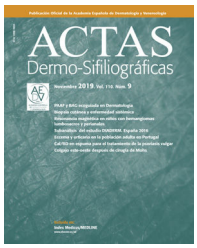
ACTAS Dermo-Sifiliográficas 114 (2023) T240–T246

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

ACTAS Dermo-Sifiliográficas

Full English text available at www.actasdermo.org



CONTROVERSIES IN DERMATOLOGY

[Translated article] Clinical Relevance of Cherry Angiomas

N. Pastor-Tomás[a,*], **J. Bañuls**[b], **E. Nagore**[c]

[a] *Servicio de Dermatología, Hospital General Universitario de Elda, Elda, Alicante, Escuela de Doctorado, Universidad Católica de Valencia San Vicente Mártir, València, Spain*
[b] *Servicio de Dermatología, Hospital General Universitario de Alicante-ISABIAL, Alicante, Departamento de Medicina Clínica, Universidad Miguel Hernández, Sant Joan d'Alacant, Alicante, Spain*
[c] *Servicio de Dermatología, Instituto Valenciano de Oncología, València, Facultad de Medicina, Universidad Católica de Valencia San Vicente Mártir, València, Spain*

Received 13 July 2022; accepted 24 October 2022

KEYWORDS
Cherry angioma;
Senile angioma;
Drugs;
Cancer;
Melanoma;
Immunosuppression

Abstract Cherry angiomas are the most common vascular tumors of the skin. They are particularly prevalent in the general population and become more common with age. Although an association with cancer was suggested at the end of the 19th century, when these tumors were first described, it could not be demonstrated. For many decades, therefore, cherry angiomas were considered to have no clinical relevance other than their association with age. A number of studies in recent years, however, have shown a link between cherry angiomas and exposure to various toxic substances and medications, benign and malignant diseases, and immunosuppression, rekindling interest in these lesions and providing clues for a better understanding of their etiology, pathophysiology, and clinical relevance.

PALABRAS CLAVE
Angioma en cereza;
Angioma senil;
Fármaco;
Cáncer;
Melanoma;
Inmunosupresión

Relevancia clínica de los angiomas en cereza

Resumen Los angiomas en cereza son los tumores vasculares cutáneos más frecuentes. Son muy prevalentes en la población general y esta prevalencia aumenta con la edad. Aunque, en sus primeras descripciones en la literatura, a finales del siglo XIX, se relacionaron con el cáncer, dicha asociación no pudo demostrarse posteriormente por lo que, durante muchas décadas, se han considerado unas lesiones asociadas al proceso del envejecimiento sin otro significado

DOI of original article: https://doi.org/10.1016/j.ad.2022.10.037
* Corresponding author.
E-mail address: nataliaderma@gmail.com (N. Pastor-Tomás).

https://doi.org/10.1016/j.ad.2022.10.040

clínico particular. Sin embargo, en los últimos años, han sido objeto de un mayor interés al ser publicados algunos estudios que muestran una asociación con la exposición a diversos tóxicos y fármacos, enfermedades malignas y no malignas y la inmunosupresión que pueden ayudar a conocer mejor su etiopatogenia y su relevancia clínica.

Introduction

Cherry angiomas, also known as capillary angiomas, senile angiomas, or Campbell de Morgan spots, are the most common type of cutaneous vascular tumor. Clinically, they appear as bright red or purple round or ovulated, dome-shaped papules of variable size ranging from hardly visible to several millimeters in diameter. Some lesions may form polypoid lesions. They present preferentially on the trunk and proximal part of the limbs, and are not so common on the acral zones and face. They affect both sexes equally, can occur in several members of the same family,[1] and, although onset may occur during adolescence, the lesions generally appear in individuals in their twenties and increase in number as the affected individuals age. The pathophysiologic mechanisms are, however, not well known.

The first brief reference to these lesions was made in the book *On the Origin of Cancer* by the surgeon Campbell de Morgan, published in 1872. In that book, the author described these lesions as ''small outgrowths of warty or vascular or dermoid structures'' that appear frequently in patients with cancer.[2] Leser and Trélat[3] also believed that the incidence of these lesions was greater in patients with internal cancers, suggesting that they were of clinical significance, particularly when onset occurred in early adult life and in great number. In 1909, Sampson Handley[2] highlighted in an article that the common belief at the time of a link between cherry angiomas and cancer was not well supported by evidence. Murison et al.[2] in 1947 conducted a study of cherry angiomas in 1300 patients in 3 hospitals and found that the number and size of the angiomas increased with age. Although angiomas were slightly more common in patients with cancer than in those with nonmalignant disease, this difference was not large enough to be clinically significant. Other authors concurred with those authors about the absence of a link between cherry angiomas and cancer, considering these lesions as a normal process associated with aging and not related to any other diseases.[4,5]

Since then, the prevailing opinion within the scientific community is that there was no link with cancer. So for a long time, study of these lesions and their pathophysiologic mechanisms and clinical significance had been very limited despite their high prevalence. However, in recent years, these lesions have once again attracted interest due to publications that report a possible association between exposure to certain toxins and drugs and certain diseases, immunosuppression, and cancer (Table 1).

Association With Toxic Agents and Drugs

The development of eruptive cherry angiomas has been reported as a result of severe cutaneous damage after exposure to alkylating agents (nitrogen and sulfur mustards)[6–8] and other toxic agents (2-butoxyethanol, bromides).[9,10]

Mustard gas is a sulfur mustard used as a chemical weapon. As a blistering agent, it causes blisters on the skin. It has been suggested that, after exposure to this agent, angiomas develop due to release of proangiogenic cytokines during the epidermal repair process, although an effect on cell DNA cannot also be ruled out.[8] Askari et al.[7] conducted a study in Iranian individuals exposed and not exposed to mustard gas with and without cherry angioma. Those authors analyzed serum levels of prolactin (PRL) and other cytokines that participate in regulation of angiogenesis during several pathophysiological processes such as tumor growth, wound healing, inflammation, and ischemia (monocyte chemotactic protein 1 [MCP-1/CCL2], CC chemokine ligand 5 [RANTES/CCL5], interleukin [IL] 8 [IL-8/CXCL8], and fractalkine/CX3CL1 [chemokine ligand 1]). They found significantly lower PRL levels and significantly greater CCL2 levels in the group exposed to mustard gas with angiomas compared with exposed individuals without angiomas. The 16K-PRL form is able to inhibit angiogenesis in vivo and in vitro,[7] and CCL2 intervenes in the angiogenic process.[7]

Nitrogen mustards, although also used as chemical weapons, have been used more widely as topical chemotherapy agents for treatment of cutaneous T-cell lymphomas and vitiligo. The onset of cherry angiomas has been reported in patients with vitiligo treated topically with nitrogen mustards.[6] It is thought that the appearance of angiomas in these patients is more likely a response to the mutagenic effects of nitrogen mustards on cell DNA, which would explain the increased proliferation of endothelial cells.[6]

The appearance of multiple angiomas has also been reported with other drugs. Thus, it has been observed in a patient with psoriasis treated with cyclosporine,[11] and in patients treated with ramucirumab.[12,13] Release of vascular endothelial growth factor (VEGF) by psoriasis plaques and immunosuppression caused by cyclosporine were hypothesized as responsible for the case associated with cyclosporine. Ramucirumab is a drug used for its antiangiogenic properties in the treatment of gastric, colorectal, and nonsmall cell lung cancer. It selectively binds to the extracellular domain of the VEGF receptor 2 (VEGFR2),

Table 1 Summary of Clinical Associations in cherry Angiomas: Possible Pathophysiologic Mechanisms That Support These Associations and Case Reports in the Literature.

Associations	Possible pathophysiologic mechanisms	Cases published/literature
Toxins and drugs		
Alkylating agents (nitrogen mustards/mustard gas)[6–8]	These cause serious skin damage that increases release of proangiogenic factors in response Possible mutagenic effect on cell DNA that increases proliferation of endothelial cells	Isolated case reports/case series
2-Butoxyetanol[9]		In 1 publication, after acute exposure, 6 of 7 individuals developed multiple eruptive angiomas
Bromides[10]		Only report of the association is in 2 laboratory technicians chronically exposed
Cyclosporine[11]	VEGF production by psoriasis plaques and immunosuppression	One case associated with psoriasis treatment
Ramucirumab[12–14]	Upregulates angiogenic pathways not mediated by VEFT (FGF) *KDR* mutations that encode VEGRF2 may confer a proliferative advantage Association with chemotherapeutic agents, for example, taxanes, can activate other proangiogenic factors	Isolated case reports published
Tamsulosin[15]	Blocks the alfa1A and alfa1D adrenergic receptors, leading to vasodilation	Association found in a case-control study
Clopidogrel[15]	Antiangiogenic properties	Protective effect against development of angiomas found in a case-control study
Nonmalignant diseases		
Pregnancy/diabetes/dyslipidemia/acromegalia[5,16–18]		Case/control studies/case series published
Immunosuppression and cancer		
Human herpes virus 8[19]	Induces neoangiogenic activity in infected cells Induces expression of cell factors with proangiogenic activity (VEGF, MCP-1, AFT4, mTOR, and ANGPTL4) Association with states of immunosuppression	In a study, HHV8 was detected in 52.9% of samples from subjects with multiple angiomas compared with no cases in subjects with few angiomas
Multicentric Castleman disease[20]	Overproduction of IL-6 leading to B-cell proliferation and VEGF secretion	Isolated case reports published
Chronic GvHD[21]	Can release angiogenic factors (VEGF and FGF) Immunosuppressive therapy used can play a role in the association	Isolated case reports published
Extracutaneous cancer/nonmelanoma skin cancer[25–27]		Association described in some case-control studies
Uveal melanoma[23,24]	Somatic mutations have been identified in *GNAQ* and *GNA11* in cherry angiomas that are shared with uveal melanoma	In 1 study, patients with uveal melanoma had a higher prevalence of cherry angiomas compared with the general population

Table 1 (*Continued*)

Associations	Possible pathophysiologic mechanisms	Cases published/literature
Cutaneous melonoma[26–30]	Proliferation-activating mutations or mutations in genes associated with DNA repair mechanisms induced by UV radiation could play a role in the development of angiomas Genetic susceptibility could also play a role if the pathways were also implicated in the etiopathogenesis of cancer/melanoma.	A significant association between presence of multiple cherry angiomas and history of melanoma in several case-control studies In a cohort study, a significant association was found between presence of multiple cherry angiomas and history of a second melanoma

Abbreviations: ANGPTL4, angiopoietin-like 4; FGF, fibroblast grown factor; HHV8, human herpes virus 8; MCP-1, monocyte chemotactic protein 1; mTOR, mammalian target of rapamycin; UV, ultraviolet; VEGF, vascular endothelial growth factor; VEGFR2, vascular endothelial growth factor receptor 2.

blocking the proangiogenic effects of VEGF.[12] The development of angiomas during ramucirumab treatment is an uncommon paradoxical effect. The mechanism by which this drug can induce vascular cutaneous tumors is still unknown. One case was attributed to a mutation in the *KDR* gene (which encodes VEGFR2) thereby conferring a proliferative advantage, although upregulation of other complementary angiogenic pathways not mediated by VEGF such as fibroblast growth factor (FGF) cannot be ruled out.[14] Immunosuppression[12] and association with other chemotherapies such as taxanes[13] have also been proposed as potential mechanisms. Combination of ramucirumab with paclitaxel may lead to an imbalance between angiogenesis inhibition and other proangiogenic factors activated by paclitaxel.[13] Most cases of angioma development in association with ramucirumab treatment have been reported on the head and neck. Choi et al.[13] considered that UV radiation could have contributed to the development of angiomas on sun-exposed areas as such radiation can induce angiogenesis by upregulating VEGF and downregulating the endogenous angiogenesis inhibitor thrombospondin 1.

Nazer et al.[15] conducted a case–control study of risk factors associated with cherry angiomas. Exposure to tamsulosin was independently and significantly associated with angiomas (odds ratio [OR] 3.5; 95% confidence interval [CI] 1.4–8.9; $P = .009$), whereas clopidogrel had a protective effect (OR 0.3; 95% CI 0.1–0.9; $P = .028$). Tamsulosin selectively blocks adrenergic alfa1A and alfa1D receptors, leading to smooth muscle relaxation in the prostate and bladder, although it can also act on blood vessels leading to vasodilation whereas clopidogrel has recently been shown to have an antiangiogenic effect.[15]

Association With Other Nonmalignant Processes and Diseases

Cherry angiomas have also been associated with pregnancy,[16] diabetes mellitus,[5] and lipid profile disorders.[17] In a case–control study, patients with diabetes had a greater number of cherry angiomas than those without diabetes.[5] In another study, Darjani et al.[17] found that levels of total cholesterol, triglycerides, and low-density lipoproteins were significantly greater among patients with angiomas compared with those without angiomas. For those authors, development of angiomas may be a response to endogenous production of angiogenic factors triggered by elevated atherogenic factors. However, the study by Nazer et al.[15] did not find any association between the presence of cherry angiomas and pregnancy, diabetes, and dyslipidemia, and likewise did not find an association with other diseases studied, such as coronary artery disease, cerebrovascular accidents, rheumatoid arthritis, asthma, thyroid disease, chronic renal disease, and cirrhosis.

It has also been reported that cherry angiomas are more prevalent in acromegalic patients than in the general population.[18]

Association With Immunosuppression and Cancer

Cherry angiomas have been associated with human herpesvirus 8 (HHV8).[19] HHV8 is the causal agent of Kaposi sarcoma (KS) and has been linked with other neoplasms including rare lymphoproliferative disorders such as multicentric Castleman disease (MCD) and primary effusion lymphoma.[19] It is an oncogenic virus, particularly in states of immunosuppression, which induces strong neoangiogenic activity in infected cells, but also causes reprogramming of cell transcription inducing expression of cell factors with proangiogenic activity such as VEGF, MCP-1, ATF-4 or activator transcription 4, mammalian target of rapamycin (mTOR), and angiopoietin type 4.[19]

These proangiogenic properties are those that have led to an investigation into whether HHV8 could be implicated in the pathogenesis of vascular proliferative lesions other than KS. Borghi et al.[19] studied the association between HHV8 infection and different cutaneous vascular lesions in a series of 29 individuals (17 samples from individuals with multiple cherry angiomas, 2 samples from individuals with a limited number of cherry angiomas [paucilesional form], 4 classic KS nodules, genital angiokeratoma, 2 pyogenic granulomas, and 3 samples from healthy skin). HHV8 was found to be present in all samples from patients with KS and 52.9% of samples from patients with multiple capillary angiomas.

In contrast, the virus was not detected in samples from patients with paucilesional forms of cherry angiomas or samples from healthy skin. For those authors, HHV8 likely acts as a cofactor in the context of local or systemic immunosuppression rather than playing a direct role in the development of cherry angiomas.[19]

Although many of the cases of MCD are associated with HHV8 infection, eruption of multiple cherry angiomas has also been reported in a patient with MCD not infected with HHV8. In that case, the appearance of angiomas was attributed to aberrant levels of IL-6, leading to B-cell proliferation and VEGF secretion.[20]

The appearance of angiomas has also been reported in patients with chronic sclerodermatous graft-versus-host disease (GvHD).[21] Possible pathophysiologic mechanisms proposed for the development of angiomas in such patients include release of angiogenic factors such as VEGF and FGF, although immunosuppression associated with concomitant use of other drugs such as cyclosporine cannot be ruled out.[21]

The association between cherry angiomas and cancer in general and skin cancer in particular is a controversial topic as these lesions are very prevalent in the general population. However, in recent years, some authors have found evidence of a possible association.

At the molecular level, low levels of microRNA-424 (miRNA-424) and elevated levels of MEK1 or cyclin E1 have been found in senile angiomas that could lead to abnormal cell proliferation in these tumors.[22] In addition, recently, somatic *GNAQ*- and *GNA11*-activating mutations have been detected in a series of cherry angiomas. These findings have also been reported in uveal melanoma, blue nevus, and blue-nevus-associated melanoma, although the *GNA14* mutations have been reported more frequently.[23] Paolino et al.[24] found that 63% of a series of 33 patients with uveal melanoma also had more than 10 cherry angiomas, a higher prevalence than that found in the general population (41–48%).

In a study that evaluated the presence of cherry angiomas in skin from the thorax of 50 patients with unilateral breast cancer, a significantly higher number of angiomas was found in the involved breast than the contralateral one.[25]

Borghi et al.[26] found that advanced age, immunosuppressive therapy, skin cancers (melanoma and nonmelanoma skin cancer), and extracutaneous cancers were factors significantly associated with the presence of multiple cherry angiomas (>30) in a cross-sectional study of 1302 patients.

In a second phase of the study, the association between cherry angiomas and skin cancer was assessed.[27] A significant association was found between the presence of at least 10 cherry angiomas (arbitrarily denoted as eruptive by the authors) and melanoma in patients aged 50 years or less (OR 6.9; 95% CI 4.0–11.9) and in the intermediate-aged group of 51–70 years, although the association was weaker (OR 1.9; 95% CI 1.2–2.9), with significance lost in those aged more than 70 years. The association between eruptive angiomas and other cancers, whether nonmelanoma skin cancers and extracutaneous cancers, was significantly greater in younger patients. Exposure to immunosuppressive therapy was variable and more clearly associated with cherry angiomas.

In another recent study published by the same group, the presence of at least 10 cherry angiomas was associated with melanoma in all age groups, although the association was strongest in those aged 40 years or less. In addition, the strength of the association was similar to that found for presence of 2 or more atypical nevi (OR 2.1; 95% CI 1.6–2.7 for atypical nevi and OR 2.3; 95% CI 1.7–2.9 for cherry angiomas).[28]

The aforementioned 2 studies published by that group are subject to certain limitations worth noting. First, they were retrospective studies so it is impossible to know whether or not the angiomas preceded melanoma development. In addition, they were conducted in dermatology departments specialized in melanoma, and so a selection bias cannot be ruled out. Finally, other potential variables associated with the appearance of angiomas were not analyzed, and so the angiomas could in fact be confounding factors. The use of the term ''eruptive angiomas'' to define the presence of 10 or more angiomas is confusing because ''eruptive'' refers to the onset of lesions in a short time period and, also, the choice of a cutoff (in this case very low) to classify patients with many or few angiomas was arbitrary and could lead to different results if a different cutoff had been chosen.

Betz-Stablein et al.[29] published a study whose aim was to describe the frequency and anatomical site of cherry angiomas in 163 individuals in the general population of Brisbane, Australia, and their association with clinical, demographic, phenotypic, and sun-exposure characteristics. These characteristics were collected through a questionnaire administered at baseline. The site and number of angiomas were determined by a full 3D body scan. In the multivariate analysis, male sex, advanced age, pale skin, Caucasian descent other than British/Irish, green- or hazel-colored eyes, and personal history of melanoma were significantly associated with an increased number of angiomas. Individuals with a personal history of melanoma were those with a stronger association with the number of angiomas; they had 3 times more angiomas than those without melanoma.

In our longitudinal study published recently, the presence of 50 or more cherry angiomas was an independent risk factor (with adjustment for age) for the development of a second melanoma in patients with sporadic melanoma (hazard ratio 3.9; 95% CI 1.7–9.1).[30]

Conclusions

Although the first references to cherry angiomas in the scientific literature associated them with cancer, subsequent studies were unable to demonstrate the link. The fact that these are very prevalent lesions in the general population and are found healthy individuals and the generalized belief, held for more than a century, that these are clinically irrelevant lesions, have hindered determination of their etiopathogenesis and their true clinical significance as there are limited studies on the subject. However, in recent years, certain epidemiological evidence has pointed to an association between exposure and different toxins and drugs, and some nonmalignant diseases and, above all, cancer and immunosuppression. For many of these associations, the development of cherry angiomas could correspond to an imbalance between proangiogenic and antiangiogenic factors with a predominance of the former. For the association with cutaneous cancer, although

there are no data to demonstrate the fact, the possible influence of proliferation-activating mutations induced by UV radiation could play a role in the development of angiomas. Other factors, such as genetic susceptibility, as yet not fully elucidated, could likewise play a role if the corresponding pathways are also implicated in the etiopathogenesis of cancer.

However, the true clinical relevance of cherry angiomas requires further investigation of risk factors and epidemiological studies that include these characteristics in different contexts.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. Gao X-H, Wang L-L, Zhang L, Hong Y-X, Wei H, Chen H-D. Familial nevus flammeus associated with early onset cherry angiomas. Int J Dermatol. 2008;47:1284–6, http://dx.doi.org/10.1111/j.1365-4632.2008.03855.x.
2. Murison A, Sutherland J, Williamson A. De Morgan's spots. Br Med J. 1947;1:634–6, http://dx.doi.org/10.1136/BMJ.1.4505.634.
3. Wertheim L. De Morgan's spots. Br Med J. 1947;1:824, http://dx.doi.org/10.1136/bmj.1.4509.824-a.
4. Weber F, Handley W. De Morgan's spots. Br Med J. 1947;1:864, http://dx.doi.org/10.1136/bmj.1.4510.864.
5. Shah K, Shah A, Shah P. Campbell de Morgan's spots in diabetes mellitus. Br J Dermatol. 1966;78:493–5, http://dx.doi.org/10.1111/j.1365-2133.1966.tb12256.x.
6. Ma H, Zhao G, Shi F, Wang Y. Eruptive cherry angiomas associated with vitiligo: provoked by topical nitrogen mustard? J Dermatol. 2006;33:877–9, http://dx.doi.org/10.1111/j.1346-8138.2006.00200.x.
7. Askari N, Vaez-Mahdavi M-R, Moaiedmohseni S, Khamesipour A, Soroush M-R, Moin A, et al. Association of chemokines and prolactin with cherry angioma in a sulfur mustard exposed population—Sardasht-Iran cohort study. Int Immunopharmacol. 2013;17:991–5, http://dx.doi.org/10.1016/j.intimp.2012.12.016.
8. Firooz A, Komeili A, Dowlati Y. Eruptive melanocytic nevi and cherry angiomas secondary to exposure to sulfur mustard gas. J Am Acad Dermatol. 1999;40:646–7, http://dx.doi.org/10.1016/s0190-9622(99)70460-3.
9. Raymond LW, Williford LS, Burke WA. Eruptive cherry angiomas and irritant symptoms after one acute exposure to the glycol ether solvent 2-butoxyethanol. J Occup Environ Med. 1998;40:1059–64, http://dx.doi.org/10.1097/00043764-199812000-00005.
10. Cohen AD, Cagnano E, Vardy DA. Cherry angiomas associated with exposure to bromides. Dermatology. 2001;202:52–3, http://dx.doi.org/10.1159/000051587.
11. De Felipe I, Redondo P. Eruptive angiomas after treatment with cyclosporine in a patient with psoriasis. Arch Dermatol. 1998;134:1487–8, http://dx.doi.org/10.1001/archderm.134.11.1487.
12. Espinosa Lara P, Medina-Puente C, Riquelme-Oliveira A, Jimenez-Reyes J. Eruptive cherry angiomas developing in a patient treated with ramucirumab. Acta Oncol. 2018;57:709–11, http://dx.doi.org/10.1080/0284186X.2017.1410287.
13. Choi J, Byun H, Lee J, Park J. Multiple cherry angiomas and pyogenic granuloma in a patient treated with ramucirumab and paclitaxel. Indian J Dermatol Venereol Leprol. 2020;86:199–202, http://dx.doi.org/10.4103/ijdvl.IJDVL_184_19.
14. Lim Y, Odell I, Ko C, Choate K. Somatic p.T771R KDR (VEGFR2) mutation arising in a sporadic angioma during ramucirumab therapy. JAMA Dermatol. 2015;151:1240–3, http://dx.doi.org/10.1001/jamadermatol.2015.1925.
15. Nazer R, Bashihab R, Al-Madani W, Omair A, AlJasser M. Cherry angioma: a case–control study. J Fam Community Med. 2020;27:109–13, http://dx.doi.org/10.4103/jfcm.JFCM_293_19.
16. Barter R, Letterman G, Schurter M. Hemangiomas in pregnancy. Am J Obs Gynecol. 1963;87:625–35, http://dx.doi.org/10.1016/0002-9378(63)90056-5.
17. Darjani A, Rafiei R, Shafaei S, Rafiei E, Eftekhari H, Alizade N, et al. Evaluation of lipid profile in patients with cherry angioma: a case–control study in Guilan, Iran. Dermatol Res Pr. 2018;2018:4639248, http://dx.doi.org/10.1155/2018/4639248.
18. Akoglu G, Metin A, Emre S, Ersoy R, Cakir B. Cutaneous findings in patients with acromegaly. Acta Dermatovenereol Croact. 2013;21:224–9.
19. Borghi A, Benedetti S, Corazza M, Gentili V, Ruina G, di Luca D, et al. Detection of human herpesvirus 8 sequences in cutaneous cherry angiomas. Arch Dermatol Res. 2013;305:659–64, http://dx.doi.org/10.1007/s00403-013-1346-5.
20. Fajgenbaum DC, Fajgenbaum D, Rosenbach M, van Rhee F, Nasir A, Reutter J. Eruptive cherry hemangiomatosis associated with multicentric Castleman disease: a case report and diagnostic clue. JAMA Dermatol. 2013;149:204–8, http://dx.doi.org/10.1001/jamadermatol.2013.1552.
21. Adamski H, le Gall F, Cartron L, Dauriac C, Lancien G, Wechsler J, et al. Eruptive angiomatous lesions associated with graft-versus-host disease. Br J Dermatol. 2003;149:667–8, http://dx.doi.org/10.1046/j.1365-2133.2003.05504.x.
22. Nakashima T, Jinnin M, Etoh T, Fukushima S, Masuguchi S, Maruo K, et al. Down-regulation of mir-424 contributes to the abnormal angiogenesis via MEK1 and cyclin E1 in senile hemangioma: its implications to therapy. PLOS ONE. 2010;5:e14334, http://dx.doi.org/10.1371/journal.pone.0014334.
23. Liau J, Lee J, Tsai J, Chen C, Chung Y, Wang Y. High frequency of GNA14 GNAQ y GNA11 mutations in cherry hemangioma: a histopathological and molecular study of 85 cases indicating GNA14 as the most commonly mutated gene in vascular neoplasm. Mod Pathol. 2019;32:1657–65, http://dx.doi.org/10.1038/s41379-019-0284-y.
24. Paolino G, Cicinelli M, Brianti P, Prezioso C, Bulotta A, Rizzo N, et al. Eruptive cherry angiomas and uveal melanoma: beyond a simple association. Clin Exp Dermatol. 2021;46:946–8, http://dx.doi.org/10.1159/000511101.
25. Guastafierro A, Verdura V, di Pace B, Faenza M, Rubino C. The influence of breast cancer on the distribution of cherry angiomas on the anterior thoracic wall: a case series study. Dermatology. 2019;235:65–70, http://dx.doi.org/10.1159/000493974.
26. Borghi A, Minghetti S, Battaglia Y, Corazza M. Predisposing factors for eruptive cherry angiomas: new insights from an observational study. Int J Dermatol. 2016;55:e598–600, http://dx.doi.org/10.1111/ijd.13330.
27. Corazza M, Dika E, Maietti E, Musmeci D, Patrizi A, Borghi A. Eruptive cherry angiomas and skin melanoma: a fortuitous association? Melanoma Res. 2019;29:313–7, http://dx.doi.org/10.1097/CMR.0000000000000563.

28. Borghi A, Dika E, Maietti E, Scuderi V, Forconi R, Patrizi A, et al. Eruptive cherry angiomas and skin melanoma: further insights into an intriguing association. Dermatology. 2021;237:981–7.
29. Betz-Stablein B, Koh U, Edwards H, McInerney-Leo A, Janda M, Soyer H. Anatomic distribution of cherry angiomas in the general population. Dermatology. 2022;238:18–26, http://dx.doi.org/10.1159/000517172.
30. Pastor-Tomás N, Martínez-Franco A, Bañuls J, Peñalver JC, Traves V, García-Casado Z, et al. Risk factors for the development of a second melanoma in patients with cutaneous melanoma. J Eur Acad Dermatol Venereol. 2020;34:2295–302, http://dx.doi.org/10.1111/jdv.16341.