CASE REPORT

Psychotic depression due to giant condyloma Buschke–Löwenstein tumors

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Abstract
A 63-year-old patient, with no psychiatric history, was admitted in the psychiatric department with depressed mood, loss of interest in activities, apathy, insomnia, attention deficit, irritability, social withdrawal, prejudice and abandon delusions. Cerebral computed tomography (CT) scan was normal but the general physical examination revealed a voluminous tumor in the inguino-pubic-ano-genital area measuring 350/80/40 mm, which appeared 15 years ago and grew gradually leading to local rickety hygiene and also to depression, especially in the last time period when the tumor grew faster. The DSM-IV-TR diagnostic was affective disorder due to general medical condition. Surgical exams concluded it was a giant exophytic tumor and was recommended a pre-operative abdominal CT scan, which did not revealed metastatic spread. The treatment consisted in wide radical excision into the tumor-free resection margins. Anatomopathological exam concluded condyloma acuminatum – Buschke–Löwenstein tumor (BLT), a very rare borderline tumor. In post-operative period, progress of depression was spectacular, with the full mental recovery by decreasing the antidepressant and antipsychotic medication, fact that strengthen the initial diagnostic of depression due to a general medical condition. Conclusions: Patients diagnosed with BLT may develop mental disorders especially with devaluation and low self-esteem, social withdrawal and secondary functional impairment. Due to the malignancy risk in such tumors and also the psychiatric unfavorable recovery prognostic in case of continuous general medical condition, the only effective treatment is tumor resection with surgical, oncological, psychiatric postoperative revaluation.

Keywords: depression, surgery, Buschke–Löwenstein tumor, morphopathology.

Introduction
Condyloma acuminatum or Buschke–Löwenstein tumor (BLT) is a very rare tumor, generally presented in case report, frequently located in the ano-genital region, assuming that it appears secondary to a sexually transmitted disease, destroying underlying tissue [1].

BLT is a locally destructive and infiltrative tumor, cauliflower-like and it is thought to be induced by human papillomavirus (HPV), most commonly HPV types 6 and 11 and occasionally types 16 and 18 [2–5].

It was first presented by Buschke in 1986, by Buschke and Löwenstein in 1925, named by them “condyloma acuminatum-like” of the penis [6].

Even though BLT has a histopathological benign character, it has a malign behavior.

The verrucous carcinoma diagnoses can be difficult due to the lack of malignant cytological characteristics, especially if biopsy implies only the surface epithelium. Therefore, large and deep biopsy is required, carefully performed sections and detailed histopathological exams. Verrucous carcinoma or Buschke–Löwenstein giant condyloma may represent an intermediary stage between penile condyloma and epidermoid carcinoma [7].

Usually, in the first line stands the excision surgical exam, and the histopathological exam is absolutely required to exclude squamous cell carcinoma for which a radical aggressive surgery is mandatory [8].

The coexistence of BLT and squamous cell carcinoma in the same site, changes the behavior and progress of the lesion [9].

Patient, Methods and Results
A 63-year-old patient, widowed, without psychiatric history, brought by his family in psychiatric emergency for depressed mood, delusional interpretation, apathy, abolition, lack of interest, poor hygiene, irritability, hetero-aggression, weight loss secondary to decreased appetite and socially isolation. The patient lived alone for the last 10 years and the only treatment before admission was with Verapamil 240 mg/day for paroxysmal supraventricular tachycardia.

Family medical history and personal history did not revealed something important. The patient does not smoke, neither consumes alcohol or drugs.

At admission, the patient did not present hallucination, only thought disturbances, especially devaluation and incurability delusions with low self-esteem and also persecutory and abandon delusions related to his daughter who was living abroad for many years. The patients had insomnia and irritability.

From the psychiatric point of view, the evaluation of the depression stage was made through tracking the scores obtained by applying the following scales: Hamilton Depression Rating Scale (HDRS) – 17 items version,
Global Assessment of Functioning (GAF) and Clinical Global Impression Scale (CGI).

The patient’s mental status, functioning and global clinical impression were evaluated by HDRS – 17 items version, GAF and CGI. At admission, the HDRS – 17 items score was 29, GAF score was between 50–41, indicating serious symptoms and serious occupational and functional impairment (normal score 100). CGI score was 5.

Patient’s state was evaluated at baseline and weekly, for four months (including pre- and post-operative period). We declared that the patient responded to treatment when the HDRS score decreased at least with 50% toward the baseline score, and fully recovery was declared when HDRS score was ≤7.

Because of his old age and also the slightly spatial disorientation, which afterwards was determined as being apathy derived, the patient was neuro-cognitive evaluated but the MMSE score and the watch test were normal. Beside these scores, the dementia diagnostic was excluded by performing a brain scan that was also normal.

Blood and urinary tests were normal. The results at immunological tests anti-HIV1 and anti HIV2 were non-reactive. Syphilis tests: RPR (Rapid Plasma Reagin)/VDRL (Venereal Disease Research Laboratory) were negative.

Neurological examination and EEG showed no pathological elements, but the clinical examination revealed a giant, cauliflower-like tumor, in the anal and genital region, initially appeared 15 years ago, slow growing and progressive, with initial genital growth, anal afterwards. The patient did not address oneself to a doctor all these years, thinking that there is something shameful, showing lately deteriorated mental status and functionality, along with the significant increase in tumor size.

Surgical and dermatological examinations concluded that it is an ano-genital neglected tumor (causing serious perianal hygiene problems).

It was observed serious impairment in the quality of life because of poor hygiene in the ano-genital region and also because of the depression due to medical condition.

For the psychiatric symptoms, we started the treatment with Risperidolum 2 mg/day, Tianeptinum 12.5 mg three times/day and Divalproex sodium 1000 mg/day. For cardiac issues, the cardiologist maintained Verapamil at the initial dose.

After several days of treatment, when the HAMD score improved from 17 to 23 items, the patient was transferred in the department of general surgery for tumor therapeutic conduct, with organic affective disorder diagnosis (DSM-IV-TR) and specialized psychiatric treatment.

Clinical examination revealed inguino-pubano-ano-genital tumor, cauliflower, about 350/80/40 mm, large base of implantation, irregular borders, color ranging from dark-purple to white-pink, surface with small areas of necrosis overinfected, firm flesh.

Accurate diagnosis is on the biopsy and histological examination.

Grossly examination shows a multi-fragment piece 355/79/38 mm, cauliflower aspect, irregular edges, hard consistency, with small areas of necrosis overinfected, color ranging from black-purple to white-pink.

Histopathological examination reveals massive epidermal hyperplasia, hyperkeratosis and parakeratosis. Part of keratinocytes shows keratinization but without identifying keratin pearls (Figures 4 and 5).

Some keratinocytes had nucleus with prominent nucleoli and large cytoplasm.

Keratinocytes with granular vacuolization, large
cytoplasm and nucleus with large prominent and visible nucleoli are presented in Figure 6.

Lymphohistiocytic inflammatory infiltrate is often present (Figure 7). Tumor cells have discrete cytoplasmic nuclear atypia, but they were not detected in blood or lymphatic vessels.

Are seen rounded masses that invade the dermis and contiguous structures (Figure 8).

Figure 3 – Three months post-operative image: inguino-pubogenital and ischiorectal region with complete cure.

Figure 4 – Histopathological examination reveals massive epidermal hyperplasia, hyperkeratosis and parakeratosis: (a) Papillomatosis florid area with hyperkeratosis. HE staining, ×40; (b) Epidermal papillomatosis, acanthosis, hyperkeratosis. Koilocytic atypia. HE staining, ×100; (c) Epidermal papillomatosis hyperplasia and koilocytic atypia present in the epidermis surface. HE staining, ×100; (d) Koilocytic atypia and dyskeratosis. HE staining, ×200.

Figure 5 – Massive hyperplasia of epidermis with endophytic growth, papillomatosis, koilocytic atypia and deep dermal papillae with rounded contours: (a) Epidermal hyperplasia with hyperkeratosis, deep dermal papillae with rounded contours. HE staining, ×40; (b) Massive hyperplasia of epidermis with endophytic growth. HE staining, ×100.
Figure 5 (continued) – Massive hyperplasia of epidermis with endophytic growth, papillomatosis, koilocytic atypia and deep dermal papillae with rounded contours: (c) Epidermal hyperplasia (acanthosis) and massive hyperkeratosis papilloma. HE staining, ×100; (d) Epidermal hyperplasia, papillomatosis, koilocytic atypia. HE staining, ×200.

Figure 6 – Keratinocytes with granular vacuolization, large cytoplasm and nucleus with visible nucleoli. HE staining, ×100.

Figure 7 – Epidermal hyperplasia and papillomatosis, with the presence of lymphoplasmocytary inflammatory infiltrate. HE staining, ×100.

In conclusion, clinical and pathological examination revealed that it is a giant Buschke–Löwenstein tumor (BLT), a rare tumor with an aggressive development by growth and invasion of surrounding tissues.

Post-operative surgical, oncological and psychiatric examinations showed that evolution was favorable.

Patient was evaluated weekly in first month and then at two weeks to the end of four months of treatment. Mental evolution was spectacular after surgery, so at one-month post-operative the HDRS score decrease with more than 50% compared with baseline.

After four month of treatment, final score for HDRS was <7, CGI-S = 1, CGI-I = very much “improvement” at endpoint compared to her condition at baseline (CGI-S = CGI for severity of illness and CGI-I = CGI for improvement), final GAF score = 100. All these results concluded that our patient was normal, not at all ill and he had a higher functionality with progressive and total recuperation.

Discussion

BLT is rarely, with an estimated incidence of 0.1% in the general population and it is sexually transmitted [3, 4].

Condyloma acuminatum was excluded because histopathological images thickening of the stratum corneum, endophytic increases and deeper invasion argues for giant condyloma.

Microscopic images are suggestive for giant condyloma of Buschke and Löwenstein.
The ratio between men and women is 3:1. BLT is more common in men and the mean age of occurrence is around 50 years. BLT can give recidivism and malignant transformation. It is a tumor with broad-based implantation and who can cause local destruction and infiltrative phenomena [11–13].

Benign condyloma are usually caused by HPV types 6 and 11, whereas HPV types 16, 18, 31 and 33 are often found in lesions with neoplastic transformation [14–16].

Besides those mentioned above, some authors consider that precarious hygiene and promiscuity had incriminated in causing BLT. Infection and viral factors also play an important role in the etiology of BLT, such as immunosuppression on HIV or HTLV-1, and chronic infection, but also other factors such uncircumcised patients, and relapsing genital warts [5, 17].

Death occurs in about 20% of patients. There have been reported cases of malignant transformation of BLT into squamous cell carcinoma, which can therefore show metastatic spread [18].

In the case of our patient, the onset was in also in genital area by papillomatosis injuries similar condyloma acuminatum by, taking after 15 years of evolution the appearance of inguino-pubo-ano-genital cauliflower tumor, without deep invading and not gives the distance impairments.

Because BLT is rarely, different types of treatment are reported for giant condyloma. The type of treatment depends on many factors, including the location of the giant condyloma, how much invaded deep and surface, the size, the unsuccessful previous therapies.

The literature describes other therapeutic methods for the treatment of BLT. Thus, Tyngh et al., in 1998, describes a therapeutic solution with Podofilox solution and gel like the first option of treatment for condyloma acuminatum [19].

Also, it is described as a therapeutic method cryotherapy by itself or in combination with topical 5-Flourouracil in relatively small BLT [20, 21].

There are authors who report cases successfully treated with combination therapy, chemo-radiotherapy [22, 23] and some cases in which surgical excision was preceded by chemo-radiotherapy [24].

There have also been reported cases in which it was used as a treatment for BLT, carbon dioxide laser vaporization [25–28].

Studies have shown that regional radiotherapy is not very useful since may induce undifferentiating of the tumor cells, stimulating a rapid progression of the lesion to the malignant degeneration [29–31].

The surgical excision is still the first line of treatment for BLT with a higher success rate (63–91%) and lower risk of recurrence [9].

In our case, the oncologist felt that the patient should be monitored and reviewed regularly just for the moment considering that total tumor excision was the best option for treatment.

It is very interesting the impact of this disease on the patient’s psyche and just slow growth over time, without any pain in some patients, but also the feeling of shame, make the disease was detected in the tumor stages reach giant sizes.

In cases with painful tumor, the more it puts a question, why these patients were not addressed from time to a doctor, the more as condylomata are often disfiguring and disrupt the patients sex life as they can cause itching, burning, pain, and postcoital bleeding [1].

Accidental discovery of such a case in a psychiatric department intrigued us to do a review of the literature, which concluded there was no published articles focusing on the impact on the functionality and the sexual life of such a patient. Certainly, the impact can be expected to be negative, but we did not find neither noting mentally, social and family factors that led to lack of addressability at a physician until the giant size of the tumor stages.

Thus, the reported cases we found that one patient was homeless, another alcoholic [16], others were diagnosed with HIV [2, 32]. In the case of our patient, he was a widower for many years and lived alone. Regarding the lack of addressability by a doctor, he said he felt ashamed and guilty, which is why he did not want his family to know the problem.

Other conditions: circumcised several years previously for phimosis [33], immunosuppression in the case of a young woman, which had been treated with electro-cauterization for multiple small condyloma acuminatum on the vulva and with approximately one month prior to the relapse of the vulvar condylomata she had been treated with high doses of systemic glucocorticoids for a recurrent severe anaphylactic reactions [34].

Studies on the influence of clinical depression on morbidity and mortality in oncology, as well as those related to depression as a factor of malignancy are less numerous, despite the high prevalence of depressive disorder in patients with cancer.

However, it was shown that patients diagnosed with depression before surgical management of malignant brain astrocytoma have a lower survival rate than those who had not pre-operative diagnosis of depression, independent of the degree of disability, tumor grade and ways of treatment [35].

At their turn, patients with breast cancer diagnosed with depression have a high risk of mortality compared to patients without depression [36]. This requires the appropriate programs to reduce the depression before and during treatment and after treatment [37]. Most specialized studies also obviously the coexistence of cancer and depression is associated with a significantly increased risk of death, and the effect of depression on the risk of death varies depending on the type of cancer [38].

The correlation between depression scores in patients with advanced cancer, calculated using the Edinburgh Scale (EDS) and the risk of death was also statistically significant, an increase of one point in EDS score increased by 7% risk of death [39].

Most studies on depression cancer patients focused on: improving quality of life; pathogenesis (immune dysfunction may be a common pathogenic factor for depression and cancer) [40, 41] screening tools available, interference depression in cancer development that affect adherence to treatment, immune and endocrine functions [42] and specific treatment approaches [43–45].

Longitudinal studies on the presence of depression...
in cancer survivors were few and the association between pre-operative depression and survival of patients require further investigation. According to some of these studies, the prevalence of depression was higher among survivors of cancer of the stomach, even after treatment [46] and fear of recurrence is a common concern of former oncology patients [47]. Wide perineal excision with histopathological margins control is the best surgical choice in the treatment of BLT if the anal canal is not involved [48].

In our case, histopathological examination showed that does not were still signs of malignancy of the tumor, which made surgical excision only be the optimal method of treatment, but because of the risk of malignancy of these types of injuries, the patient will remain under regular control made by oncologist, surgeon, psychiatrist and psychologist to prevent tumor recurrence and secondary depression.

Conclusions

Larger studies are needed and a more detailed analysis of psychological, social and environmental factors at future cases reported with giant BLT. Our recommendation is for the authors to stop more to the causes that led at so late addressability to a doctor. Knowing the relationship between depression and cancer, the patients with such tumors must be regularly investigated after tumor excision to treat any secondary depression because depression persistent may increase the risk of malignancy existing in this type of tumors.

References

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