

Cutaneous metastasis of internal carcinomas, our experience in 94 cases

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Abstract

Cutaneous metastasis is a neoplasia involving the dermis and/or hypodermal tissue with no contiguity with the primary tumor.

Materials and methods: A retrospective and descriptive study was conducted on all patients with diagnosis of cutaneous metastasis consulting the POBA Dermatology Department between 1993 and 2008. Features taken into account were: primary tumor, gender, age, location, clinical aspect, number of lesions, lapse between primary tumor detection and appearance of metastasis, and survival time after diagnosis of metastasis. The diagnosis was confirmed histopathologically in all patients.

Objectives: To calculate incidence; to identify clinical variants; to determine the cases where metastases preceded the primary tumor, and were the sign that led to diagnosis; and to compare the results with international and national statistics.

Results: A total of 94 patients with diagnosis of cutaneous metastasis were studied: in 65 patients, the primary tumor was in breast, 9 in lung, 3 in kidney, 3 in stomach, 2 in colon, 2 in ovary, 2 in bladder, and 1 case in rectum, parotid gland, liver, esophagus, and osteosarcoma, respectively. In the remaining 3 patients, metastasis preceded diagnosis of the primitive tumor. Most of the cutaneous metastases involved women (76 percent), with breast cancer as first cause. In men, amounting to 24 percent of the patients, most frequent was lung metastasis, followed by kidney and stomach. Most affected age group ranged from 50 to 70 years. Most frequent location was chest and abdomen. Rare locations were palm of hand, fingers and toes. Survival was less than 2 years after detection of metastasis.

Conclusions: Our findings are similar to the published data. In our case material we emphasize: rare locations: palm of hand, fingers, and toes; glans metastasis of osteosarcoma not found in the literature; clinical variants not described (granuloma annulare-like, pagetoid, and eczematous (Dermatol Argent 2009; 15(2):117-124).

Key words: cutaneous metastasis, primary cancer, clinical variants.

Introduction

Metastasis [Greek *meta* (after, beyond), and *stasis* (stop, stagnate)]¹ is any neoplastic lesion arising from another noncontiguous neoplasia.

By cutaneous metastasis, we mean a neoplastic lesion involving dermis and/or subcutaneous cell tissue not contiguous to the primary tumor.

It must be differentiated from direct extension, that is the neoplastic lesion produced directly by the primary tumor mass;² thus, direct propagation occurs by contiguity of implantation, and is not a metastasis.

For dissemination, a metastasis requires a **lymphatic pathway** and/or a **hematogenous pathway**.

By the **lymphatic pathway**, the neoplastic cells reach the skin directly (through the thoracic duct-subclavian vein-general circulation, with subsequent cutaneous permeation; or by retrograde via, due to obstruction of the lymphatic lumen by the tumor embolus, and subsequent centrifugal deviation to the skin.³

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By the hematogenous pathway, the tumor may disseminate through venous vessels to the left heart cavity; it is less frequent by arterial pathway, not only due to the arterial wall structure, but also due to the higher intraluminal pressure.⁴⁻⁶

The mechanism to produce a cutaneous metastasis comprises several steps or stages:⁵⁻⁷

1. Detachment of primary tumor.
2. Invasion and intravasation of the neoplastic cell within the vessel.
3. Passage through the blood and/or the lymphatic circulatory system.
4. Stoppage (stasis) in a receptor bed vessel.
5. Extravasation through the vessel wall, and invasion of the receptor tissue bed.
6. Proliferation in the tissue.

Cutaneous metastases of internal neoplasias have a 0.8 to 8 percent incidence.⁸ They may be a tumor sign in advanced states, or the first clinical manifestation of an unknown visceral neoplasia. We stress the importance of the dermatologist in the diagnosis of an unknown primary tumor through cutaneous metastasis.

Classic clinical forms of metastases are divided in: *early*, erysipeloid or inflammatory, and telangiectatic; and *late*, nodular and cuirass.

The **atypical** clinical variants include bullous, sclerodermiform, cicatricial, umbilical, dysmetabolic papula-like, zosteriform, and alopecic variants.⁹

Objectives

- To calculate incidence of cutaneous metastases.
- To identify clinical variants.
- To determine proportion of cases wherein metastasis preceded the primary tumor and was the sign that led to diagnosis.
- To compare data and results with international and national statistics.

Materials and methods

A retrospective and descriptive study was conducted on all patients with diagnosis of cutaneous metastasis of internal carcinoma consulting the Dermatology Department of Policlínico Bancario in the period 1993-2008.

- We analyzed:
 - triggering primitive tumor
 - gender
 - age
 - location
 - clinical aspect
 - number of metastasis

- lapse between primary tumor detection and appearance of metastasis
- survival after diagnosis of metastasis

- Diagnosis were confirmed by histopathological and immunohistochemical studies for orientation on probable triggering tumor in patients with unknown primitive tumor.

Results

A total of 94 patients with diagnosis of cutaneous metastasis were studied: in 65 patients the primary tumor was in breast, 9 in lung, 3 in kidney, 3 in stomach, 2 in colon, 2 in ovary, 2 in bladder, and 1 case in rectum, parotid gland, liver, esophagus, and osteosarcoma, respectively.

In the remaining 3 cases, metastasis preceded the primitive tumor.

Most affected age group ranged from 50 to 70 years. Predominant primary tumor appeared in breast (70 percent of the cases), followed in frequency by lung cancer (10 percent) (**Chart 1**).

Average lapse between primary tumor and metastasis ranged from 2 and 5 years (**Chart 2**).

Of the cutaneous metastases, 76 percent were in female patients, and breast cancer was the first cause in women, with 65 patients (94 percent of the cases). Following in frequency are ovary in 2 cases, and lung, rectum, and bladder in 1 case. In males (24 percent of the cases) most frequent was lung metastasis with 8 cases (37 percent). Following in frequency are kidney and stomach with 3 cases each, colon with 2 cases, bladder, parotid gland, liver, esophagus, and osteosarcoma with one case each. Described in detail are age, location, number of lesions and clinical variant in the 2 dominant tumors: breast cancer and lung cancer.

The 65 breast cancer metastasis cases appeared in females, and the age of 76 percent of patients ranged from 50 to 80 (**Chart 3**).

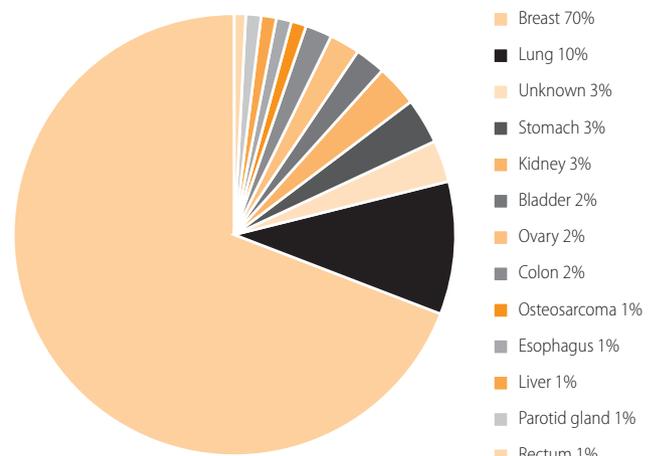


Chart 1. Primary tumor.

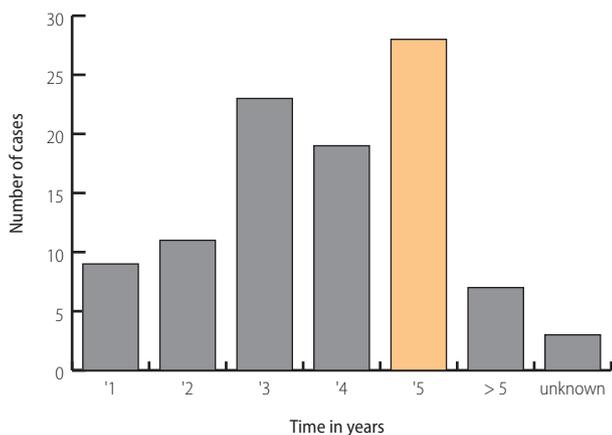


Chart 2. Lapse between primary tumor and metastasis.

TABLE OF VALUES FROM CHART 2.

Up to 1 year	9 cases
Up to 2 years	11 cases
Up to 3 years	23 cases
Up to 4 years	19 cases
Up to 5 years	28 cases
More than 5 years	7 cases
Unknown	3 cases

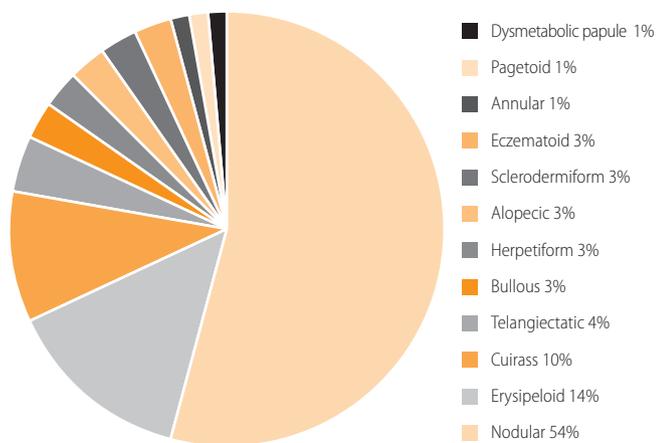


Chart 4. Breast cancer metastases. Clinical features.

VALUES OF CHART 4.

Nodular	39 cases
Erysipeloid	10 cases
Cuirass	7 cases
Telangiectatic	3 cases
Bullous	2 cases
Herpetiform	2 cases
Alopecic	2 cases
Dysmetabolic papule	1 case
Sclerodermiform	2 cases
Annular	1 case
Eczematous	2 cases
Pagetoid	1 case

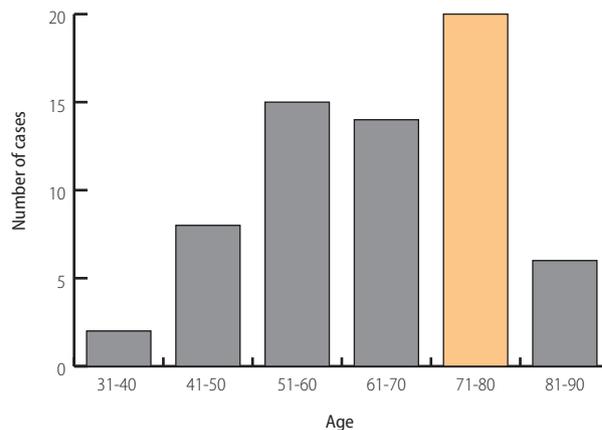


Chart 3. Breast cancer metastasis. Incidence per age.

TABLE OF VALUES FROM CHART 3.

31 to 40 years	2 cases
41 to 50 years	8 cases
51 to 60 years	15 cases
61 to 70 years	14 cases
71 to 80 years	20 cases
81 to 90 years	6 cases

Single presentation form was found in 42 cases, and multiple lesions in 25 patients.

Lesions were located in mammary area in 34 cases, chest 18, back 10, arm 6, presternal 6, ribs 5, flank 5, axilla 5, scalp 3, clavicular area 1, pubis 1, leg 1 and neck, 1 case.

In 56 percent of cases, lesions involved the mammary (34 cases) and the chest (18) area. The age was divided in decades, with a dominance ranging from 50 to 80 years (76 percent) (**Chart 3**). Predominant clinical variant was nodular, with 39 cases corresponding to 54 percent of the total. The rest of variants are described in **Chart 4**, with predominance of erysipeloid (10 cases). Variants not described in the literature are: eczematous, pagetoid, or granuloma annulare-like.

In some patients two clinical forms appeared simultaneously or during the course of the disease. Cases 17 and 18 combined nodular and erysipeloid variants, case 55 combined nodular and telangiectatic variants, case 28 combined erysipeloid form and two years later nodular and telangiectatic forms, case 65 combined nodular clinic form and herpetiform some years later. Lung cancer metastasis amounted to 9, 8 of which were in males.

The age of onset was: 41 to 50 years 1 case, 51 to 60 years 3 cases, 61 to 70 years 4 cases, 71 to 80 years 1 case, maintaining dominance in males between 50 and 70 years.

Single clinical forms were seen in 6 cases, and multiple in 3 cases. Their locations were: scalp 4 cases as predominant site, back 2, face 2, toe, shoulderblade area, neck and arm 1 case.

The nodular form was the most frequent clinical variant (70 percent of the cases). Other variants were in plaque, alopecic and telangiectatic.

Follow-up was completed in 88 cases, 75 patients evolved to death: 39 patients died in the first year (52 percent of the cases) and 16 patients in the second year (21 percent of the cases).

Discussion

Most frequent was breast cancer metastasis, with 76 percent of the total of cases and 94 percent for females. In males, predominant primary tumor was in lung, with 37 percent of the patients. These figures are similar to those found in the literature.^{1,7,10}

In contrast, colon cancer metastasis stated as second in frequency both in females and males was displaced by those originated in ovary and stomach, respectively.^{1,10}

Time lapsed between primary tumor diagnosis and metastasis detection was from 2 to 5 years.

The age group wherein most cases were recorded was between 50 and 70 years. Data is consistent with the literature.^{1-3,9}

All primitive tumors were described by other authors, except osteosarcoma.¹¹⁻¹⁶

Multiple metastases are defined as lesions found in various body sites. Taking into account this concept, 42 cases were found as single variant and 25 with multiple lesions in breast cancer metastasis; 6 patients with single lesions and 3 with multiple lesions in lung cancer metastasis.

Reviewed data indicate higher incidence in multiple lesions, because they do not take into account the above described concept, and consider that multiple metastases occur when there is more than one lesion.^{3,7,17}

Most frequent location of breast cancer metastasis was on chest and breast, with 56 percent of the total cases. Following in frequency are the back and the scalp.

Lung cancer metastases were located on scalp in 34 percent of patients.

Among the rare locations we highlight: one breast cancer metastasis located on a leg, one lung cancer metastasis located on a toe^{18,19} (**Figure 1**), a lesion on palm of the hand (**Figure 2**) with origin in a renal carcinoma, and two lesions located on a foot sole and thumb tip with origin in a liver carcinoma (**Figure 3**).

Of the clinical variants of breast cancer metastasis we point out the nodular form as the most frequent, followed by the erysipeloid form. The two cases with herpetiform clinical features had breast cancer as primary tumor and were preceded by an



Figure 1. Lung cancer metastasis located on a toe.



Figure 2. Renal carcinoma metastasis in palm of the hand.



Figure 3. Metastasis located on thumb tip originated from a liver carcinoma.



Figure 4. Bullous clinical appearance of a breast adenocarcinoma metastasis.



Figure 5. Pagetoid or bowenoid variant of a breast adenocarcinoma metastasis.

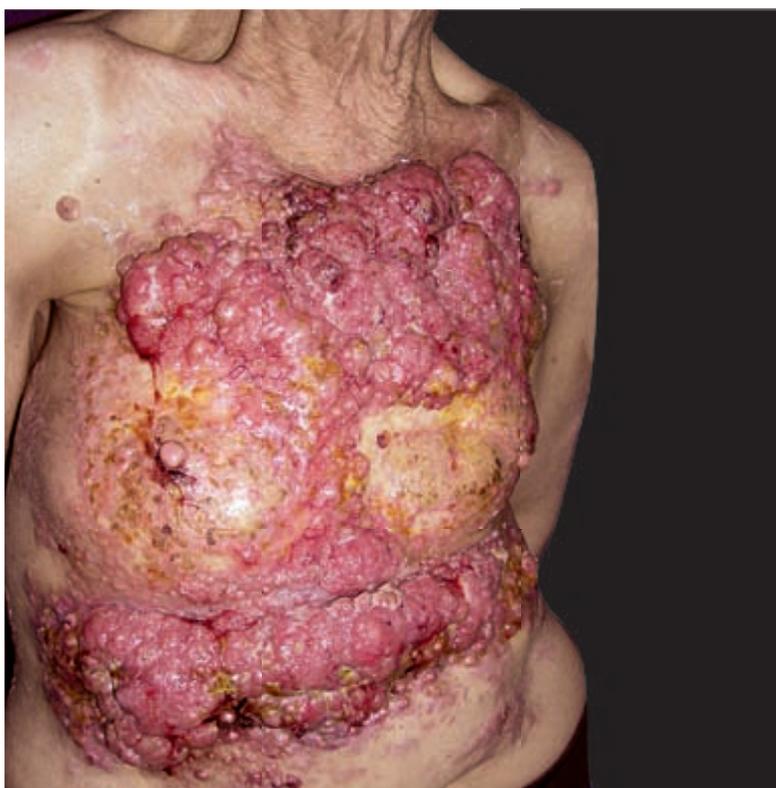


Figure 6. In cuirass breast carcinoma metastasis.

hemorrhagic and ulcerated type aggressive herpes zoster, and then metastatic nodes appeared on it in linear distribution.²⁰⁻²³

As rare variants, 2 cases are mentioned with bullous clinical presentation²⁴ (**Figure 4**). We point out variants not described in the literature: pagetoid or bowenoid (**Figure 5**); eczematous, where lesions were seated on the mastectomy scar and extended to the breast and arm of the other side; and granuloma annular-like, which clinical features were found reported as “annulare centrifugum type”.²⁵

The clinical in cuirass variant, described in patients with years of survival to the primary tumor, generally begins with nodular forms that with time converge as a cuirass.²⁶⁻²⁹

Of the 7 cases with this metastasis variant stands out a female patient showing lesions extended on all the chest and abdomen (**Figure 6**).

We do not consider sclerodermiform and in cuirass as synonyms.

The alopecic forms were only found on scalp.^{30,31} Patients with nodular forms evolved to the cuirass form.³²

The number of clinical variants was greater than the 65 cases found, because some patients showed 2 clinical forms simultaneously or during the disease evolution.

Primary tumors causing metastasis in the umbilical area were stomach, colon and ovary, in data consistent with the literature.³³⁻³⁶

Rectum adenocarcinoma metastasis appeared as an inflammatory plaque located in abdomen, in a similar way to uterus or stomach metastasis.^{16,37}

Noteworthy was the extension of a metastatic lesion in a patient with primary bladder tumor of erysipeloid type involving abdomen, flank and both thighs.³⁸

Parotid gland cutaneous metastasis are rare.³⁹ The case shown in the case material appeared as an extensive infiltrated hemorrhagic plaque in cuirass involving left side of the face, ear, neck and chest, whereon multiple nodes developed (**Figure 7**).

Esophagus carcinoma metastasis involved the floor of the mouth; the tumoral mass extended forward and behind the lower incisors^{40,41} (**Figure 8**).

We reported one case of penis metastasis of an osteosarcoma. Lesions of nodular aspect were distributed on the gland (**Figure 9**). Cutaneous osteosarcoma metastases are exceptional, and no genital location has been published so far.

In 3 patients, the cutaneous metastasis led to diagnosis of unknown primary tumor. Diagnosis

of lung cancer was reached through a scalp lesion; and in the two other cases, metastases on chest and axilla came from a breast cancer.

Different theories have been suggested to explain the affinity of metastasis for scalp. Perhaps it occurs because it is a nonmobile, highly irrigated area.^{2,3,7,42-44}

Of the 94 cases, 11 were located on scalp, with alopecic and nodular clinical forms; 5 cases had a lung primary tumor, 3 a breast tumor, 2 a kidney tumor, and one case a bladder tumor.

Histological study of the lesions may lead to the diagnosis of the primary tumor: the adenocarcinoma is related to breast, lung, digestive tract and ovary neoplasias. In the case of an epidermoid carcinoma, it may be in lung, esophagus and oral cavity. If it is a undifferentiated or anaplastic tumor, it may be in lung or breast.^{46,47}

Diagnosis presumption is confirmed by immunohistochemical techniques⁴⁵ (Table 1).

Follow-up was completed in 88 cases, 75 patients evolved to death: 52 percent of patients died in the first year, and 21 percent died in the second year. These facts correlated with the data found in the literature, since 73 percent of patients died in the 2 years subsequent to the metastasis diagnosis.^{3,29,48}

Conclusions

Our findings are similar to those found in the reviewed literature:

- Higher incidence of cutaneous metastasis in females.
- Predominant primary tumor:
 - Females: breast cancer
 - Males: lung cancer
- Most affected age group: between 50 and 70 years.
- Most frequent location: on chest

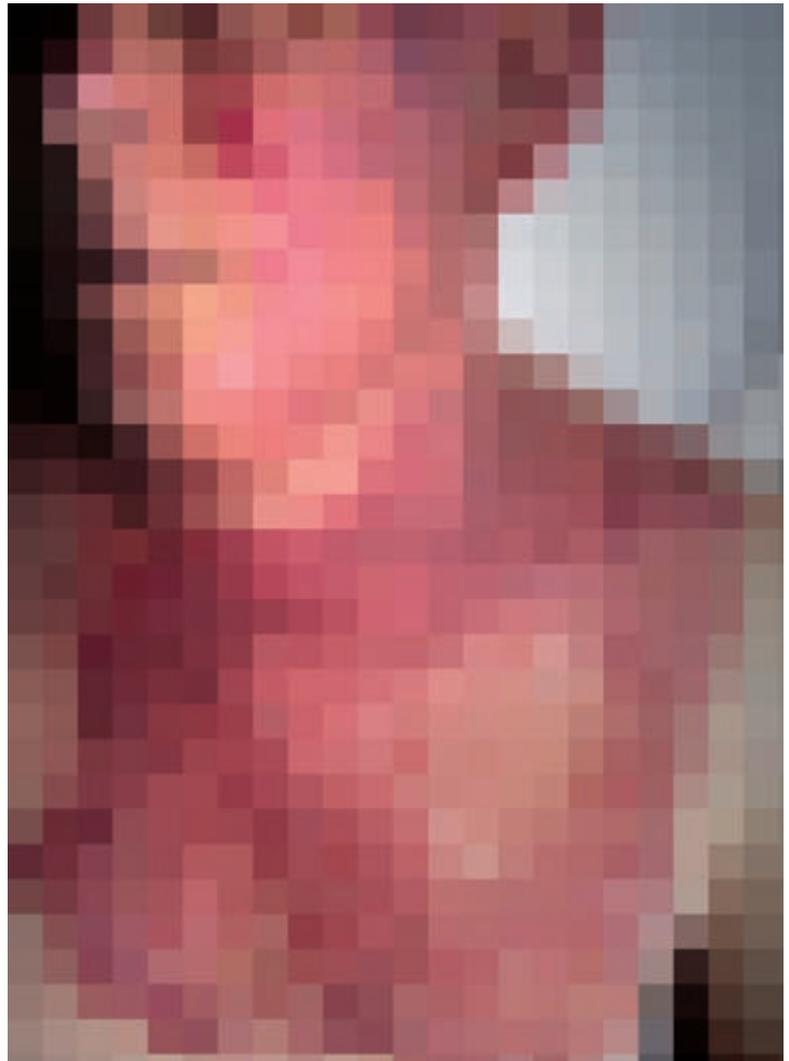


Figure 7. Parotid gland adenocarcinoma metastasis.

- Survival less than 2 years after diagnosis of metastasis.

In our case material, we highlight:

- Rare locations: palm of the hand, fingers and toes.
- One location, not found in the literature, glans metastasis of osteosarcoma

TABLE 1. IMMUNOHISTOCHEMISTRY FOR DETECTION OF UNKNOWN PRIMARY TUMOR.

	Vim	CK 7	CK 20	CA 15.3	CA 19.9	Renal	CA 125	Hep.	CEA	TTF-1	Alpha fp	Thyroglobulin
Breast duct cancer	-	+	-	+	-/+	-	-/+	-	+	-	-	-
Colon adenocarcinoma	-	-	+	+	+	-	-/+	-	+	-	-	-
Pancreas adenocarcinoma	-	+	+	+	+	-	-/+	-	+	-	-	-
Renal carcinoma	+	-/+	-	+	-	+	-	-	+	-	-	-
Serous ovary cancer	-	+	-	+	-	-	+	-	-	-	-	-
Mucinous ovary cancer	-	+	+	+	+	-	+	-	+	-	-	-
Liver carcinoma	-	-	-	-/+	-	-	-	+	-	-	+	-
Thyroid cancer	+	+	-	+	+	-	+	-	-/+	+	-	+
Lung adenocarcinoma	-/+	+	-	+	+	-	-	-	+	+	-	-

Vim: vimentin. **CK:** citokeratin. **TTF-1:** Thyroid transcription factor. **Alpha fp:** alpha fetoprotein. **Renal:** anti-renal cancer cell Ab (clone 66-4C2). **Hep:** anti-hepatocyte Ab (clone OCH 1E5).



Figure 8. Esophagus carcinoma metastasis in floor of the mouth.



Figure 9. Osteosarcoma metastasis in penis.

- Not described clinical variants: granuloma annulare-like, pagetoid and eczematous.
- The importance of a dermatologist in diagnosis of unknown primary tumor through cutaneous metastasis.

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