consider LGV or syphilis as our initial differential diagnosis. In the present epidemiological context, we emphasize the importance of high clinical suspicion to avoid undetected cases in order to interrupt the chains of transmission. Considering the steady increase of cases reported in Africa since 1970 and present-day globalization, it would be wise to consider monkeypox in the differential diagnosis when evaluating genital ulcer diseases.

Finally, we would like to highlight our patient’s remarkable improvement after one day of antibiotic therapy with doxycycline, with resolution of fever and lymphadenopathy reduction. A case report of MPXV treated with doxycycline for suspected rickettsial infection has been described in the literature, where the patient presented fever resolution within the first 24 h of treatment. This clinical improvement could be explained by the natural evolution of the disease, by the anti-inflammatory properties of doxycycline or by an unknown mechanism.

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The principal investigator had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Giant congenital melanocytic naevus with a novel CUX1–BRAF fusion mutation treated with trametinib

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Dear Editor, Giant congenital melanocytic naevi (GCMN) are rare, large melanocytic proliferations, caused by genetic mutations that interfere with the normal proliferation, differentiation and migration of melanoblasts. Apart from cosmetic disfigurement, these naevi may be complicated with pain, pruritus, neurocutaneous melanosis and higher risk of melanoma. Somatic mutations mainly in NRAS but also in BRAF and in other genes have been described in GCMN. Both NRAS and BRAF mutations activate the mitogen-activated protein kinase (MAPK) pathway, which increases proliferation and survival of melanocytes.

A 4-year-old girl with a GCMN in a bathing trunk distribution presented with a rapidly growing right flank mass accompanied by recent swelling of the inguinal area, perianal and genital pruritus, and pain.

Physical examination revealed a large brown plaque affecting the lower trunk, buttocks, genital and inguinal areas with rough consistency, covered with fine hair. Multiple accompanying smaller naevi over the trunk and extremities were observed. A 4-cm round mass was noted in the right flank area, as well as inguinal lymphadenopathy and genital swelling (Figure 1a,b). Imaging studies demonstrated enlargement of right inguinal lymph nodes (LN) coalescing to a 5-cm mass with swelling of the perineum, and retroperitoneal lymphadenopathy along the iliac chain without involvement of the spinal canal. Positron emission tomography-computed tomography revealed an excessive metabolic activity in the right flank mass while only a mild signal in the inguinal LN (Figure 1d–i). At that point, excision of the right flank mass was performed. Histopathological findings showed epithelioid melanocytes with significant atypia, mitotic figures (8–12 per mm²), hypercellularity and abrupt margins between the tumour nodule and surrounding naevus. The tumour abuts the deep margin focally in the centre of the specimen. The findings were nonconclusive for either an atypical proliferative nodule or transformation to melanoma.

Biopsy of the suspected inguinal LN demonstrated small naevus cells without atypia. Next-generation sequencing of DNA extracted from the mass for melanoma mutational hot spots, including BRAF, NRAS, KRAS, was negative. However, comprehensive genomic profiling (FoundationOne® Heme) performed on DNA extracted from the GCMN was positive for a novel fusion mutation of CUX1–BRAF. Although this fusion has not been functionally characterized, other fusions with similar breakpoints in BRAF have been reported as...
constitutively active, causing hyperactivation of the MAPK pathway,⁵ therefore supporting the notion that this mutation is driving the GCMN in our patient.

Following the surgical procedures, the patient still reported intractable perianal–genital pain and pruritus persisted. As an attempt to suppress melanocytic proliferation in the GCMN and thus improve the patient’s symptoms, we initiated trametinib treatment [MAPK kinase enzyme (MEK) inhibitor] at a dose of 0·6 mg daily. Two weeks after initiation of treatment, the patient reported a significant improvement in pain and pruritus. Currently, 22 months under treatment with trametinib, clinical improvement continues. Pain and pruritus have resolved and swelling has improved. Mild fading of hyperpigmentation has been observed in the GCMN (Figure 1c).

Repeated imaging demonstrated improvement in oedema of the entire naevus, normalization of lymphadenopathy, and no new suspicious foci with excessive metabolic activity (Figure 1d-II). The patient had mild elevation of liver function tests (aspartate aminotransferase up to 59 U L⁻¹, normal ≤34 U L⁻¹), which has been stable under recurrent monitoring. Mild elevation of creatinine phosphokinase (338 U L⁻¹, www."

![Figure 1](image-url)
normal ≤145 U L⁻¹) and mild scalp hair loss were also noted. All abovementioned abnormalities are known adverse effects of trametinib.

The presence of a GCMN can have a dramatic effect on a patient’s life, with associated higher risk of neurological complications, malignancy, cosmetic effect and more.¹ As already mentioned, GCMN result from postzygotic activating mutations in the MAPK pathway, interfering with the normal proliferation, differentiation and migration of melanoblasts and melanocytes.²–⁴ The possibility of using MEK inhibitor treatment in selected GCMN cases has been suggested previously,⁵ but to our knowledge, only one patient with GCMN (due to a AKAP9–BRAF fusion mutation) was treated with a MEK inhibitor, with encouraging results.⁶ Our patient presented with a novel BRAF mutation (CUX1–BRAF), which has not been reported previously in GCMN. Previous data imply a connection of this mutation to malignancy development,⁷ possibly via loss of the regulatory domain of BRAF. Hence, these alterations might be sensitive to MEK inhibition. Initiation of trametinib treatment in our patient brought a rapid improvement of pain and pruritus, as well as gradual resolution of objective findings, such as oedema and pigmentation of the naevus. Our findings show that patients with BRAF-mutated GCMN can benefit from MEK inhibitor treatment. Data are available only on request due to privacy/ethical restrictions. Further investigations regarding the long-term effect of this treatment, as well as its effect on the risk of melanoma development in GCMN, are warranted.

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Consensus on the clinical management of chronic radiation dermatitis and radiation fibrosis: a Delphi survey

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Dear Editor, Chronic radiation dermatitis and fibrosis (CRDF) has been defined as skin changes that develop more than 90 days after the cessation of radiation therapy. It encompasses dyspigmentation, epidermal thinning, dermal atrophy and telangiectasias.¹ As no consensus on standard of care exists, we created an international, multidisciplinary, consensus-based approach for the terminology, risk factors, treatment and management of CRDF.

A multidisciplinary panel of 27 providers (25 physicians and two nurse practitioners) participated in the Delphi-method survey, which consisted of two independent rounds of questionnaires followed by a consensus meeting between panellists. Of the 25 physicians, 19 were dermatologists and six were oncologists, two of whom were radiation oncologists. Strong consensus was achieved once ≥70% of respondents strongly agreed or agreed with a statement. Moderate consensus was achieved if 50–69% of respondents strongly agreed or agreed with a statement. Statements that achieved moderate consensus were reviewed in detail for modification and inclusion in the second Delphi round. Statements that failed to reach consensus (<50% of participants agreeing or strongly agreeing) were dismissed unless a group member felt further discussion could benefit inclusion in the next round.

The first and second rounds in the Delphi process consisted of 63 and 27 questions or statements, respectively. We achieved strong consensus for 15 statements and moderate consensus for 16 statements. Thirty-two statements failed to reach consensus and were eliminated. This process and the results are summarized in Table 1. Consensus points determined by this collaboration of physicians can be used to aid the decision making of clinicians treating patients with CRDF and are outlined below.

Treatment features increasing the likelihood of CRDF that reached strong consensus include reradiation, initial radiation...