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## CASE REPORT

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# Forensic Dermatopathology and Internal Disease

**ABSTRACT:** The gross and microscopic analysis of skin lesions at autopsy can help the pathologist understand diseases and injuries inflicted premortem, perimortem, or postmortem. From January 2003 to January 2004, skin findings at autopsy were closely examined by a dermatologist and sampled for microscopic analysis at the Southwestern Institute of Forensic Sciences. Dermatologic abnormalities in some of these cases led to the discovery of internal disease and allowed for a more complete understanding of the pathologic disease processes affecting the individual. We present four autopsy cases with skin manifestations of internal disease, including pseudoxanthoma elasticum, calciphylaxis, the sign of Leser Trelat, and papular mucinosis, and demonstrate the usefulness of the dermatological assessment at autopsy. In all cases, discovery of these skin lesions and internal disease manifestations allowed contributing factors to the death of the individual to be uncovered.

**KEYWORDS:** forensic science, dermatopathology, skin, disease

The skin is the interface between an individual and the environment and, therefore, plays a major role in the external examination during autopsy. Skin findings can help the examiner understand diseases and injuries inflicted premortem, perimortem, or postmortem. Many natural disease processes that cause death, or contribute to the cause of death, have cutaneous findings. A careful examination of the skin in non-traumatic deaths can suggest specific diseases that are then confirmed by internal examination and microscopic analysis. In some cases, the skin findings are not distinctive or specific to a particular entity on gross examination, and a skin biopsy should be taken to allow for a closer investigation. For example, blisters and erosions are commonly discovered during the autopsy; however, the differential diagnosis for the cause of the skin lesions is broad and may include burns, decomposition blisters, primary skin blistering disorders, blistering drug reactions, coma bullae, and several others. The histology of these entities is quite different, and histopathologic examination may allow for the cause of the blister to be determined.

Forensic dermatopathology is a field that has had limited attention. The skin is sometimes overlooked or only given a cursory examination during autopsy; however, a more careful examination may lead to clues regarding internal disease, events around the time of death, or the post-mortem environment. The literature has only one paper concerning forensic dermatopathology, which was written over twenty years ago (1). The subject has not been revisited, and the skin is only briefly mentioned in the forensic literature through case reports.

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Close examination of the skin and the understanding of cutaneous signs may aid the investigator in discovering internal findings that may have otherwise been overlooked or would not have been attributed to the correct cause. Even if the external findings are not diagnostic, microscopic analysis should be performed, as the findings can be important. Only one report in the literature acknowledges this point, in the description of a case of a 28-year-old male who died suddenly after apparently having a seizure at home (2). Internal examination revealed severe glossitis, epiglottitis, and inflammation of the upper respiratory tract. The patient also had 'mucocutaneous lesions' that involved only 1–2% of his body surface area. Although the skin lesions may have been overlooked, given the minimal involvement, a biopsy was consistent with Stevens-Johnson syndrome and provided a diagnosis and cause of death.

Recently, skin findings at the Southwestern Institute of Forensic Sciences have been closely examined by a dermatologist and sampled for microscopic analysis. In many cases, skin findings have led to the discovery of internal disease and a more complete understanding of pathologic disease processes. We report four of these cases to demonstrate the usefulness of this approach in autopsy.

### *Case 1*

A 49-year-old white female sustained 8% total body surface area burns and inhalation injury after apparently tripping over her space heater and starting a house fire. The patient was asystolic on arrival to the outside hospital and her carboxyhemoglobin level was 60%. Past medical history included blindness, refractory hypertension, and depression. On external examination, there was a large brown firm plaque with peripheral erythema, erosions, and blisters on the back and right flank, consistent with burns. There were also fine yellowish papules in the intertriginous areas. A punch skin biopsy was performed on one of the lesions in the right inguinal crease. Internal examination was not performed. The skin biopsy revealed fragmented and clumped, irregular basophilic fibers

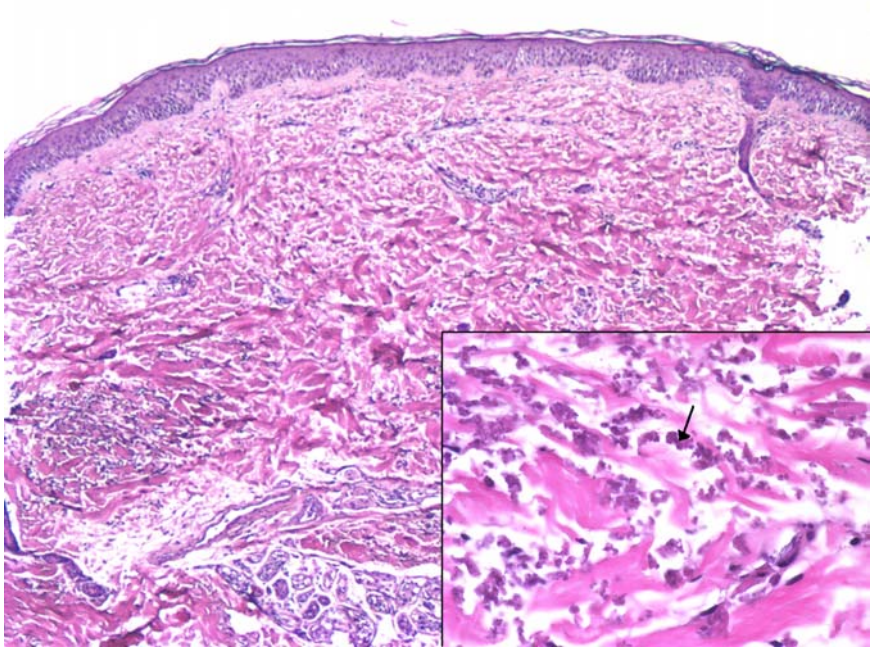

FIG. 1—*Diffuse, extensive, fragmented and clumped, irregular basophilic fibers (arrow) coursing through collagen bundles are consistent with a diagnosis of pseudoxanthoma elasticum. A sparse chronic inflammatory infiltrate, comprised mainly of lymphocytes, is present around some of the basophilic fibers.*

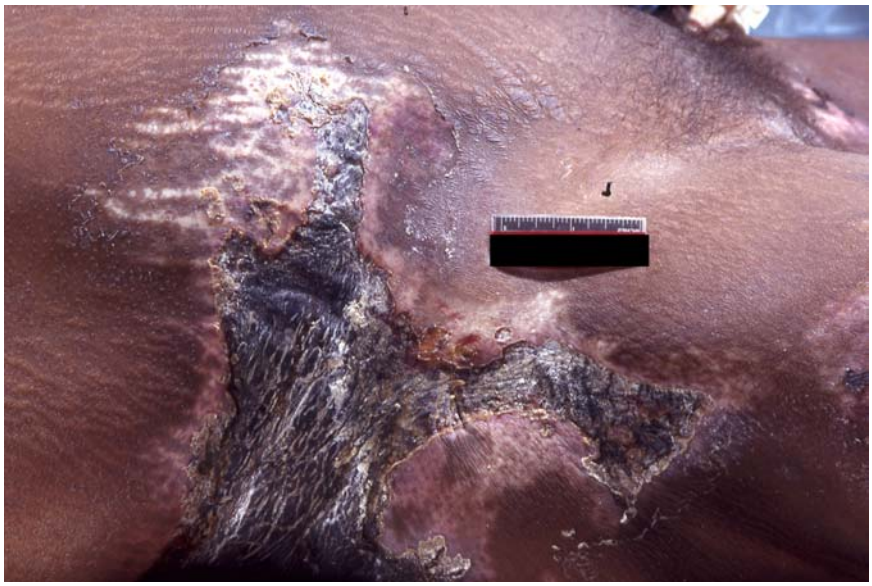

FIG. 2—*Large necrotic stellate ulcerations on her flanks (6 × 9 inches) , characteristic of calciphylaxis.*

on routine hematoxylin-eosin (H&E) histopathologic examination (Fig. 1), which was consistent with a diagnosis of pseudoxanthoma elasticum (PXE).

PXE is a genetic disorder, and the defect has recently been mapped to the ABCC6 gene on chromosome 16 for both the autosomal dominant and recessive forms (3). PXE leads to clumped, distorted, calcified elastic fibers which manifest as disease in many organ systems. Patients typically develop flat, yellowish papules on the skin in flexural areas that sometimes coalesce and resemble "plucked chicken skin." Most patients also develop angioid streaks in the eye that may lead to blindness, and many develop progressive calcification of medium sized arteries that leads to hypertension and myocardial infarction at a young age. The diagnosis of PXE allowed this patient's clinical findings to be attributed to one cause. Knowledge of this genetic disease was useful, given the possibility of significant morbidity and mortality in other affected family members who may not be aware of this possibility, and genetic counseling could be offered.

### *Case 2*

A 24-year-old African American female was witnessed to collapse at home and was in asystole when the paramedics arrived. There were no signs of trauma, and her mother reported she had not been feeling well. The patient had a history of end-stage renal disease, hypertension, and congestive heart failure, which was unusual for her age. External examination revealed large necrotic stellate ulcerations (8–10 cm in diameter) on her bilateral flanks (Fig. 2). A skin biopsy was taken from the periphery of the ulcer.

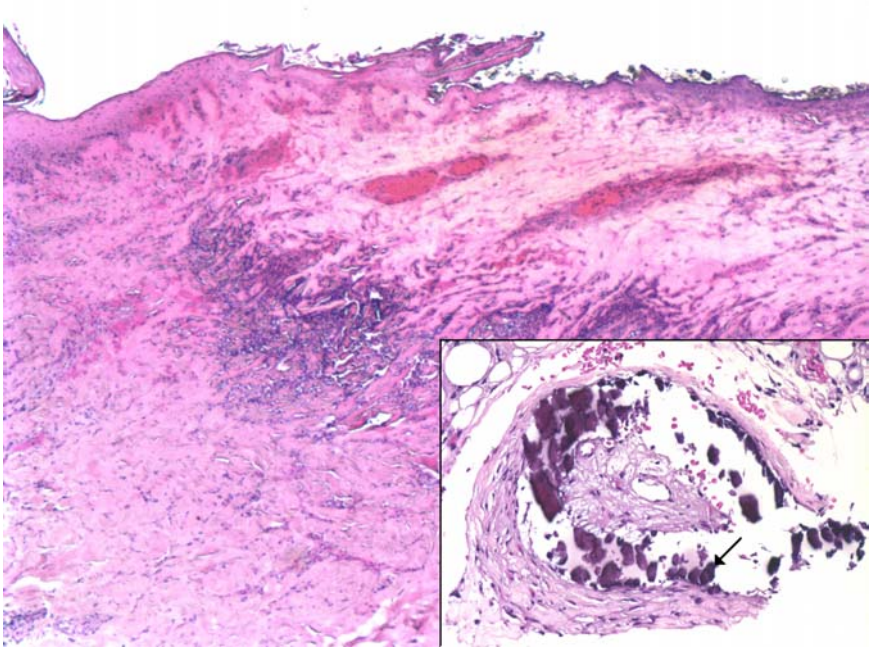

FIG. 3—*Calcification within vessels (arrow) and thrombi in the dermis, confirming the diagnosis of calciphylaxis.*

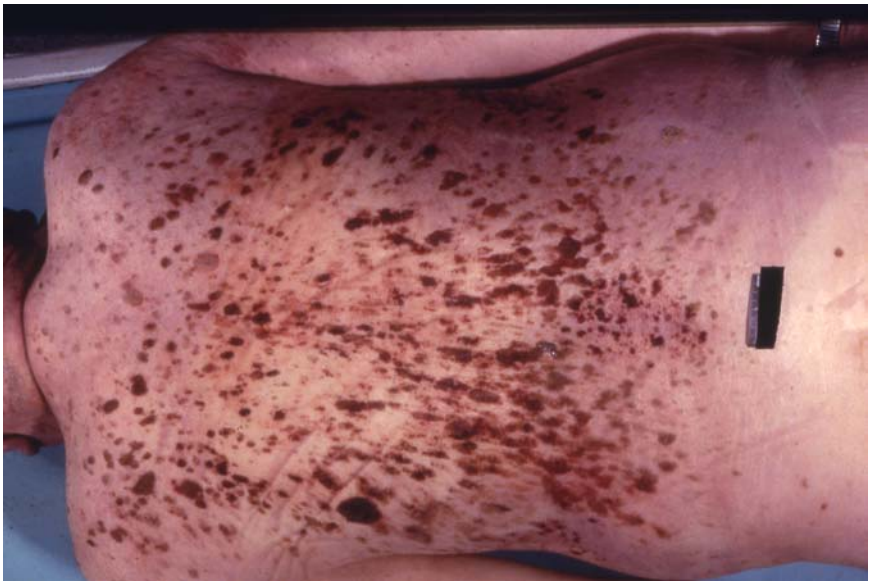

FIG. 4—*Numerous, almost confluent, brown, stuck-on appearing, verrucous papules and plaques, consistent with eruptive seborrheic keratoses.*

An internal examination was not performed. The skin biopsy revealed calcification and thrombi within the vessels of the dermis, consistent with calciphylaxis (Fig. 3).

Calciphylaxis is a vasculopathy that develops most often in patients with renal insufficiency, but other risk factors include female sex, obesity, diabetes mellitus, hypercoagulable states, and dialysis initiated within the past year. The most apparent consequence is the ischemic damage and necrosis that develops in the skin and subcutaneous tissues; however, ischemic involvement of other organs may also be extensive (4). Death is not uncommon within a few months and is usually due to sepsis or visceral involvement. Recognizing this entity at autopsy allows the examiner to realize possible comorbid illnesses of the patient and to guide the autopsy with the understanding of the likely causes of death.

*Case 3*

A 65-year-old white male was found dead in his home with a gunshot wound to the right side of the head and a gun near his hand. The patient had a history of hypertension, atherosclerotic cardiovascular disease, a brain neoplasm for which he had been surgically treated, and suicidal ideation. An external examination revealed a five inch curvilinear scar in the right temporal scalp, as well as evidence of recent surgery, including a parietal/temporal bone flap held in place with wire and a burr hole. The patient also had numerous, almost confluent, brown, stuck-on appearing, verrucous papules and plaques on the trunk, scalp, and face (Fig. 4). A skin biopsy of one of the brown papules was taken and revealed epidermal hyperplasia with anastomosing rete pegs and keratin-filled pseudocysts, consistent with seborrheic keratoses. Autopsy showed a cavitary defect involving the right posterior frontal lobe of the brain. Adjacent

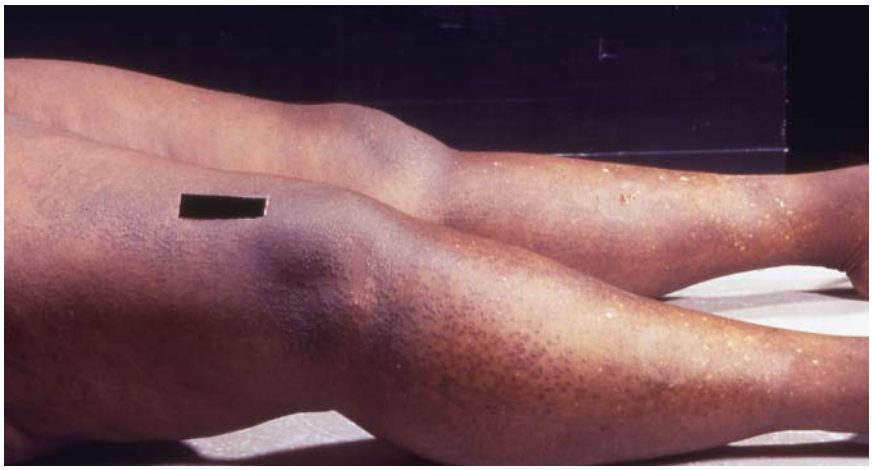

FIG. 5—*Innumerable hyperpigmented and flesh colored papules on the extremities which had been previously diagnosed as papular mucinosis.*

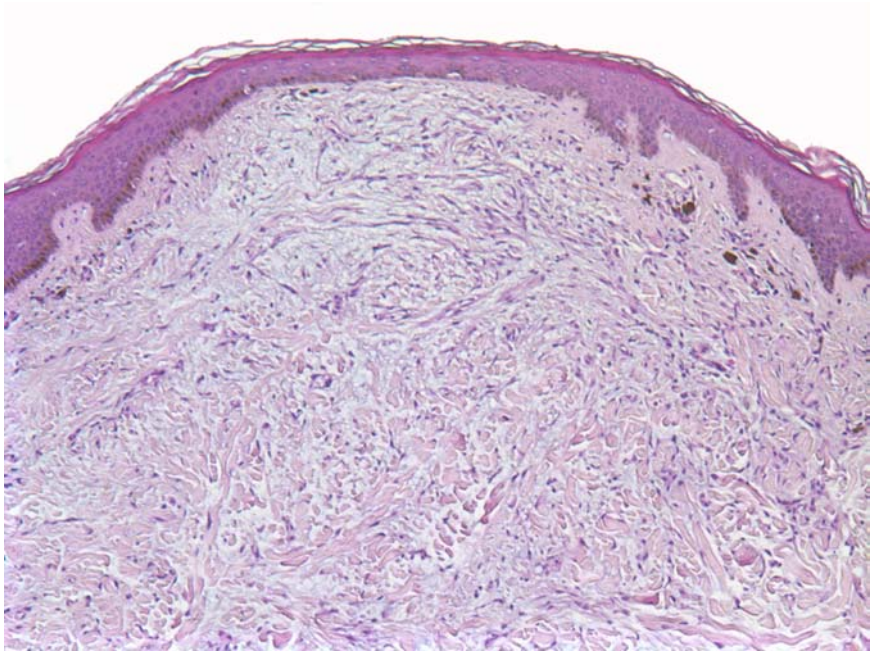

FIG. 6—*Mucin deposition and fibroblast proliferation in the papillary and upper reticular dermis characteristic of papular mucinosis.*

to the cavity, there was a multiloculated cystic structure within a brown discolored focus of parenchyma. A section of the discolored brain parenchyma revealed a multiloculated cyst containing granular debris, cholesterol clefts, and focal hemorrhage surrounded by gliosis with macrophages. There was no residual tumor seen. The eruptive, extensive nature of the seborrheic keratoses, combined with the history of a brain tumor six-month prior, was consistent with the sign of Leser-Trelat.

The sign of Leser Trelat is the sudden appearance or growth of seborrheic keratoses in association with the discovery of internal malignancy. The term "eruptive seborrheic keratoses" is given to these lesions since they appear rapidly. A review of sixty cases(5) of the sign of Leser Trelat showed that the time for the evolution of multiple seborrheic keratoses in these cases ranged from a few days to one year. The cutaneous findings and the discovery of the malignancy usually occurred within a few months of each other, and the appearance and remittance of the skin lesions may parallel the course of the cancer. The most common types of cancer associated with this sign are gastrointestinal adenocarcinomas and lymphoproliferative disorders; however, case reports associated with brain neoplasms have been described (6,7). Although it is controversial whether this sign exists, the occurrence of eruptive, extensive seborrheic keratoses have led to the discovery of internal malignancy and may help guide the autopsy examination.

*Case 4*

A 48-year-old African American female was witnessed to collapse at home and was taken to the local hospital. She was asystolic on arrival and attempts to revive her failed. The patient had a history of hypertension, congestive heart failure, and a rare skin condition known as papular mucinosis. The external examination revealed innumerable hyperpigmented and flesh colored 2–3 mm firm papules on the face, ears, trunk, and extremities (Fig. 5). The skin was also diffusely indurated and slightly bound down. An internal examination was not performed. A skin biopsy of one of the papules

demonstrated immense mucin deposition and a fibroblast proliferation in the papillary and upper reticular dermis, characteristic of papular mucinosis (Fig. 6). The patient was regularly followed by the dermatology clinic at the medical school and had a known diagnosis of papular mucinosis with an associated monoclonal gammopathy.

Papular mucinosis, otherwise known as scleromyxedema, is an idiopathic disorder that manifests as flesh-colored, hyperpigmented, or erythematous skin papules with a predilection for the face, neck, upper trunk, and upper extremities. Affected patients can have a chronic, progressive course, and those with diffuse involvement frequently develop cutaneous, gastrointestinal, muscular, neurologic, cardiac, and pulmonary complications. These may include scleroderma like changes, monoclonal paraproteinemia, dysphagia, peripheral neuropathy, weakness, dyspnea, myocardial infarction, and heart block. The pathogeneses of the extracutaneous manifestations are unclear since there is limited histopathologic data and relatively few autopsy reports of this entity (8). Given that this patient had severe, diffuse skin disease, an internal examination may have offered insight into the etiology of her heart disease and possibly the pathogenesis of the extracutaneous manifestations of papular mucinosis.

## Conclusion

In these four cases, the close analysis of skin findings at autopsy led to the confirmation of a serious genetic disease and notification of the family, explanation for sudden death in a young person, association of skin findings with internal malignancy, and may have provided the opportunity to better understand the pathogenesis of a poorly understood disease process. Without the information obtained through the gross and microscopic examination of the skin, complete autopsies would have accurately determined a cause of death; however, many such cases are not routinely autopsied in large busy offices. In some cases, the knowledge gained through the dermatological assessment allowed the examiner to determine the likely cause of death without an internal examination. In other cases, the cutaneous changes directed the pathologist to more closely examine particular organ systems and focus the internal examination.

The goal of this paper is to raise awareness of the useful supplemental information that may be obtained through gross and microscopic analysis of skin lesions at autopsy. Examination of distinctive findings by a dermatologist at the time of autopsy may be optimal; however, this is rarely available. Skin lesions can be photographed, biopsied, and later analyzed by a dermatologist or dermatopathologist in consultation in order to gain the necessary information. The close analysis of skin findings at autopsy may help the investigator to discover pertinent internal findings and gain a greater understanding of the disease process leading to death.

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