

Erythrodermia Associated to Lung Cancer

Simu Lia-Maria¹, Morariu S.H.¹, Turcu M.², Podeanu Maria-Daniela³, Șincu Nina⁴, Marian D.⁵

¹ Department of Dermatology and Venereology, University of Medicine and Pharmacy Tg. Mureș

² Department of Pathology, University of Medicine and Pharmacy Tg. Mureș

³ Department of Radiology and Imaging, University of Medicine and Pharmacy Tg. Mureș

⁴ Department of Infectious Diseases, University of Medicine and Pharmacy Tg. Mureș

⁵ Department of Surgery, University of Medicine and Pharmacy Tg. Mureș

There are a few skin lesions which are connected with internal malignancies, being important especially if they appear prior to neoplasia. We are presenting the case of a patient who had desquamative erythrodermia associated to lung carcinoma. The patient was also diagnosed with a cerebral metastasis. The appearance of skin lesions suggested the presence of a subacute immune vasculitis, this was confirmed by immunohistochemical examinations, which revealed a leukocytoclastic vasculitis. Given the fact that previous erythematous lesions improved during the treatment of cerebral metastasis, the recurrence of erythrodermia suggests the evolution of metastasis. On the other hand, we can not rule out the possible role of the received chemotherapy in the development of the vasculitic process. The observation that these events do not occur in all cancer patients leads to the conclusion that the triggering mechanisms responsible for these paraneoplastic syndromes are individually conditioned

Keywords: cutaneous paraneoplastic syndromes, leukocytoclastic vasculitis

Introduction

Skin, paraneoplastic syndromes caused by lung cancer, are conditioned by the immuno-allergic response of the body to cancerous tissue. In this response intervene proteolytic agents' aggression, the reactivity of sympathetic and parasympathetic nervous system, the mucopolysaccharides and electrolytes metabolism and also blood supply and presence of risk factors.

These lesions are autonomous, nonmalignant, without cell atypia. They may evolve concurrently with cancer, or before them. In all cases they represent an element of seriousness in the development of cancer. The most authors agreed that the main mechanisms responsible for producing skin lesions are: insufficient intake of oxygen and increasing carbon dioxide, secretion of polypeptidic factors and autoimmune reactions that are added [1, 2].

We present a clinical case of erythrodermia. This patient was clinically examined and investigated using imaging and laboratory tests. Previously, he had been diagnosed with a form of lung neoplasm. The 44 year-old male patient was diagnosed with lung cancer 2 years prior to presentation. The tumor was in the upper right lobe and he underwent upper right lobectomy followed by radiation therapy and chemotherapy. Histopathological examination revealed a papillary adenocarcinoma with undifferentiated areas with outbreaks of large atypical cells which were arranged in glandular structures with papillary epithelial atypical hyperplasia. Also, there were extensive areas of necrosis and territories comprising undifferentiated atypical cells. Ten months after surgery, head CT showed a right emisferial mass with extensive area of edema with dimensions of 17.3-mm – single brain metastasis – which led to 24 sessions of cobaltotherapy, so that within one month the metastasis shrinked to 5.1 mm.

On the skin, the patient presented an intense desqua-

mative erythrodermia, predominantly on the scalp and internal sides of the upper and lower limbs.

Biopic skin examination showed the following changes: moderate acanthosis of epidermis and in the dermis there were hyperplasia of small vascular structures with a single row of endothelial cells and few peritelial cells, that had wide lumen and a post capillary venule aspect. Around these vessels were constantly infiltrated with lymphocytes, histiocytes and neutrophils some of which were to be disintegrated. The appearance suggested the presence of a subacute immune vasculitis. Immunohistochemical examinations allowed to specify what types of cells the perivascular inflammatory infiltrate contained. They were represented by macrophages and T lymphocytes, for B lymphocytes the result was negative. Because of the destruction of few neutrophils we have considered this lesion as a leukocytoclastic vasculitis.

Discussions

Histopathological changes are included in the group of immune vasculitis which occur in collagenoses (lupus erythematosus, poliarteritis nodosa), may evolve in viral infections (Coxsackie, herpetic), after consumption of drugs (penicillin) but also in presence of internal malignancies [1, 2, 3]. Skin biopsy reveals the presence of vascular and perivascular infiltration of polymorphonuclear leukocytes with formation of nuclear dust (leukocytoclasia), extravasation of erythrocytes, and fibrinoid necrosis of the vessel walls. This process is dynamic and a biopsy of a lesion taken too early or too late in its evolution may not reveal these findings. The presence of eosinophils has been correlated with drug-associated disease [4, 5]. Leukocytoclastic vasculitis's pattern can occur in any vasculitic syndrome but also may occur in nonvasculitic diseases such as neutrophilic dermatoses, at the base of leg ulceration, or in some



Fig. 1. Desquamative erythrodermia



Fig. 2. Detail – lower limb

insect bite reactions. Careful clinical-pathologic correlation is necessary. Immunofluorescent staining may reveal immunoglobulins (immunoglobulin G, immunoglobulin M) and complement components (C3, C4) deposited on the skin basement membrane, which are suggestive of immune complex deposition. In Henoch-Schönlein purpura, IgA deposits may be found [6].

Most cases of paraneoplastic vasculitis occur before or concurrent with cancer diagnosis [7]. Associated manifestations of a leukocytoclastic vasculitis such as hypertrophic pulmonary osteoarthropathy can be also observed [8]. Failure of a vasculitis to respond to conventional therapy should raise questions about underlying malignancy. The most frequent form of vasculitis as paraneoplastic phenomenon is leukocytoclastic vasculitis. Effective treatment of the cancer enhances the likelihood of improvement in vasculitis [9]. The vasculitic lesions can be also disseminated – systemic vasculitis [10]. Since vasculitic paraneoplastic syndromes, including cutaneous leukocytoclastic vasculitis, may develop before the clinical presentation of malignant tumors, most of the authors strongly suggest that in apparently idiopathic cutaneous leukocytoclastic vasculitis, patients should be evaluated for the presence of occult malignancy that could be curable by early detection [11].

These skin lesions may be explained through the existence of immune complexes containing IgG and complement which are deposited on the capillary walls causing their deterioration. The presence of antineutrophil cytoplasmic antibodies (ANCA) can be demonstrated in many patients with vasculitis. These antibodies destroy azurophilic granulations of polymorphonuclear leukocytes but also lysosomal enzymes of monocytes or cytoplasmic components of endothelial cells. These antibodies are evidenced by immunofluorescence or immunohistochemical examination. Proinflammatory cytokines released by tumor cells favor expression of surface antigens that have affinity for antineutrophilic antibodies (ANCA) resulting in neutrophil degranulation and alterations of endothelial cells. It is mentioned a case of a patient with bronchioloalveolar carcinoma who has developed cutaneous vasculitis with highly positive p-ANCA titer [12]. The immune vasculitis of the skin was frequently mentioned in the context of malignancy, not only in lymphoma or leukemia but also in carcinoma [7]. The period of time in which cancer and vasculitis occur is also important, so that more than 12 months raise questions about the connection between these two conditions [9].

In our case, previous erythematous lesions were improved during diagnosis and treatment of cerebral metas-



Fig. 3. Detail – hypogastric region

tasis. The recurrence of erythrodermia (cutaneous vasculitis) suggests the evolution of metastasis. On the other part, the chemotherapy administered to this patient could have caused the vasculitic process, so, we cannot rule out its role in this case.

Conclusions

It has been mentioned the triggering role of lung malignancies in cutaneous immune vasculitis and also in other syndromes: Leser-Trelat, palm's keratosis, ichthyosis acquisita, Bowen's disease, scleroderma, pemfigus, erythema gyratum repens, acanthosis nigricans, palmoplantar hyperkeratosis (thilosis), Bazex acrodermatosis, hipertrichosis lanuginosa acquisita.

Cutaneous vasculitis is reported mostly in connection with hematologic malignancies (leukemia, lymphoma) but recently, vasculitis is reported to be associated with bronchial or gastrointestinal tract carcinoma [4,14]. In our case, leukocytoclastic vasculitis could have been caused by the evolution of the metastasis but the coexistence of radio- and chemotherapy prevents us to strongly assign the erythrodermia only to the tumor.

The observation that these events do not occur in all cancer patients leads to the conclusion that the triggering mechanisms responsible for these paraneoplastic syn-

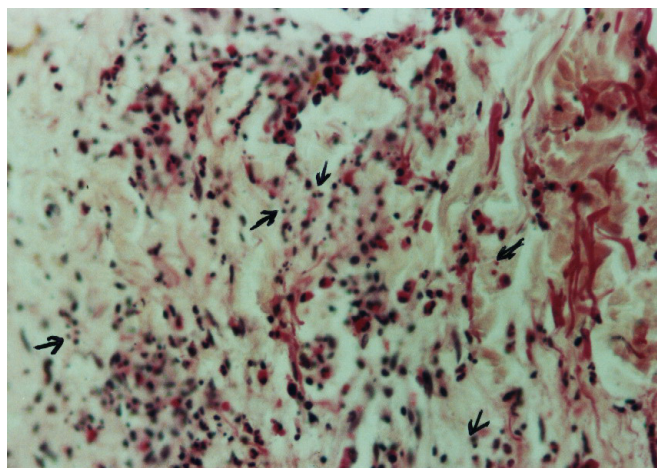


Fig. 4. Microscopic appearance of the skin – lymphocytic and histiocytic perivascular infiltrates and some neutrophils which are to be desintegrated (leukocytoclasia), HE, ob 20x

dromes are individually conditioned. The clinical significance of these conditions is represented by the moment of their occurrence, especially when the onset of the skin lesions precedes the evolution of the internal malignancy.

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