Patients Who Have Multiple Skin Cancers Develop New Skin Cancers at a Constant Rate

Research in North America and Australia has shown that people with a history of multiple nonmelanoma skin cancers (NMSCs) are at a higher risk of developing new NMSCs than the general population. In North America, it was found that up to 50% of patients with NMSC developed a new NMSC within 5 years. The percentage was higher in Australia, where 2 prospective studies found that 50% of women and 70% of men develop new NMSCs within 5 years. The main risk factors for new skin cancer formation were the number of skin cancers removed and male sex. In Australia, it was found that all patients who had 3 or more skin cancers (multiple skin cancers) developed another skin cancer within 6 years; however, it was uncertain whether the rate of development of new skin cancers decreased over time. We report the rate of new NMSC formation in high-risk patients who were followed up for 10 years.

Patients, Methods, and Results. The materials and methods have been described elsewhere. In brief, during a 1-year period (1988-1989), all new patients with NMSC seen by one of us (D.C.) were enrolled in the study. Patients were reviewed regularly and new skin cancers were removed. All skin cancers were histologically verified. Of 481 patients entered in the study, 361 were followed up for 10 years, and 166 of them had multiple NMSCs. The number of new NMSCs removed in the first 3 years of review (years 1-3) and in the last 3 years (years 8-10) were recorded. All NMSCs found at the site of a previously removed skin cancer were deemed to be recurrences and were not included in the study.

In the first 3 years of follow-up, men had an average of 5.2 new NMSCs (range, 1-12) and women had an average of 3.5 (range, 1-12). In the last 3 years of follow-up, men had an average of 3.3 new NMSCs (range, 2-12) and women had an average of 3.6 (range, 2-10). These differences between the sexes were not statistically significant (P=.70).

Comment. The study found that patients at high risk of forming new skin cancers continued to develop new tumors at a constant rate, even after 10 years of review. The patients had changed their lifestyles after their NMSCs were removed and were better about protecting their skin from sun damage. They used sunscreen regularly and wore clothes that reduced exposure to sun. However, these changes did not influence the development of new NMSCs. This suggests that in this group, once enough exposure of UV light has occurred to cause a skin cancer, irrevocable damage of enough magnitude is done to ensure a constant rate of new skin cancer formation despite subsequent improvement in skin protection.

One possible reason for the poor prognosis of patients with multiple skin cancers is that there is evidence that they have weaker immune systems than the normal population. Patients with multiple NMSCs have weaker cell-mediated immunity and lower lymphocyte counts than do normal controls or patients with fewer skin cancers. There was a correlation between the number of skin cancers removed and the weakness of cell-mediated immunity as measured by cutaneous reactions to recall antigens. There was also a correlation between the number of skin cancers removed and the reduction in lymphocyte counts and CD4/CD8 ratios. Women were found to have a significantly higher CD4/CD8 ratio than men, which could be one reason why women have a better prognosis than men.

The results of this study indicate that careful review of patients with multiple skin cancers is needed because they all develop new cancer formation. They also underscore the need to prevent skin damage from occurring in the first place by reducing the amount of UV light that reaches the skin. Once a skin cancer develops, the patient could be in a group that develops multiple tumors, which means a lifetime of new skin cancers. There is as yet no means of predicting which patients will fall into this group.


A Copy Editor Has No Right to Distort an Author’s Meaning

In my letter to the editor in the May 2001 issue of the ARCHIVES, the crux of my thesis was set forth in a single sentence that, when written by me and sent off to the ARCHIVES, read as follows: “But some colleagues disposed favorably to dermatologic surgery, I...”
among them, are concerned about a distressing trend in that field to cosmetology and to the failure of leaders like Drs Brody and Coleman to decry it.” A copy editor for the ARCHIVES took the liberty of changing the sentence to read thus: “But some colleagues disposed favorably to dermatologic surgery, I among them, are concerned about a distressing trend in that field to the name cosmetology and to the failure of leaders like Drs Brody and Coleman to decry it.”

The issue that I wrote about is not the name, but rather the transformation of a magnificent, multifaceted discipline, namely, dermatology, into a self-serving industry dedicated to facade, to wit, cosmetology. Changing the words distorted completely the meaning of my missive.

Furthermore, words were added to sentences that also changed the meaning I had sought to convey. For example, I wrote these lines: “Anyone who has been engaged in the active practice of dermatopathology for the past 30 years will attest to the curious paradox of a plummet in the quality of performance of skin biopsies by dermatologists concurrent with the surge to dermatologic surgery” to which the copy editor added the words “for treatment.” One of the themes of my piece is that, all too often, dermatologic surgery is used for physiologic phenomena rather than for treatment of disease. The addendum to my sentence again distorts the meaning intended by it.

Last, in the essay I sent to the ARCHIVES the term “stratum dysjunctum” was spelled correctly. The copy editor changed it for publication to “stratum disjunctum”!

I write now to rectify the distortions and the reaffirm my meaning.

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1. Ackerman AB. Dermatologic surgeons will determine what's in their name: both high quality and high standards. Arch Dermatol. 2001;137:663-664.

In reply

Dr Ackerman did indeed ask the copy editor to delete the words “for treatment” when he saw the edited copy before publication. Failure to do so was our oversight and I apologize for this. The other changes that Dr Ackerman objects to, however, were all present in the edited copy that he saw for approval before publication and he raised no objections to them at that time—in fact, he complimented the copy editor for “a superb job of copy editing.” In copyediting, there is always the danger that, in trying to clarify the meaning, the copy editor might change the meaning. It is for this reason that we sent the edited copy to the author for approval before publication. I apologize that, in this case, the process did not produce a letter that met the author's satisfaction.

Cheryl Iverson
Managing Editor, Archives Journals

Perineal Ulcerations as the Presenting Manifestation of Hemangioma

We read with great interest the article by Knispel and Shaw on cutaneous ulceration as the initial presenting manifestation of a hemangioma of infancy, which appeared in the “Off-center Fold” section of the March 2001 issue of the ARCHIVES. We agree that this manifestation represents an important, albeit uncommon, clinical presentation of hemangioma of infancy. In addition to the report by Rekant and Katz that was cited by the authors, we reported 3 cases of perineal ulcers as the presenting manifestation of a hemangioma of infancy, as well as a fourth case with an identical presentation in the perioral area.

Although Drs Knispel and Shaw found histologic examination of skin biopsy specimens helpful in their case, the histologic findings were not diagnostic in our cases even when viewed retrospectively after the clinical diagnosis became obvious. Skin biopsy specimens did demonstrate increased cutaneous vascularity but not to a degree significantly different from that which can be seen at the edge of ulcers due to other causes.

In summary, while we agree with Knispel and Shaw that hemangioma of infancy can present with cutaneous ulceration without evidence of hemangioma initially and that this represents an important diagnostic consideration in newborns with perineal (or perioral) ulcerations, the histologic findings may not always be diagnostic. In cases with equivocal or nondiagnostic histologic findings, erythrocyte-type glucose transporter protein (GLUT-1) staining, which has recently been found to be a specific marker for hemangiomas of infancy, may be helpful in distinguishing ulcerations due to hemangioma of infancy from other causes of cutaneous ulceration.

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In reply

We were pleased to learn of the article by Liang and Frieden that was published in Pediatrics in 1997 concerning their 4 cases of ulcerated perineal and perioral hemangiomas and to be introduced to glucose transporter isofrom 1 as a new immunohistochemical marker for hemangiomas of infancy.

Clinicians who are not managing hemangiomas of infancy rarely have the opportunity to observe the progression...
and resolution of these lesions. Photographs show the ulceration in our patient when he was 3 weeks old (Figure, A), the fully developed hemangioma when he was 4 months old (Figure, B), and the beginnings of resolution when he was 9 months old (Figure, C). Figure, C, was taken 1 month after an intralesional injection of triamcinolone acetonide (10 mg/mL) was administered into the most raised nodule. The rapid response suggests possible benefit from the use of intralesional corticosteroid injection in this setting.

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VIGNETTES

Pigmentary Demarcation Lines in Pregnancy

Pigmentary demarcation lines (PDLs) are borders of abrupt transition between 2 zones of skin, one more deeply pigmented and the other with a lighter pigmentation. Pigmentary demarcation lines follow the Voigt lines, which delimit the distribution of peripheral nerves and are usually observed among black and Japanese subjects, but only rarely in white subjects. On the basis of their location, 5 groups of PDLs have been identified and labeled A through E.1 Types A, B, and C PDLs are the most common and are detectable in white people.1 Recently, lines on the face have been described and labeled as type F PDLs.2

We report a case of a type B PDL that developed on the lower extremities of an Italian woman during the second trimester of pregnancy. To our knowledge, this phenomenon has been reported once in the literature in a white woman.3

Report of a Case. A 28-year-old white woman with skin phototype IV and in the 28th week of her otherwise normal first pregnancy was referred to us for a peculiar pigmentation on her posterior lower legs. The pigmentation started during the third to fourth month of gestation. The patient was not aware of this pigmented pattern before pregnancy and stated that her history was negative for systemic diseases or contraceptive pills.

Results of the physical examination showed that the line of demarcation began at midperineum, curved to the posteromedial thigh, and extended to the inner base of the heel through the popliteal fossa and the medial calf. The lines were bilateral and symmetrical (Figure). In-
creased pigmentation of the areolae, nipples, genitalia, and linea nigra was evident.

The results of the biopsy of the hyperpigmented skin showed mild hyperpigmentation of the basal layer of the epidermis without inflammatory infiltrate or melanophages in the upper dermis.

After a normal delivery, the PDL started to fade during the first week post partum and disappeared on the thighs within 3 to 4 months, but they persisted, although barely noticeable, on the legs from the popliteal fossa to the heel.

This pigmented pattern remained unchanged during the patient's second pregnancy, 3 years later. At the most recent follow-up consultation, 5 years after the first pregnancy, results of the examination disclosed a bilateral and symmetrical type B PDL from the popliteal fossa to the heel. The line was sharply demarcated, but the difference between the darker and the lighter areas was very slight.

Comment. The pigmented pattern of our patient was diagnosed as a type B PDL on the basis of its clinical and histopathologic features. Pregnancy can induce accentuation of a preexisting PDL or the appearance of new lines. Appearance of a type B PDL during pregnancy has been well documented in the literature, and 14% of black women present with such a pigmented pattern during pregnancy. To our knowledge, our patient represents the second case of a type B PDL reported in a white pregnant woman.

Increased pigmentation of a type B PDL during pregnancy in a black woman was reported by Fulk. When PDLs appear during pregnancy, a concomitant local factor may be involved in addition to the high levels of estrogen, progesterone, and melanocyte-stimulating hormone. The role of hormones in inducing a type B PDL is supported by the report of persistent type B PDLs in a white nonpregnant woman receiving long-term estrogenic medication.

Compression of peripheral nerves issuing at the space between S1 and S2 by the enlarged uterus has been proposed as a causative mechanism of these lines. Some cases of pregnancy-associated PDLs were accompanied or preceded by an overlapped erythematous component, and the fact that erythema and pigmentation disappeared soon after delivery supports this hypothesis.

Furthermore, type B PDLs may not appear in all of a woman's pregnancies and may be present only for a limited time during pregnancy, especially at the end. This finding may be explained by the possible presence of a local trigger factor occurring only in some pregnancies or during some periods of the same pregnancy. In our patient, the type B PDL appeared during the first pregnancy, fading until barely noticeable on the legs, where they remained unchanged during the second pregnancy.

In white people, the association between type B PDLs and pregnancy has been rarely reported in the literature, but, since PDLs are asymptomatic, we consider that they are probably overlooked or undiagnosed.

Further studies should be performed to quantify the relative incidence of type B PDLs of the lower limbs in the white population and to determine their frequency during pregnancy. In any case, a type B PDL may be considered another less frequently recognized physiologic change related to pregnancy.

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Successful Treatment of Impetigo Herpetiformis With Oral Cyclosporine During Pregnancy

Impetigo herpetiformis is an uncommon pustular dermatosis that typically occurs during pregnancy. Clinically and histologically, it bears some resemblance to pustular psoriasis, and the two conditions are discussed within the same entity. Systemic glucocorticosteroids are widely used for the treatment, whereas cyclosporine was also used in one case after delivery. We herein report a case of impetigo herpetiformis that did not respond well to systemic corticosteroids and required cyclosporine administration.

Report of a Case. A 26-year-old pregnant woman without history of psoriasis experienced a sudden onset of severely pruritic erythema and pustules on the chest at 27 weeks' gestation. This was her third pregnancy; the first one resulted in delivery of a healthy, full-term infant, and the second one ended in a spontaneous abortion in the first trimester. During the previous pregnancies, she had no skin problems. She was treated with topical application of clobetasol propionate and systemic oral prednisolone, 45 mg/d (1 mg/kg of body weight). The treatment resulted in transient partial response, and the disease exacerbated in a few days. On her admission at 29 weeks' gestation, erythematous plaques bordered by tiny pustules were scattered on her trunk and extremities (Figure 1). Results of skin biopsy showed spongiosis and pustules with neutrophilic infiltrate in the epidermis (Figure 2). In the dermis, diffuse inflammatory infiltration of polymorphonuclear neutrophils and lymphocytes was found.
The diagnosis of impetigo herpetiformis was established. Oral cyclosporine at a dosage of 5 mg/kg daily was added to the prednisolone therapy. Within a few days, marked reduction in the disease activity was noted, and the prednisolone dosage was gradually tapered from 45 mg/d to 20 mg/d. At 32 weeks' gestation, she experienced exacerbation of the disease. The cyclosporine dosage was increased to 10 mg/kg daily (plasma cyclosporine trough level, 107 ng/mL), and the disease was well controlled. Cyclosporine dosage was decreased to 5 mg/kg gradually. At 36 weeks of gestation, she was delivered of a healthy infant weighing 2382 g without any birth defect. The cyclosporine and prednisolone dosages were gradually reduced, and all therapy was stopped 6 weeks after the delivery.

Comment. To our knowledge, this is the first case report of impetigo herpetiformis treated with cyclosporine during pregnancy. The case did not respond well to high-dose systemic corticosteroid therapy. Considering the risks to the mother and the fetus, we decided to administer cyclosporine rather than to increase the prednisolone dosage to greater than 1 mg/kg daily; the risks of corticosteroid at this dosage are well documented. A few cases of pustular psoriasis during pregnancy have been treated with cyclosporine, resulting in good control of psoriasis, and these patients were delivered of healthy infants.3,4

Cyclosporine is categorized in "C" in Food and Drug Administration pregnancy categories.5 In animal studies, cyclosporine is embryotoxic, but not teratogenic in high dosages (30 mg/kg daily for rats, or 100 mg/kg daily for rabbits).3 In humans, a report of 629 pregnancy outcomes in transplant recipients receiving cyclosporine therapy showed its relatively safe nature.6 The possible association between cyclosporine administration and spontaneous abortion and/or low birth weight could not be denied so far. The risk for immunosuppression in the mother and the child should be considered carefully. When all risks and benefits are counted and systemic corticosteroid therapy fails, cyclosporine therapy may be an option for the treatment of impetigo herpetiformis during pregnancy.

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Follicular Toxic Effects of Chimeric Anti–Epidermal Growth Factor Receptor Antibody Cetuximab Used to Treat Human Solid Tumors

Report of a Case. A poorly differentiated rectal adenocarcinoma with unresectable liver metastases developed in a 58-year-old man with no significant medical or dermatological history. He under-
went a course of therapy including intravenous fluorouracil and leucovorin calcium that was terminated prematurely because of toxic effects, pelvic radiotherapy, and low anterior rectal resection. Despite subsequent chemotherapy with irinotecan hydrochloride, the liver metastases enlarged, and a treatment protocol incorporating irinotecan hydrochloride and cetuximab (ICM-C225) (520 mg weekly) was started at the Memorial Sloan-Kettering Cancer Center, New York, NY. Within 1 week, erythematous follicular papules and pustules developed. These affected virtually all cutaneous surfaces, including the scalp, face, shoulders, trunc, buttocks, and extremities, but spared palmar, plantar, and mucosal surfaces (Figure). Results of a skin biopsy revealed neutrophilic suppurative folliculitis; special stains for microorganisms produced negative results. Topical clindamycin phosphate solution and triamcinolone acetonide cream were prescribed. Given the severity of his reaction, the third dose of cetuximab was withheld. As his eruption improved within 2 weeks and his tumor mass decreased, cetuximab therapy was resumed. This resulted in a worsening of his eruption, which was controlled to some extent using topical steroids and anti-inflammatory medications.

Comment. Growth factor blockade represents a novel strategy for cancer treatment. The epidermal growth factor receptor (EGF-R) is a transmembrane protein encoded by the c-erb-B proto-oncogene that dimerizes on ligand binding, initiating mitogenic intracellular signal cascades through its tyrosine kinase activity. Its principal endogenous ligands include EGF and transforming growth factor α. Cetuximab is a chimeric monoclonal antibody that effectively binds EGF-R, blocking its signal transduction pathway and causing internalization and down-regulation of transmembrane EGF-R. As EGF-R is overexpressed in many solid tumors, and as cetuximab has shown antitumor efficacy and safety in animal models of human cancer, cetuximab is currently being investigated in patients with head and neck, colorectal, lung, renal, and pancreatic cancers. The adverse effects of cetuximab are generally limited to constitutional symptoms. However, it has significant cutaneous toxic effects, including follicular rashes, acneiform eruptions, nail bed changes, and seborrheic dermatitis-like eruptions. Follicular rashes occur in approximately one third of patients.9

The probable explanation of these skin reactions may lie in the role of EGF in the development and maintenance of hair follicles. Failure of hair follicles to enter the catagen stage develops in transgenic mice expressing an EGF-R dominant-negative mutation in the basal layer of the epidermis and the follicular outer root sheath, which causes severe inflammatory follicular necrosis and alopecia.2 Similarly, EGF-R–null hair follicle buds grafted onto nude mice demonstrate an inability to progress from the anagen to telogen stages, resulting in inflammation and alopecia within weeks.6 These studies suggest that EGF-R has a central role in follicular physiology. The addition of EGF or transforming growth factor α to cultured human sebaceous-pilosebaceous infundibula causes infundibular keratinocyte disorganization mimicking changes seen in acne,7 suggesting that proper maintenance of follicular keratinization requires a delicate range of EGF-R activity. Familiarity with the follicular toxic effects of cetuximab is important not only because it is a novel antitumor agent that is likely to gain more widespread use, but also because of its in vivo confirmation of the significant role of EGF-R in follicular homeostasis.

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No Detection of Human Herpesvirus 8 in Different Types of Cutaneous Angiosarcoma

Angiosarcomas of the skin arise almost exclusively in the following clinical settings: (1) the face and scalp, usually in elderly individuals; (2) the lymphedematous extremities; and (3) skin that has been previously irradiated (postradiation angiosarcomas). The detection of human herpesvirus 8 (HHV-8) DNA in tumor tissue of acquired immunodeficiency syndrome (AIDS)–associated Kaposi sarcoma (KS) by Chang et al has originated the debate on the relevance of HHV-8 (also known as KS-associated HHV) in the pathogenesis of malignant tumors. Moreover, there are contradictory reports concerning the presence of HHV-8 DNA sequences in angiosarcomas. A recent report confirmed the presence of HHV-8 in disseminated angiosarcoma and reported the presence of HHV-8 in 3 additional cases, although many authors deny its presence in angiosarcoma. All studies concerning the detection of HHV-8 did not take into account the different types of angiosarcoma. Thus, we investigated different types of angiosarcoma (idiopathic, lymphedema-associated, and postradiation angiosarcoma) concerning the presence of HHV-8, using the highly sensitive polymerase chain reaction (PCR) technology for detection of HHV-8–specific DNA.

Materials and Methods. Specimens. Formalin-fixed, paraffin-embedded lesional tissue specimens obtained between 1986 and 1998 from 19 cutaneous angiosarcomas of 9 patients were obtained from the histopathology archives of the Department of Dermatology, Graz, Austria.

Ten specimens were from 5 patients with idiopathic angiosarcoma, 5 specimens were from 2 patients with lymphedema-associated angiosarcoma, and 4 specimens were from 2 patients with postradiation angiosarcoma. The diagnosis of angiosarcoma was confirmed in all cases by conventional histopathologic examination and by immunohistochemical staining with CD31 monoclonal mouse anti-human endothelial cell antibody (PECAM-1; Dakopatts, Copenhagen, Denmark). Nine biopsy specimens of KS from a previous study (4 specimens of lesional skin of 3 patients with classic KS and 5 biopsy specimens of lesional skin of 4 patients with AIDS-related KS) served as positive controls. Biopsy specimens of 3 hemangiomata, 1 specimen of nonlesional skin, and 1 specimen of lichen planus were used as negative controls. On the molecular level, all samples were analyzed in a blinded version without knowledge of the individual diagnoses.

DNA Preparation. Five adjacent 6-µm-thick slices were cut from each sample block of the formalin-fixed, paraffin-embedded biopsy material. To avoid cross-contamination, the blade of the microtome as well as disposable gloves were changed between the preparation of samples. DNA was extracted as described with modifications with separate sets of supplies and pipetting devices using disposable tips and plungers. Briefly, the sections were deparaffinized, scraped off, and resuspended in a digestion buffer (0.2M Tris-hydrochloride [pH 8], 10mM EDTA, 1% sodium dodecyl sulfate, and 1 mg/mL of proteinase K). After incubation at 55°C overnight, the proteinase K was inactivated by boiling the solution at 95°C for 10 minutes. Two microliters of this DNA solution served as template for the following PCR reactions.

Polymerase Chain Reaction. DNA amplification of the 233–base pair (bp) KS330 fragment specific for HHV-8 was performed by nested PCR with an outer primer pair (KS-1, KS-2) and an inner primer pair (KS-3, KS-4). In a first step, 2 µL of the DNA solution was used as template for amplification reactions in a final volume of 25 µL containing 50mM potassium chloride, 10mM Tris-hydrochloride, 1.5mM magnesium chloride, 200µM each of deoxyribonucleotide triphosphate (dATP, dCTP, dGTP, and dTTP), 0.5 U of Taq DNA-polymerase (Perkin Elmer Biosystems, Weiterstadt, Germany), and 2.5pM of each primer of the “outer” primer pair (KS-1 and KS-2). In a programmable thermocycler (Perkin Elmer), samples were set to heat at 95°C for 5 minutes. Subsequently, 40 cycles of PCR were performed at 94°C for 60 seconds, 63°C for 30 seconds, and 72°C for 30 seconds. For internal PCR, 0.5 µL of the outer products was used as template for amplification of a 160-bp fragment using the primers KS-3 and KS-4, under the following conditions: 94°C for 30 seconds, 60°C for 30 seconds, and 72°C for 30 seconds. After non-denaturing gel electrophoresis and subsequent staining with ethidium bromide, the amplification products were visualized by UV-light transillumination. To confirm that DNA of sufficient quality and quantity was obtained from all analyzed samples, in each sample a 207-bp fragment of the human β-actin gene was amplified.

Southern Blot Analysis. Specificity of the amplification products was confirmed by Southern blot analysis. The 160-bp “inner” PCR products of all samples were electrophoretically separated on a 2% agarose gel, vacuum blotted onto a nylon membrane (Boehringer, Mannheim, Germany), and hybridized with an internal radioactive, phosphor 32–labeled oligoprobe as previously described.

Results. Results of PCR and subsequent Southern blot analysis of DNA obtained from formalin-fixed samples of all angiosarcomas were negative for the 233-bp HHV-8 DNA sequence except for the 9 specimens of KS serving as positive controls.

Comment. The discovery of a new human herpesvirus in KS tissue of patients with AIDS by Chang et al in 1994 has opened a new dimension in oncology. Human herpesvirus 8 has since been detected not only in AIDS-associated KS, but also in all other types of KS (classic, endemic, and iatrogenic), supporting a fundamental contribution of HHV-8 to the pathogenesis of KS not necessarily associated to immunosuppression. This observation raises the question of whether HHV-8 can also be associated with other hemangioproliferative disorders.
There are a large number of benign vascular lesions, such as hemangiomas, lymphangiomas, or pyogenic granulomas, that were not found to contain the HHV-8 DNA sequence. Remarkably, there are contradictory data concerning the presence of HHV-8 in angiosarcoma. McDonagh et al detected HHV-8 sequences by PCR in 7 (29%) of 24 angiosarcomas, using, as we did, the same primer pair described by Chang et al. In this study, 20 hemangiomas and 6 hemangiopericytomas were additionally analyzed. One case of hemangioma was positive for HHV-8, but none of the hemangiopericytomas. Recently, Remick et al also found HHV-8 DNA sequences in 1 patient with disseminated angiosarcoma, as well as in 3 others of 8 angiosarcoma samples. However, other investigators could not confirm these results.

There has been much debate on etiology and pathogenesis of angiosarcoma. Chronic lymphedema and radiation therapy are now recognized clearly as relevant predisposing factors in lymphedema-associated and post-radiation angiosarcoma. Nevertheless, the exact pathogenesis of these tumors is far from understood and a link between HHV-8 and this neoplasm has been suggested. All reports in the literature failed to investigate different types of angiosarcoma; thus, it was suggested for us to do that. However, HHV-8 DNA sequences could not be detected in any of our cases of different types of angiosarcoma, suggesting that individual cases of different angiosarcoma types of the skin cannot be associated with HHV-8 and that the etiology of some of these conditions remains unclear.

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