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Case Report

Giant Congenital Melanocytic Naevus: A Case Report and the Potential Risk Factor of Autoimmunity

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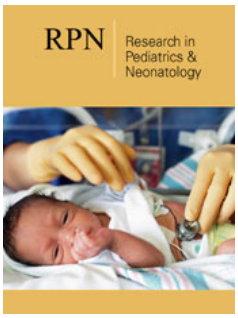

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Abstract

Background: GCMN is a rare condition associated with neurological abnormalities and risk of malignant transformation into potentially fatal tumours.

Case presentation: We report a case of profound GCMN in a newborn with a maternal background of autoimmune disease.

Conclusion: There may be an unexplored shared genetic basis between an abnormal immune milieu and risk of GCMN. Management of GCMN is multifactorial and patient-centred, with no evidence for definitive treatment at present.

Keywords: Neonatology; Dermatology; Congenital; Autoimmunity

Abbreviations: GCMN: Giant Congenital Melanocytic Naevus, MAPK: Microtubule-Associated Protein Kinase

Background

GCMN are irregular, hyperpigmented naevi which span over 20cm and may have associated smaller satellite lesions [1]. Histologically, they are junctional, compound or intradermal naevi and often feature hypertrichosis. GCMN have an incidence of less than 1 in 200,000 and are either present at birth or develop from existing melanocytes in the first 2 years of life [2]. They arise largely from gain-of-function somatic mutations in the enzymes BRAF at amino acid V600 (1 in 6 cases) or NRAS at Q6 (4 in 5 cases) [3]. These mutations affect the Microtubule-Associated Protein Kinase (MAPK) signal transduction pathway, leading to abnormal proliferation of embryonic melanoblasts. Consistent with the differentiation of melanocytes from neural crest cells, GCMN are associated with syndromes including type 1 neurofibromatosis [1], lipomatosis [4] and cortical migration abnormalities [5]. Patients with multiple naevi are at greater risk of concurrent neuropathology and are recommended early MR imaging of the brain [6]. GCMN also carry risk of malignant transformation into melanoma and other, rarer neoplasms such as liposarcoma and rhabdomyosarcoma [7]. This is thought to be driven by sporadic mutations or defects in neural crest development and occurs more commonly in larger naevi [2,8].

Case Presentation

We report a case of GCMN in a newborn with a maternal background of autoimmune disease. His antenatal course was normal, and no physical abnormalities were detected with ultrasound scanning. He was born by uncomplicated vaginal delivery at term, with an

extensive GCMN on the upper back (Figure 1) and widespread satellite naevi (Figure 2). The rest of his examination, blood glucose and thyroid function tests were normal. His mother is of Sri Lankan origin, diagnosed with hyperthyroidism, psoriasis and insulin-dependent type 2 diabetes. His father is of Indian origin and is healthy. Together they have one other son who is well and there is no family history of GCMN.

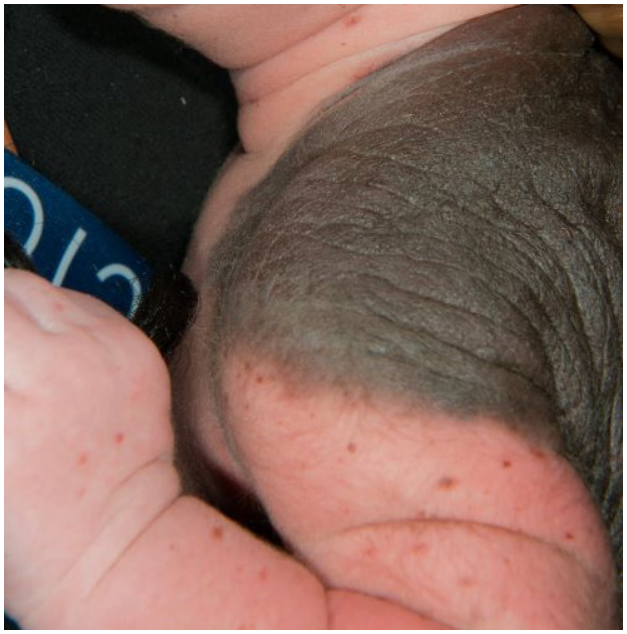

Figure 1: Large, irregular and hyperpigmented naevus with hypertrichosis.

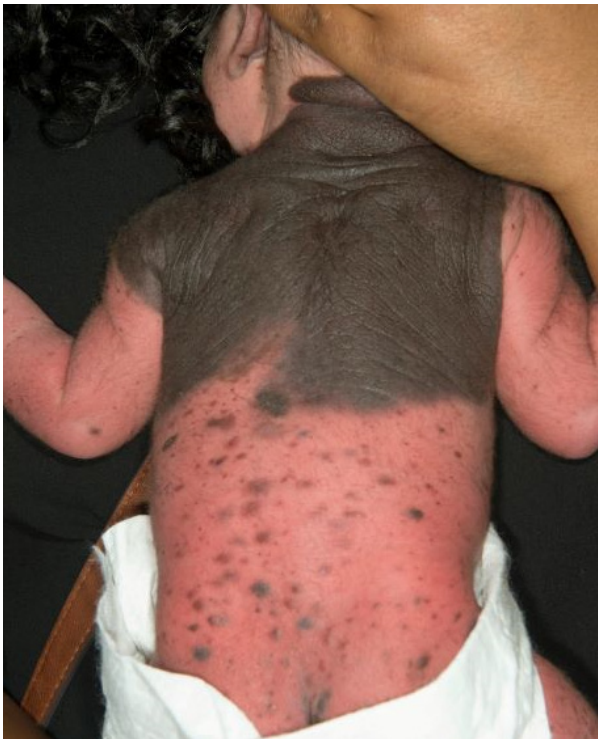

Figure 2: GCMN with widespread satellite lesions.

Discussions and Conclusions

To our knowledge, there have been no reported cases associating GCMN with autoimmune disease. There is some evidence, however, that number of melanocytic naevi is related to immunological disturbance [9,10] such as the abnormal expression of T-cells and pro-inflammatory cytokines in psoriasis [11]. Furthermore, immunomodulators which alter the cytokine profile have been reported to result in eruptions of naevi [12] as well as development of melanoma [13,14]. It could therefore be hypothesised that autoimmunity is associated with overstimulation of melanocytes [15,16] and further studies are required to characterize this relationship, the potentially underlying genetic cause and whether control of maternal autoimmune disease has a role in risk reduction of GCMN.

There are currently no universally accepted guidelines for treatment of GCMN and the benefit of surgical excision remains controversial. Recently, the genetic heterogeneity within naevi has opened the possibility of targeting GCMN with specific inhibitors [8]. Sporadic mutations in lesions have been found to activate, for example, the MAPK signaling pathway and MAPK inhibitors such as trametinib have shown some efficacy [17]. At present, however, management focuses on sun protection, regular clinical examination, patient education for early detection of malignant transformation and minimization of the potential psychosocial impacts of the condition [18].

To conclude, this is a profound example and personal perspective of a rare, congenital condition with potential for malignant transformation. We present a novel hypothesis, with evidence from this case and the wider literature of a predisposition to GCMN in those with genetic mutations also present in autoimmune disease. Further research is required to exclude solely a fortuitous concurrence between GCMN and what are relative common diseases, as well as to develop more effective, targeted treatments.

Patient's Perspective

I granted consent for publication of my baby's photographs to increase the information available about GCMN and its potential complications. When he was born, my husband and I were not expecting him to have any problems and we were frightened by the lesion. Neither we nor the midwife present had ever seen or heard of GCMN. I was worried that my background of psoriasis had a role in causing the condition and so I am pleased that his case may encourage research into whether any risk is conveyed by maternal autoimmune disease. Most of all, I hope that this report will help my son to better understand his condition, allow him to take pride and ownership over his unique GCMN and in doing so overcome any psychosocial impacts it may have on his future.

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