

ALTERAZIONI DELLE PIASTRINE E CONDIZIONI GENETICHE

## GYNECOLOGICAL INVOLVEMENT IN FEMALES WITH CONGENITAL PLASMINOGEN DEFICIENCY TYPE 1.

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**Background and aims:** Congenital plasminogen deficiency type 1 (PLGD1) is an ultrarare disease characterized by the development of fibrin-rich pseudomembranes on mucosal surfaces of several organs and systems, mainly involving the conjunctiva. In affected females, ligneous lesions may occur on the vaginal and cervical surfaces, ovaries, Fallopian tubes and endometrium. Our aim was to conduct a review of the literature on clinical manifestations and therapeutic approaches of genital involvement in females with PLGD1, including our three cases.

**Methods:** A review of the literature was conducted including terms such as ligneous cervicitis, ligneous vaginitis, ligneous endometritis, ligneous conjunctivitis and plasminogen deficiency type 1. Three patients with congenital plasminogen deficiency and genital involvement followed at our center were included in the analysis.

**Results:** Fifty-seven cases of genital ligneous pseudomembranes, consistent with the typical clinical, histological, and laboratory findings of PLGD1, have been described in the literature. These are predominantly case reports and case series, while a number of patients were included in a phase 2-3 clinical study. Nine of these cases were documented before the correlation with plasminogen deficiency was identified. Reported plasminogen activity levels ranged from <2% to 50%. The pseudomembranous lesions have been described in

the vagina, cervix, endometrium, ovaries and Fallopian tubes. Including our cases, genital lesions represented the sole clinical manifestation of the disease in 12 of 60 patients (20%), with extragenital involvement, primarily the conjunctiva, observed in the remaining patients. Main symptoms included dysmenorrhea, vaginal discharge, post-coital bleeding, and infertility (15 of 52 reported cases, 28.8%). Histological findings of pseudomembranes require a differential diagnosis with neoplasia, sometimes coexisting with the ligneous lesions. Simple excision of the pseudomembranes was associated with recurrence of the lesions. Data on the specific treatment of the gynecological area were scarce and often empirical: topical and systemic treatments included steroids, cyclosporine, estroprogestins and fresh frozen plasma. The only effective treatment was a replacement therapy with human Glu-plasminogen concentrate, already approved by the FDA. No data were found regarding the quality of life and psychological impact caused by gynecological involvement in patients with PLGD1.

**Conclusions:** In patients with PLGD1, involvement of the genital apparatus is not uncommon, it can represent the sole clinical manifestation of the disease and can lead to infertility. There are very encouraging results from replacement therapy with human plasminogen concentrate, the use of which is still limited worldwide.

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