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Take-home messages

- Despite congenital infection with HHV-6 having an established prevalence of 1%, there are few reports associating HHV-6 to disease in fetuses.
- HHV-6 has been implicated in myocarditis in adults and children, but there was no previous association with myocarditis in fetuses.
- The virus-induced myocardial injury and the subsequent reparative lesions in the heart in development may be the cause of structural cardiac defects in fetuses.

We consider that in our case, the presence of HHV-6 DNA in the myocardium, in the absence of other pathogens, suggests that the myocarditis was caused by the virus. Moreover, we suggest that the identification of the viral genome is favourable to a pathogenic relationship between the virus and the cardiac anomaly.

In our case, there are pathological findings of acute, subacute and chronic myocarditis compatible with viral persistence. The infection probably occurred early in the second trimester of pregnancy. We postulate that the virus-induced myocardial injury and the subsequent reparative lesions in the heart in development may be the cause of structural cardiac defects in this fetus.

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Progressive macular hypomelanosis Guillet-Hélénon: structural and immunohistochemical findings

In 1985 and 1988, Gerard Guillet and Raymond Hélénon, with colleagues, described a novel acquired hypopigmentation disorder in dark-skinned immigrants from the Caribbean which they named progressive macular hypomelanosis (PMH).[1 2] Over the past 20 years, many other terms have been coined for this condition, including cutis trunci variata, nummular and confluent hypomelanosis, Creole dyschromia, or idiopathic multiple large-macule hypomelanosis.[3] More than 600 PMH patients have been reported in the literature with skin phototypes II–VI, but the debate about the aetiology of this disorder is still open.

We present an immunohistochemical and ultrastructural study on disseminated PMH extending beyond the trunk. No *Propionibacterium* colonisation of skin was found despite extensive examination. The evidence for a bacterial origin is discussed in consideration of the literature.

A 29-year-old Romanian female patient (skin phototype III), who had relocated to Germany 8 years earlier, presented with a mottled hypopigmentation of her skin that had progressed over the past 12 years. At the age of 17, macules started to appear on the abdomen and then spread gradually to the flanks, axillae and back. Over the past 2 years, the patient had noticed a rapid progression to the neck, décolleté and groin without any subjective symptoms. Physical examination revealed multiple partially coalescing oval or irregular hypopigmented macules ranging in diameter from 1 to 5 cm without any scaling (figure 1A). There was no fluorescence under illumination with Wood's light (figure 1B). Other family members were not affected.

Blood tests including HIV-ELISA were unremarkable with the exception of TPPA (1:160). Standard bacterial cultures (McConkey-sheep blood agar, 37°C) from skin swabs revealed coagulase-negative *Staphylococcus aureus*. Cultures under microaerophilic and dark conditions on brain–heart infusion agar (pH 7.1, 37°C) were negative for *Propionibacterium* species. *Treponema pallidum* DNA was not found after PCR in PMH lesion.

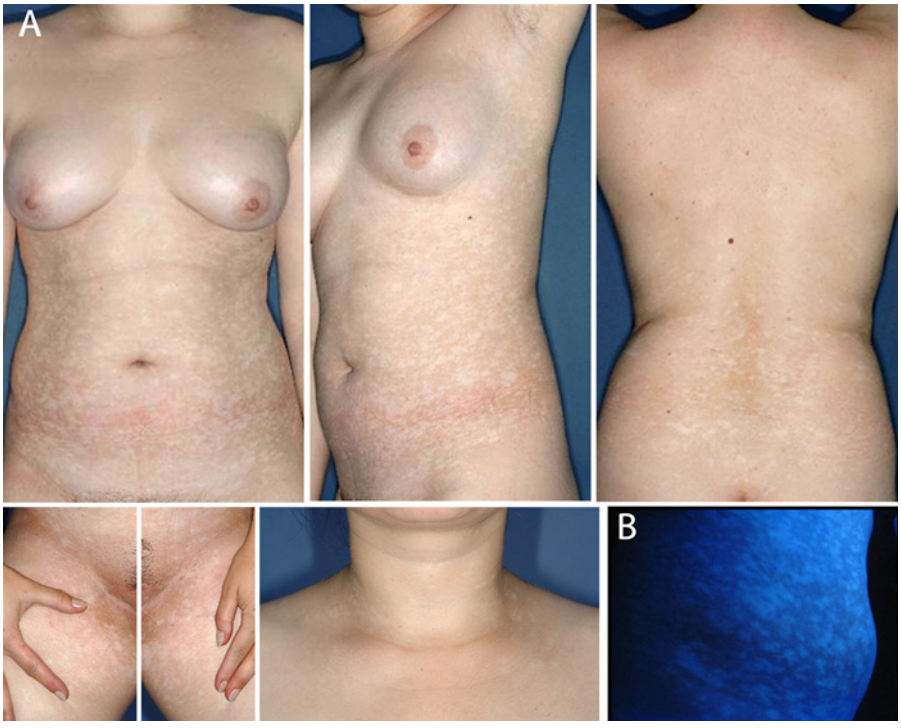

Figure 1 (A) Disseminated progressive macular hypomelanosis in a 29-year-old female patient. (B) No follicular fluorescence under Wood's light (UVA 320–400 nm), right flank part.

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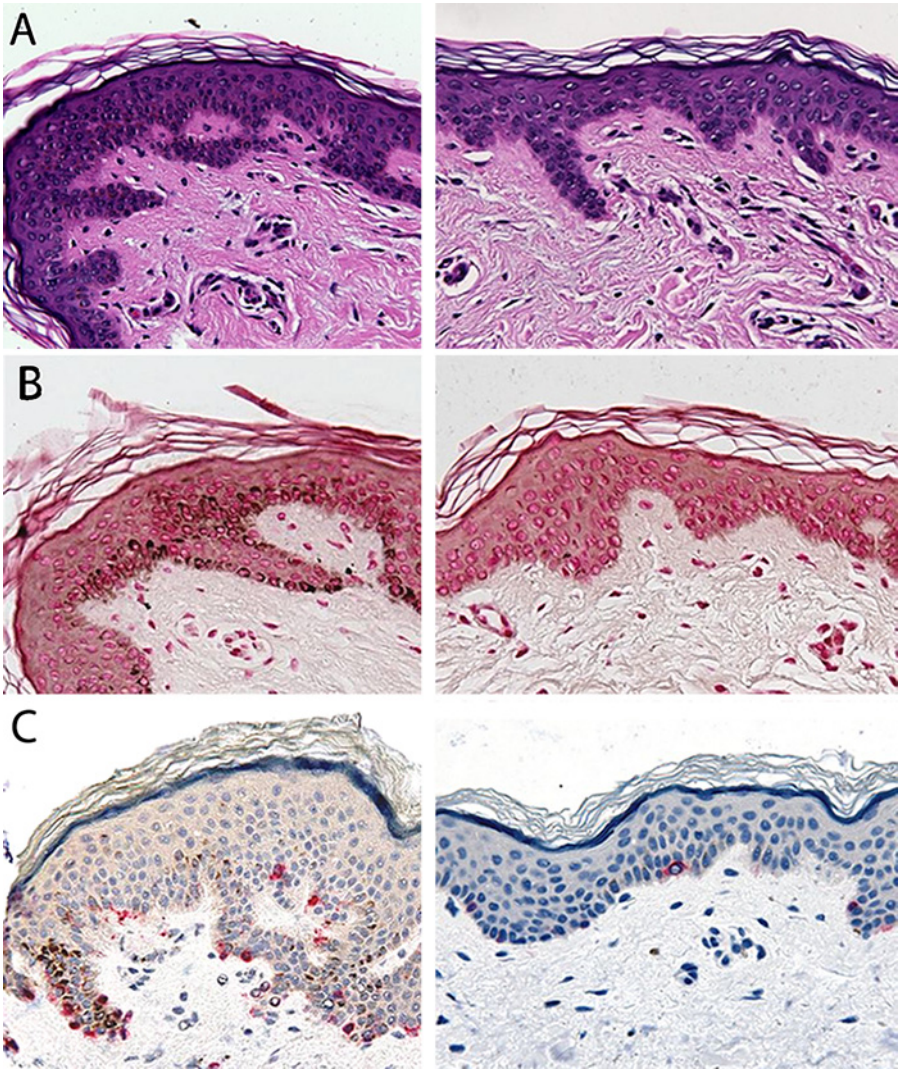

Figure 2 Histological stains and immunohistochemistry of healthy (left) and lesional (right) skin from the back: a marked reduction of pigment in the basal layer of the epidermis in lesional skin (right) on (A) H&E and (B) Fontana–Masson staining; (C) a reduction in the number of melanocytes in lesional skin (right) in Melan A staining.

A marked reduction of pigment in the basal layer of the epidermis and a sparse lymphohistiocytic infiltrate could be seen in lesional skin on H&E (figure 2A) and Fontana–Masson staining (figure 2B). Bacteria and fungi were absent in both hair follicles and inter-follicular epidermis on H&E or periodic acid Schiff-stained sections. Melan A staining showed normal melanocyte morphology but reduced numbers in the basal layer (figure 2C). Electron microscopy revealed smaller and aggregated melanosomes in the affected areas compared with unaffected skin (figure 3).

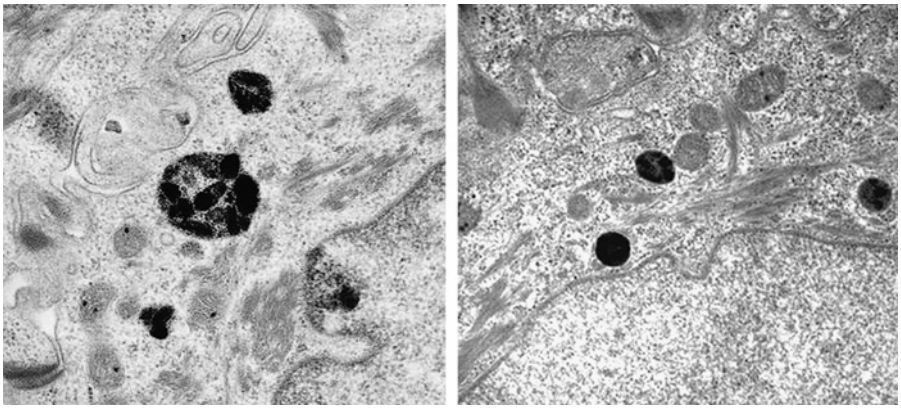

Figure 3 Electron microscopy of healthy (left) and lesional (right) skin parts of the back; immature melanosomes look smaller and aggregated in the lesional skin (×20 000).

Take-home messages

- Progressive macular hypomelanosis (PMH) is a rare aetiologically unknown pigmentation anomaly characterised by small, immature melanosomes containing low-density melanin.
- The diagnosis of PMH is based on the ultrastructural examination of melanosomes.

Phototherapy was declined by the patient. However, encouraged by a report from the literature,[4] we tried 2.5% benzoyl peroxide cream treatment twice daily for a month despite the lack of evidence of *Propionibacterium*. We did not observe any effect after 6 months' follow-up.

No consensus has been reached so far regarding the aetiology of PMH. Based on the observation of follicular red fluorescence under Wood's light in 50 from 291 PMH patients, and isolates of *Propionibacterium* from lesional, but not from healthy skin in six patients, a bacterial aetiology for PMH was proposed.[5] This provided the rationale for a randomised, within-patient, left–right comparison trial between topical antimicrobial treatment (5% benzoyl peroxide gel and 1% clindamycin lotion, bcUVA) and anti-inflammatory treatment (0.05% fluticasone cream, fUVA), both combined with UVA three times/week for 14 weeks.[4] Both treatment arms achieved temporary repigmentation or hyperpigmentation. At the 12-week examination, lesional (re)pigmentation was found to approximate the pigmentation of normal skin in both arms with a difference of 0.9 colorimetric units. A complete repigmentation was observed only in 62% (28/45) bcUVA- treated arms compared to 22% (10/45) after fUVA at the 12-week follow-up. The remaining sites showed either no or incomplete repigmentation.[4]

The study leaves many questions unanswered: To what extent does the topical treatment contribute to the effect of UVA? Other studies employing only phototherapy have demonstrated beneficial effects of UVB[6] or sun light.[7] Could the lower degree of pigmentation achieved in the fUVA arm have been brought about by corticosteroid? If the cause of PMH was an infection, why would anti-inflammatory treatment be effective as well? Why was the treatment effect transient? To evaluate the efficacy of antimicrobial therapy, treatment versus placebo, vehicle plus UVA would have been preferable.

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Why do acne patients, whose skin is densely colonised by propionibacteria, never exhibit signs of hypopigmentation or PMH? One recent study identified *Propionibacterium* species other than *Propionibacterium acnes* from the skin of 8 out of 14 PMH patients, where the remaining 6 patients were found to harbour *P acnes* exclusively on their skin.[8] This definitely put the existence of any causative or PMH-specific species in doubt.

As reported earlier in this article,[3] we did not find any signs of *Propionibacterium* colonisation of lesional skin by Wood's light examination, microbiological analysis or pathology. The diagnosis of PMH was confirmed by histology and electron microscopy. Other differential diagnosis of hypopigmentation (syphilis, pityriasis versicolor, pityriasis alba, leprosy, incontinentia pigmenti, mycosis fungoides or arsenic hypomelanosis) could be excluded by clinical signs, history, laboratory and histopathology.

The follicular fluorescence under Wood's light is obviously an indicator of *Propionibacterium* colonisation, but the prevalence of these bacteria has to be evaluated epidemiologically in PMH patients and healthy controls. Our observations as well as those of others[3] show that PMH occurs in the absence of *Propionibacterium*. We therefore rather favour the hypothesis of a genetic background of PMH as proposed by Guillet *et al*[2] with an impaired melanosomal maturation process giving rise to smaller melanosomes, containing low-density melanin.

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