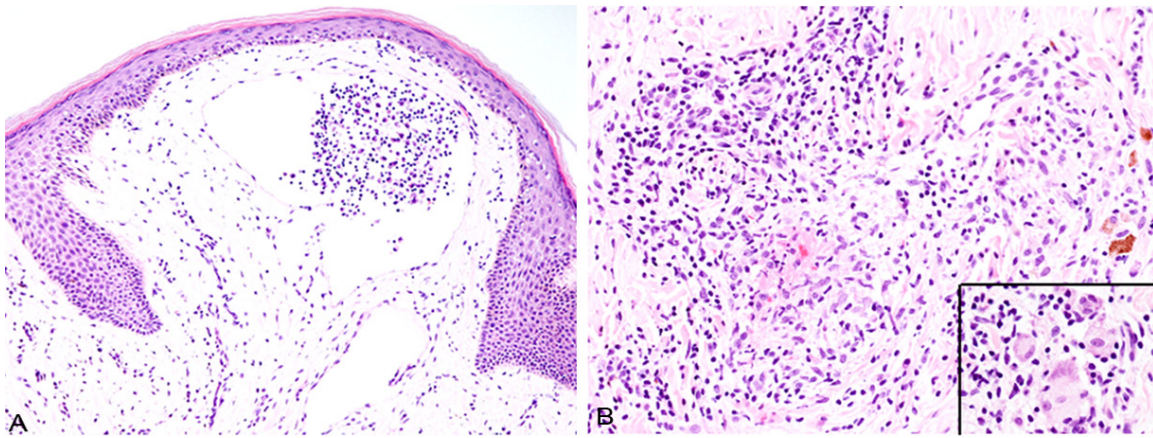


Figure 1. Histopathological features of the vulva nodule. A: Granulomatous lymphangitis. Lymphocytes and aggregated macrophages are observed within a dilated lymphatic. HE, x 100. B: Non-caseating granuloma (right) and granulomatous vasculitis (left) are noted. A few giant cells are also present (inset). HE, x 400.

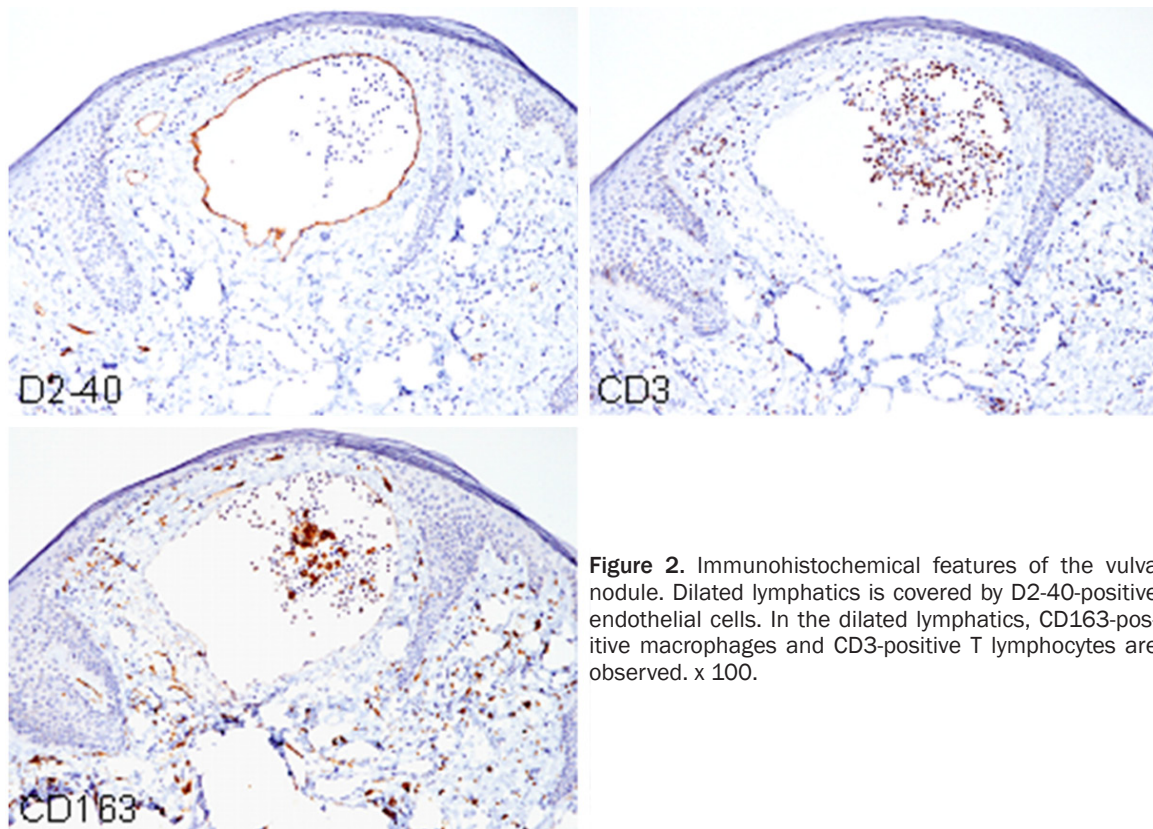


Figure 2. Immunohistochemical features of the vulva nodule. Dilated lymphatics is covered by D2-40-positive endothelial cells. In the dilated lymphatics, CD163-positive macrophages and CD3-positive T lymphocytes are observed. x 100.

A physical examination revealed that multiple skin-colored to brownish nodules, measuring 2-3 mm in diameter, were present in her vulva. Biopsy was performed under a clinical diagnosis of genital warts.

A histopathological examination of the biopsy specimen demonstrated a marked lymphangi-

ectasia in the papillary dermis (**Figure 1A**). Within the dilated lymphatics, lymphocytes and aggregates of macrophages were present, which are typical features of granulomatous lymphangitis (**Figure 1A**). The papillary dermis was extended and edematous (**Figure 1A**). In the reticular dermis, tiny non-caseating granulomas were observed, and granulomatous vas-

culitis was also noted (**Figure 1B**). A few giant cells were also present in the reticular dermis (**Figure 1B**, inset). In the superficial and deep dermis, perivascular mild lymphoplasmacytic infiltration was also observed. No eosinophilic infiltration was noted.

Immunohistochemical studies were performed using an autostainer (Ventana) by the same method as previously reported [6-8]. Granulomas were positive for CD163. D2-40-positive endothelial cells were observed in the dilated lymphatics (**Figure 2**). CD163-positive macrophages and CD3-positive T lymphocytes were present in the dilated lymphatics, however, CD20-positive B lymphocytes were rarely seen in the dilated lymphatics (**Figure 2**).

According to these results, an ultimate diagnosis of metastatic CD accompanied by both granulomatous vasculitis and lymphangitis in the vulva was made.

Discussion

The occurrence of cutaneous lesions in patients with CD is well known, and erythema nodosum and pyoderma gangrenosum are the most common cutaneous manifestations of CD [2]. Metastatic CD refers to cutaneous granulomatous lesions occurring in patients with CD without continuity of the gastrointestinal tract. Less than 70 cases have been reported in the English-language literature since the disease was first reported in 1965 [1-5]. The most common histopathological characteristics is superficial and deep non-suppurative sarcoidal granulomas with giant cells [2]. Emanuel and Phelps reported histopathological features of 12 cases of metastatic CD [2]. In their series, granulomatous vasculitis and massive edema of the dermis (both papillary and reticular dermis) were characteristic features and present in 2/12 cases, in addition to granulomatous inflammation; rich eosinophilic infiltrate was also observed in 67% of cases [2]. Therefore, they concluded that these three features are useful for diagnosis of metastatic CD and can be used histopathologically to distinguish it from cutaneous sarcoidosis [2]. The present case displayed granulomatous vasculitis and edema of the papillary dermis, but no eosinophilic infiltrate was observed.

Lymphangiectasia can develop in connection with numerous conditions, such as long-stand-

ing lymphedema (including infection and inflammation), surgery, radiation therapy, trauma, and lymphatic obstruction by tumors [4]. CD can also cause lymphangiectasia of the external genitals [4, 5]. Handfield-Jones *et al.* first reported two cases of CD with lymphangiectasia of the vulva, which were initially misdiagnosed as genital warts [5], and Mu *et al.* also documented a case of vulvar lymphangiectasia mimicking genital warts in a CD patient [4]. The multiple vulvar nodules of the present case were initially diagnosed as genital warts, and lymphangiectasia in the papillary dermis of the present case may represent multiple nodules.

Moreover, granulomatous lymphangitis is characterized by the presence of intra- or perilymphatic sarcoidal granulomas with lymphangiectasia. This condition is known to be associated with CD, cheilitis granulomatosa, and Melkersson-Rosenthal syndrome, and idiopathic cases have rarely been documented [9]. Murphy *et al.* summarized the previously reported 44 cases of granulomatous lymphangitis [9]. These patients were mostly young females and 82% of cases involved CD [9]. The vulva is the most common site of granulomatous lymphangitis, followed by scrotum and penis [9]. Granulomatous lymphangitis of the external genitals can present with peripheral leg edema indicating blockage of pelvic lymphatic vessels and lymph nodes, presumably by granulomatous inflammation [10]. Granulomatous lymphangitis in CD patients may also reflect obstruction of common lymph node drainage between the rectoanal region and external genitals, because most CD patients with granulomatous lymphangitis, including the present case, had anal diseases [9].

This is the first documented case of metastatic CD accompanied by both granulomatous vasculitis and lymphangitis. The diagnosis of metastatic CD in the present case was not difficult because characteristic, but rare, histopathological features such as granulomatous vasculitis and lymphangitis were present, and moreover, a clinical history of CD was available. However, a few cases of genital swelling associated with granulomatous inflammation prior to a diagnosis of gastrointestinal CD have been documented [11-13]. Therefore, granulomatous vasculitis and lymphangitis in the external genitals should be considered as a possible indicator of metastatic CD, even in cases without a history of gastrointestinal CD.

Metastatic Crohn's disease

Disclosure of conflict of interest

None.

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