

CASE REPORT

Metastasized squamous cell carcinoma developed on lupus vulgaris

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Abstract

Lupus vulgaris (LV) is the most frequent cutaneous tuberculosis, representing more than 55% of the tuberculoses with this location. Malignization can occur after a long latency (10–30 years), in 1–2% of the cases, and it is mainly in squamous cell carcinoma. The histological exam is highly important in the observation of neoplastic transformations. The authors present a 59-years-old female patient, from the rural environment, working as a farmer, with lupus vulgaris developing since her first childhood years. It started at the age of 2 years, at the right ear lobule, after the empiric perforation for earrings. The evolution was progressive, eccentric, interesting the pinna and the right cheek in the meanwhile. At the first examination, in 2002, a diffuse mass of red-yellowish infiltration was found at the level of the right ear and the right cheek. In the following two years, an ulcero-vegetating tumor developed at the level of the right ear lobule, accompanied by the presence of a right retromandibular adenopathy, of about 1 cm, which was proved by the histopathologic exam to be a squamous cell carcinoma developed from a lupus vulgaris. After scraping out the right retromandibular ganglion, detected by palpation, a histological exam showed ganglion metastasis.

Keywords: lupus vulgaris, squamous cell carcinoma, metastasis.

Introduction

Lupus vulgaris (LV) represents more than 55% of cutaneous tuberculoses and appears in individuals with hypersensitivity to tuberculin [1]. In 80% of the cases, lupus vulgaris starts in childhood, with the head (nose, cheek ears) as election location [2]. Malignization occurs after a long latency (10–30 years) [3], in 1–2% of the cases, and it is mainly in squamous cell carcinoma. In comparison with other preneoplastic lesions, malignization is rare, but it must be envisaged as long as we assist the recrudescence of tuberculosis, including the one in a cutaneous location.

The authors present a case of LV, which, after a 57-years evolution, turned into a squamous cell carcinoma (SCC), complicated in turn by a regional ganglionic metastasis. The clinical symptoms based on which malign transformation is suspected are represented by the increase in relief of the cutaneous lesion, the ulceration and infiltration of the basis.

We underline the importance of the histological exam for the diagnosis (both phase and final diagnosis), as well as the necessity of the periodic clinical examination of these patients, considering the risk of LV malignization.

Patient and methods

The patient B.S., aged 59, from the rural environment, who worked as a farmer, was hospitalized

in the Dermatology Clinic in 2004 for an ulcero-vegetating tumor interesting the right ear lobule.

According to the *anamnesis*, the patient was made to wear earrings at the age of two, after an empiric perforation (with a sewing needle) of each ear lobule. Afterwards, an inflammatory process with red-yellowish nodules, which were initially grouped at the level of the right ear lobule, insidiously started. Furthermore, through the eccentric evolution, the disease has to interest the entire pinna and the right hemifacies. The patient was first examined by a dermatologist in 2002, at the age of 57, when a slightly embossed diffuse mass of red-yellowish infiltration is found at the level of the right ear and the right cheek (Figure 1), allowing the visualization of numerous lupus nodules (tubercles), with a diameter of 3–4 mm, in vitropressure.

Personal and family pathologic antecedents were not significant. During this entire period, the patient did not take any treatment. After the clinic exam, prominent LV was suspected. The diagnostic was confirmed after the *biopsy* and the *histological exam*. A great number of tubercles, made up of epitheloid cells and gigantic Langhans' type cells (Figures 2 and 3), with a peripheral disposition of nuclei (Figure 4) were found at the dermis level. The infiltrate with mononuclear cells (lymphoid cells) can be noticed around granulomas (Figure 5). This inflammatory infiltrate is located closely to the epidermis. The epidermis presents areas of atrophy (Figure 3 – the upper left half) and ulceration (Figure 6).

At the edge of ulceration, the epidermis becomes hyperplastic and presents areas of acanthosis and papillomatosis (Figure 3 – the right half). Fibrosis areas were found around tubercles, which indicate the fact that the lesion was chronic (Figure 7). Small areas of caseification necrosis were noticed at the centre of tubercles (Figure 8).

The *intradermal reaction to tuberculin* was highly positive, and the *lung radiography* was normal. The *Ziehl-Nielsen coloration* was negative, as well as the *culture* accomplished after *cutaneous biopsy*. The investigations for finding the infection with *Treponema pallidum* and HIV were negative.

After stating the LV diagnostic, the patient followed anti-tuberculosis chemotherapy (isoniazide, rifampicine, ethambutol, pyrazinamide) through the Pneumophthisiology Service. An obvious clinical improvement was obtained at the level of the right cheek and pinna (Figure 9), but not at the level of the affected lobule, where the tumor developed in the subsequent period.

The patient was hospitalized again in the Dermatology Clinic in Craiova, in 2004, with an ulcero-vegetating tumor interesting the right ear lobule. Besides the tumor of 2/1 cm covered by a purulent crust, the *dermatologic exam* also showed a right retromandibular ganglion with the diameter of 1 cm, of a firm consistency, mobile on supra- and subjacent plans, and a tissue with a yellowish atrophic-cicatricial aspect, with big nodules, 3–4 mm prominent at the skin surface, and a couple of squamo-crusts on its surface, occupying the right cheek (Figure 10).

The excision of the tumor was accomplished with a safety margin of 5 mm, obtaining a good aesthetic result (Figure 11) from the patient's point of view. The histological exam of the tumor showed a moderate differentiated SCC. The aspect of moderate differentiated SCC, characterized by the presence of tumoral islands, mainly centered by keratin pearls was noticed in malignization areas (Figures 12 and 13). The cells had a polygonal aspect, eosinophilic cytoplasm, some with individual keratinization (Figure 14). Given this situation, right retromandibular ganglionic scraping out was performed, as the histological exam showed the presence of a SCC metastasis with the same degree of differentiation as the primitive tumor. The normal histological structure of the lymphatic ganglion was partly substituted with tumoral cell islands (Figures 15 and 16).

The patient was taken over by the Oncology Department for specific treatment.

✎ Discussions

The case we presented shows the risk of malignization of lupus vulgaris, so that the classification of this disease under the group of precancerous lesions is justified. The scientific interest in such pathology is actual as the infection caused by *Mycobacterium tuberculosis* (Koch's bacillus) still represents a main public health issue. In Romania, morbidity by pulmonary tuberculosis had a marked increase after

1990 (1990: 70‰; 1995: 102.6‰; 2001: 134.1‰; 2002: 142.2‰) being followed by a low decrease (2003: 135.7‰; 2004: 134.6‰; 2005: 123.7‰; 2006: 117.8‰), more than two times higher than the Eastern Europe average (2001: 50‰). The figure is four times higher than the Central Europe average (2001: 35.5‰) and six times higher than the Western Europe average (2001: 20‰). Cutaneous tuberculosis are rarely found in medical practice, including in Romania, but it is expected that the recrudescence of pulmonary tuberculosis, especially in the context of the HIV/AIDS pandemic shall cause the appearance of new cases of bacillary infection at the level of the skin.

Lupus vulgaris represents the most frequent form of cutaneous tuberculosis (more than 55% of the cases) and it mainly occurs in previously contaminated individuals, with a strong sensitivity to tuberculin [1, 2]. It mainly interests female individuals. Inoculation is either exogenous, either endogenous. As we have already mentioned, the election location of LV is represented by the cervico-facial region, and the inoculation of the Koch's bacillus is usually exogenous. Most of the times, lesions are caused in the nasal mucous membrane, by infected fingers or bacilliferous dust. The tegument is secondarily interested through the lymphatic way. Objects rarely make contamination, such as the perforation of the ear lobule for earring holes, as in our case; after vaccination; after tattoos with contaminated tools, etc. Endogenous inoculation (by lymphatic way or contiguity) is more frequent in LV at the level of limbs, as the tuberculosis focus is osseous or articular. We can exceptionally find hematogenous dissemination from deep focuses, after a transitional depression of immunity, usually after measles. In this last situation, the intradermal reaction to tuberculin is negative, and the patient shows disseminated LV.

The elementary lesion within the LV is a nodule (tubercle, lupoma) with a diameter of 3–4 mm, located in the deep derma, soft, yellowish, of an "apple marmalade" shade, after glass blade pressing (vitropressure). The vitropressure maneuver does not bring diagnostic benefits to colored persons [2]. The tendency of nodules is to conflate and form a polymorphic lupus plaque.

Our case was presented as a slightly embossed, diffuse mass of a red-yellowish infiltration, which allowed the visualization of numerous lupus nodules with a diameter of 3–4 mm, upon vitropressure, located at the level of the right ear and right cheek, classifying it under the clinical form of prominent lupus vulgaris.

Depending on the clinical aspect, the following forms are mentioned in the specialized literature [2, 5]:

- Flat lupus vulgaris – an atrophic, squamous plaque, with more obvious nodules at the periphery. It does not usually ulcerate, and the scar is imperfect (relapse tubercles in the area with interstitial sclerosis). Differential diagnosis must be made with: chronic lupus erythematosus (we can find erythema, follicular hyperkeratosis and cutaneous atrophy); superficial basal cell carcinoma (lupus tubercles missing at vitropressure), flat cicatricial basal cell carcinoma (frame with epitheliomatous pearls);

▪ Prominent lupus vulgaris - tubercles are larger, they are 1–4 mm prominent at the skin surface, and they give a pseudo-tumoral aspect by confluence. Except from the tumidus form (location at the level of the nasal pyramid) and the myxomatous lupus vulgaris (location

at the level of the ear lobule), the prominent lupus vulgaris has the tendency to ulcerate. The tumidus lupus must be differentiated from the chronic tumidus erythematous lupus and the sarcoidosis;



Figure 1 – Prominent lupus vulgaris

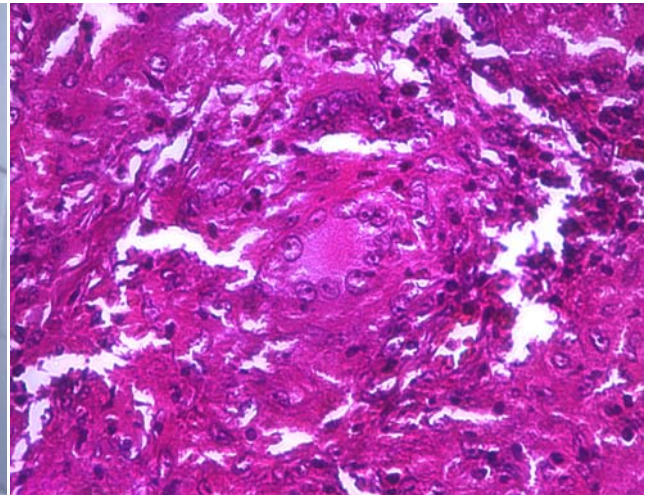


Figure 2 – Tubercles at the dermis level

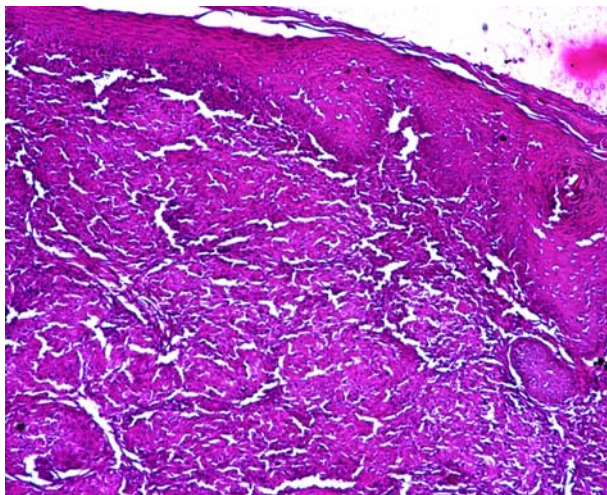


Figure 3 – The epidermis presents areas of atrophy (the upper left half); acanthosis and papillomatosis (the right half)

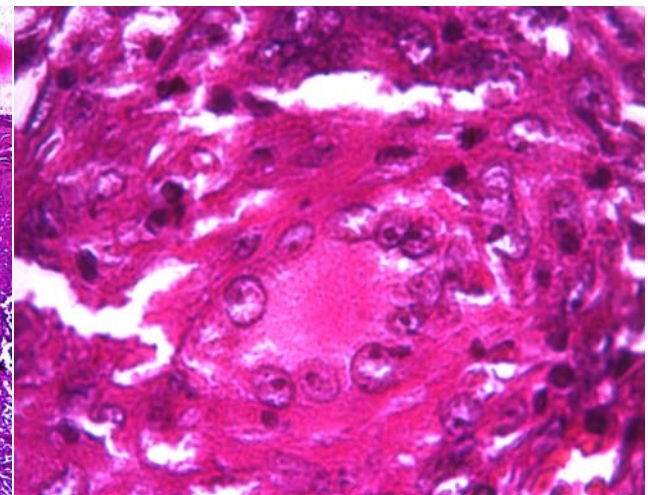


Figure 4 – Peripheral disposition of nuclei

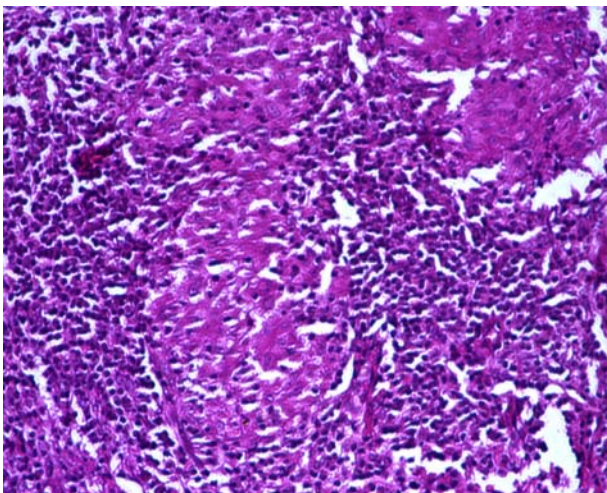


Figure 5 – The infiltrate with mononuclear cells

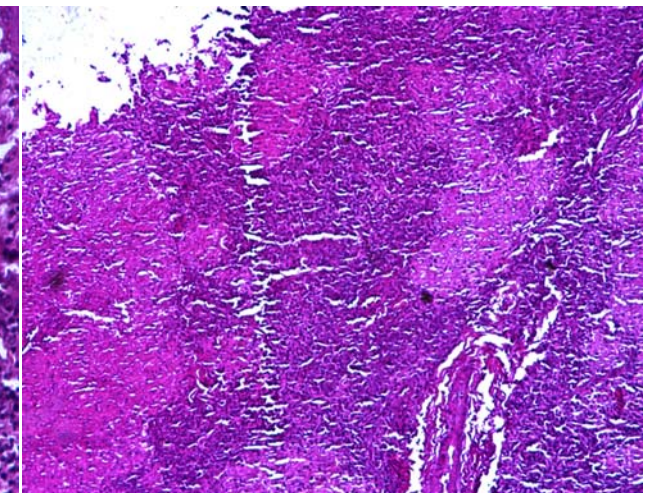


Figure 6 – Epidermis with ulceration areas

▪ Ulcerated lupus vulgaris – it is about d'emblée ulcerations or, more frequently, of secondary ulceration. It can have an ulcerocrustous, ulcero-vegetating (more frequently on the nose) or terebrating (lupus vorax)

aspect, when we find deep ulcerations that result in the destruction of cheeks, nose. Ulcerations on the limbs are superficial, arciform (ulcero-serpiginous lupus).

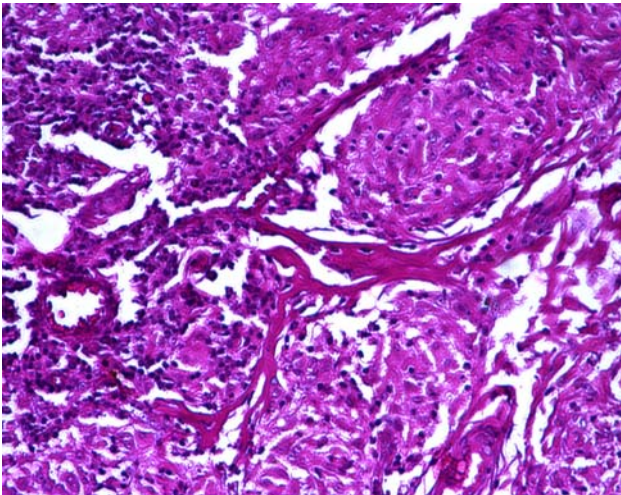


Figure 7 – Fibrosis areas around tubercles

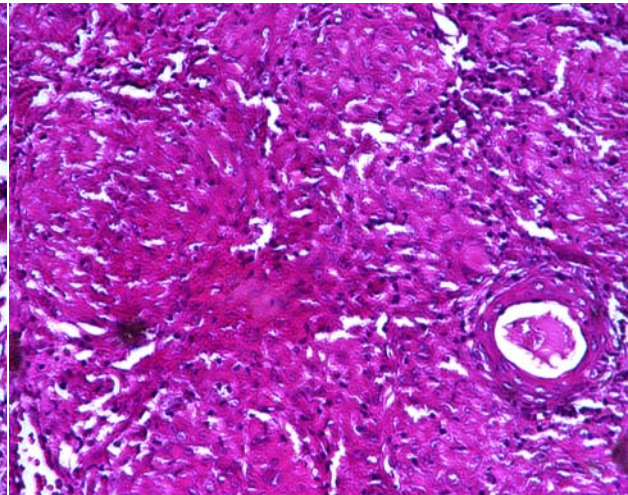


Figure 8 – Small areas of caseification necrosis at the centre of tubercles



Figure 9 – Evolution post anti-tuberculosis chemotherapy



Figure 10 – SCC on lupus vulgaris



Figure 11 – Postoperative evolution

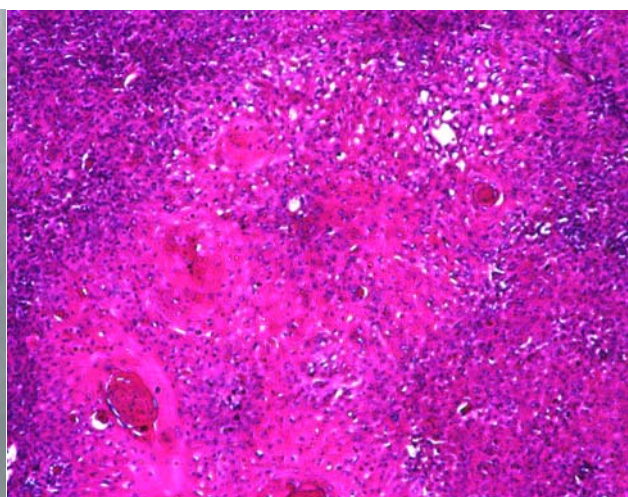


Figure 12 – Moderate differentiated SCC

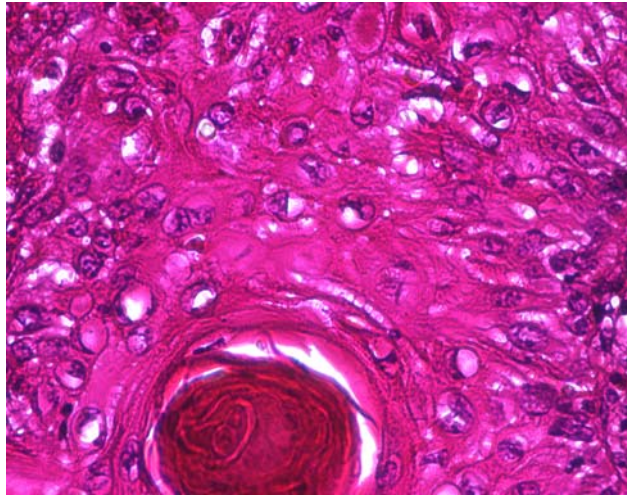


Figure 13 – Moderate differentiated SCC

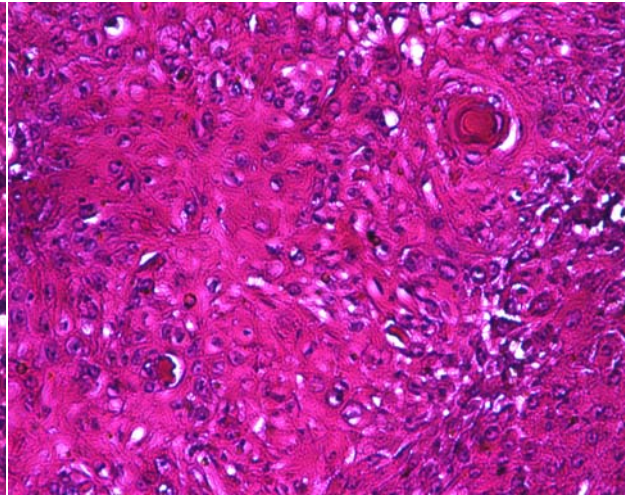


Figure 14 – Moderate differentiated SCC

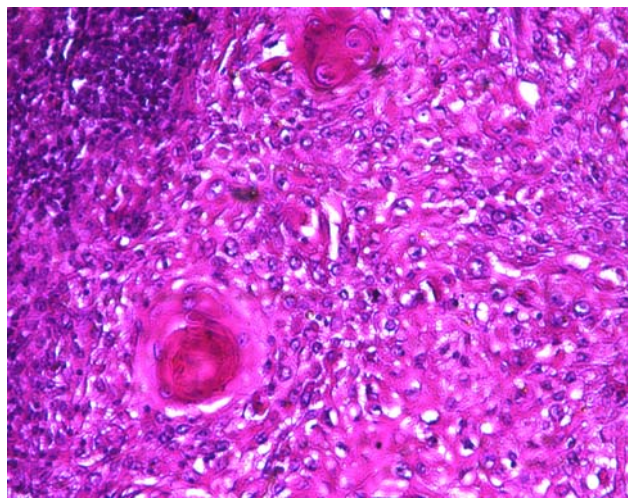


Figure 15 – Retromandibular ganglionic metastasis of moderate differentiated SCC

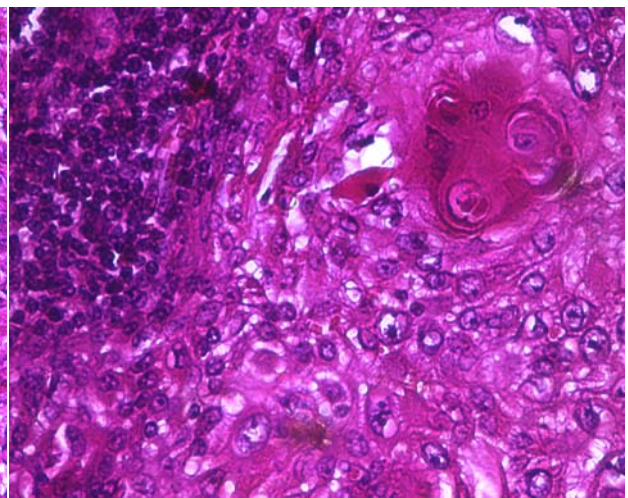


Figure 16 – Retromandibular ganglionic metastasis of moderate differentiated SCC

The positive diagnosis of lupus vulgaris was based on the clinical aspect, on the visualization of lupus tubercles in vitropressure, on the histopathologic exam and the IDR to tuberculin, which was highly positive, whereas the Ziehl-Nielsen coloration, as well as the culture performed after the cutaneous biopsy, were negative.

The tuberculous nature of the cutaneous lesion is certain when pathogenic mycobacteria (*Mycobacterium tuberculosis*, *Mycobacterium bovis*) are showed at this level. The visualization thereof is made by Ziehl-Nielsen coloration, culture in the Lowenstein environment or inoculation in guinea pigs. The low amount of LV bacilli makes that, most of the times pathogenic mycobacteria are not visualized at the level of the lesion, by these methods. The success in the establishment of the LV diagnostic is ensured by the PCR (polymerase chain reaction) technique, according to some authors [6, 7], as bacillary DNA sequences may be identified. Thus, only 6% of the cutaneous cultures from patients with lupus vulgaris were reported as positive [1].

The following criteria (relative criteria) are used with an informative value for LV diagnosis:

- The presence of Koster's follicle, by histological cups;
- The visualization of sensitivity to tuberculin;
- The coexistence of a deep tuberculosis focus;
- Positive personal or familial tuberculosis antecedents.

The differential histological diagnostic in lupus vulgaris is made with other granulomatous inflammatory reactions.

If no treatment is taken LV evolution is chronic, progressive, but slow. Along decades, it may result in invalidating mutilations, especially at the level of the nose.

Other complications, such as microstomia and ectropion have been described, depending on the location of the LV [8]. However, the most important complication is represented by the appearance of cancers, especially of the spinocellular carcinoma [9, 10].

As it is already known, squamous cell carcinomas represent 20–40% of cutaneous carcinomas and they usually start after the age of 60. They are predominant in persons with light skin, exposed to sunlight and bad weather. Many of these malign tumors start on

preneoplastic lesions, such as solar keratoses, keratotic cheilitis, cutaneous cone, keratoacanthoma, chronic radiodermatitis, leukoplakia. However rarely, chronic inflammatory dermatoses may represent the starting point of a squamous cell carcinoma. Of these, LV seems to suffer carcinomatous transformation most frequently. Malignization occurs after a long latency (after 57 years in our case). The risk of malignization was appreciated in the first part of the previous century as being 1–4% (Pautrier and Touraine), 10% (Gottran) and 10.5% (Hornberger). Researches in the area have shown that malign degeneration is more frequent in LV cases treated with ionized radiations (Roentgen-therapy) or by sclerogenic methods. As such, treatment was abandoned during the last decades; we have noticed a decrease in the malignization risk to 1–2% of LV cases.

As for malignization mechanisms, in our case the fibrosclerous and the inflammatory cicatricial processes have contributed on the one hand and the extended exposure to solar radiations on the other hand. Note that our patient was phototype II (light tegument, hair and eyes, individuals are tanned in a very difficult way and get frequent sunburns) and she worked as a farmer. We remind that the anti-tuberculosis chemotherapy resulted in an obvious improvement of the clinical picture, except at the level of the right ear lobule, in fact where the fibrosclerotic and the inflammatory processes had the highest evolution period.

Besides the squamous cell carcinoma, there is also discussed the possibility of the development of other cancers on old LV lesions, such as basal cell carcinoma and exceptional, sarcoma or melanoma [11]. Every time, the certainty diagnostic for cancer is established on basis of the histological exam. As for the diagnostic of squamous cell carcinoma on old LV, it was established through the histological exam of the tumor, after the excision thereof with safety margins. Considering the metastasizing potential (by lymphatic and/or sanguine means) of the squamous cell carcinoma, simultaneously with the clinical suspicion of retromandibular adenopathy, the regional ganglionic group was scraped out. The histological exam showed the presence of ganglionic metastasis.

Conclusions

Lupus vulgaris can turn into squamous cell carcinoma after a long variable latency, 57 years in the case of our patient.

The patient with lupus vulgaris must be periodically examined by clinical methods, and the presence of any suspect lesion imposes cutaneous biopsy, followed by the histological exam for noticing malignization in the incipient, curative phase.

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