Mastocytosis in Children Is Associated with Mutations in c-KIT

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Mastocytosis can affect both children and adults, and, depending on age at onset, its manifestations and prognosis may differ. Childhood mastocytosis generally has a good prognosis and typically presents in children under 2 years of age. Pediatric mastocytosis tends to regress spontaneously, is rarely associated with hematologic disorders, and rarely affects organs other than skin. Most patients improve substantially, or their disease resolves completely before the onset of puberty (Kiszewski et al., 2004; Ben-Amitai et al., 2005). Adult-onset mastocytosis can be severe, is commonly considered incurable, and may be associated with systemic involvement of multiple organ systems. Adult-onset mastocytosis may also be associated with clonal hematologic non-mast-cell-lineage diseases, such as myelodysplastic and myeloproliferative disorders. It can lead to rare mast cell leukemia, carrying a high risk of mortality (Valent et al., 2003). The adult-onset form of the disease is associated with c-KIT mutations, mostly in exon 17 (D816V).

Several small studies have found different frequencies of c-KIT mutations in patients with childhood-onset mastocytosis, and debate has focused on whether this form of mastocytosis is a reactive or a clonal disease (Longley et al., 1996; Buttner et al., 1998; Verzijl et al., 2007). For this reason, Bodemer and colleagues studied a relatively large cadre of patients with childhood mastocytosis (2010, this issue). These patients were enrolled at multiple sites, and each patient had a positive Darier's sign (with their disease confirmed by histopathology). The investigators examined the patients’ skin biopsies for mutations in codon 816 (exon 17, D816V) and other c-KIT mutations. They observed a high rate of mutations; 42% were found in D816V and 44% were found outside exon 17. Half of these mutations were encoded in an unexpected location: exons 8 and 9. All the mutations identified were somatic, and all caused activation of c-KIT.

Through the following questions, we examine this article in greater detail. For brief answers, please refer to the supplementary material online.

REFERENCES


QUESTIONS
1. Describe the various types of mastocytosis.
2. What was the rationale for this study?
3. Explain the methods employed.
4. What were the results?
5. What were the conclusions and implications of the study?

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