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## A case of HPV and acquired genital lymphangioma: over-lapping clinical features

*Lymphatic malformation or lymphangioma is a benign proliferation of the lymphatics accounting for 4% of all vascular malformations and 26% of all benign vascular tumors. There are several reports about genital lymphangiomas mimicking venereal lesions, such as genital warts. Hereby we described a case of a 24 year old man affected by multiple vesicles and warts in genital area. All hematological and biochemical parameters, Human Immunodeficiency Virus (HIV) and Treponema Pallidum tests, C1 - Inhibitor and C1 - Q values were within limits. An accurate fulguration and wide excision of bigger lesions were performed.*

*Histological examination showed numerous dilated lymphatic vessels in the superficial dermis with infiltration of inflammatory cells, that is a histopathological picture compatible with genital lymphangioma. Considering our clinical suspicion of condylomatosis, HPV (Human Papilloma Virus) Polimerase Chain Reaction (PCR) Genotyping, named INNO-LiPA test, was performed, that revealed a genital infection by HPV - genotype 6. We think that our case can be considered an example of HPV infection and acquired genital lymphangioma overlap clinical syndrome. The patient presented any lesions one year after the procedure at follow-up examination.*

KEY WORDS: Condyloratosi, HPV cenotyping, Lymphangion

## Introduction

Lymphatic malformation or lymphangioma is a benign proliferation of the lymphatics accounting for 4% of all vascular malformations and 26% of all benign vascular tumors<sup>1,2</sup>. Based on the clinical and pathological characteristics, lymphangiomas are broadly classified as superficial (circumscriptum) or deep (cavernous)<sup>3</sup>. There is any clear distinction between both and the only difference seems to be the extent of the malformation. Lymphangiomas also can be classified as simple, cavernous or cystic according to the size of the lymphatic vessels.

Another important distinction can be realized between congenital and acquired lymphangioma<sup>4</sup>. Congenital lymphangiomas result from a hamartomatous malformation of lymphatic vessels, while acquired lymphangiomas are the results of acquired obstruction of lymphatic vessels induced by surgical or radiation treatment of neoplasms of the breast or uterus, trauma, chronic inflammation, infection (e.g. Erysipelas, Tuberculosis) and other unknown diseases. There are several reports about genital lymphangiomas mimicking venereal lesions<sup>5</sup>. Indeed, considered those arising in other regions, lymphangiomas of genital and anal areas can be more hyperplastic, probably due to the loose connective tissue, which can cause a cauliflowerlike aspect or some smooth and umbilicated lesions, mimicking respectively genital warts or molluscum contagiosum<sup>6</sup>.

Hereby we report a rare case of acquired genital and anal lymphangioma that showed excellent results following an adequate surgical treatment.

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## Case report

A 24 year old man applied to our outpatient clinic for evaluation of multiple vesicles and warts in genital area. Some of these lesions are oozing too. Physical examination confirmed that the patient had many lesions on his inguinal area, scrotum, glans and penis (Figs. 1, 2). There was associated edema on the penis and on the lips (Fig. 3). All hematological and biochemical parameters were within limits. Both Human Immunodeficiency Virus (HIV) and Treponema Pallidum infections were also excluded. Moreover, C1 - Inhibitor and C1 - Q values, useful for diagnosis of hereditary angioedema, were normal. An accurate fulguration and wide excision of bigger lesions were performed (Fig. 4).

Histological examination showed numerous dilated lymphatic vessels in the superficial dermis with infiltration of inflammatory cells, that is a histopathological picture

compatible with genital lymphangioma. Considering our clinical suspicion of condilomatosis, immunohistochemical staining for p16 protein was carried out. Results were not clear, thus HPV (Human Papilloma Virus) Polymerase Chain Reaction (PCR) Genotyping, named INNO-LiPA test, was performed. This extra-investigation revealed a genital infection by HPV - genotype 6. After the surgical treatment, cleanse of whole genital area daily with antiseptic agents was prescribed for one month.

The patient presented any lesions one year after the procedure at follow-up examination. Lips edema disappeared completely. No complication of surgical intervention was observed.



Fig. 1



Fig. 2



Fig. 3



Fig. 4

## Discussion

Acquired progressive lymphangioma (APL), also known as benign lymphangioendotelioma, is a rare benign proliferation of lymphatic vessels caused by lymphatic malformation<sup>7</sup>. It occurs most commonly in adolescents and young adults and some reports suggest that a reactive process can play a role in the development of APL<sup>8</sup>. In our patient, the causative factor of disease probably have been due to a human papillomavirus infection. Specifically, we think that our case can be considered an example of HPV infection and acquired lymphangioma overlap clinical syndrome. It is worthwhile doing a careful differential diagnosis of APL. Histological features and an accurate clinical examination are very helpful to exclude other pathological conditions as hereditary angioedema, cystic hygroma, hernia, hydrocele, genital warts, or more rarely lymphangiomatous variant of Kaposi sarcoma and verrucous hemangiomas<sup>9</sup>.

Various treatment modalities have been suggested: observation ("watch and wait" policy), cryotherapy, sclerotherapy, carbon dioxide laser, superficial radiotherapy, surgical excision<sup>10,11</sup>. We chose to treat this patient with a wide fulguration of the interested area by electrocautery and multiple biopses of bigger lesions, because we had many doubt about diagnosis. We considered surgical management the best option for this rare pathological condition. Indeed we achieved an excellent outcome with surgery at one year follow – up examination. In conclusion, our case report is useful to remind physicians of the diagnostic challenge set by vesicular lesions in genital area, which can be often misdiagnosed and consequently mistreated.

## Riassunto

Una malformazione linfatica o linfangioma è una proliferazione benigna di vasi linfatici che costituisce il 4% di tutte le malformazioni linfatiche ed il 26% di tutti i tumori vascolari benigni. Ci sono alcuni reports di casi di linfangiomi genitali che simulano clinicamente lesioni veneree, come ad esempio condilomi genitali. Descriviamo qui un caso di un maschio di 24 anni affetto da multiple vescicole e lesioni condilomatose nell'area genitale. Tutti i parametri ematologici e biochimici, i tests per infezioni da HIV e *Treponema Pallidum*, i valori di C1-inibitore e C1-Q erano nella norma. È stata eseguita un'accurata bonifica con elettrofulgorazione ed un'ampia escissione biptica delle lesioni più grandi.

L'esame istologico ha rivelato numerosi vasi linfatici dilatati presenti nel derma superficiale con infiltrato di cellule infiammatorie, compatibile con la diagnosi di linfangioma genitale. Considerando però il nostro sospetto

clinico di condilomatosi, è stato eseguito il test di genotipizzazione delle cellule in esame con la reazione a catena della polimerasi (PCR), denominato INNO – LiPA test, che ha evidenziato anche un'infezione da papilloma virus umano (HPV) – genotipo 6. Il paziente non ha presentato alcuna lesione un anno dopo la procedura. È quindi molto probabile che la proliferazione linfangiomatosa sia stata stimolata, nel caso descritto, da un'infezione da HPV e che il paziente abbia presentato una sindrome clinica caratterizzata dalla sovrapposizione di lesioni tipiche di ambedue le condizioni. In letteratura sono descritti casi di linfangiomi genitali che "mimano" lesioni condilomatose, in realtà con l'estensione dell'utilizzo di metodiche di biologia molecolare quale è l' INNO -LiPa, non escludiamo che possano incrementarsi le diagnosi di linfangioma e infezione da HPV coesistenti nel medesimo paziente.

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