

# Abnormal Scarring With Keloid Formation After Osteochondroma Excision in Children With Multiple Hereditary Exostoses

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**Introduction:** Multiple hereditary exostoses (MHE) is an autosomal dominant condition characterized by numerous cartilage-capped exostoses/osteochondromas in areas of actively growing bone. Abnormal scarring with keloid formation after osteochondroma excision in children with MHE has not been previously described.

**Methods:** A retrospective double-cohort study was undertaken to determine if children with MHE have a higher rate of abnormal scarring with keloid formation after osteochondroma excision when compared with those with solitary osteochondroma. In the initial phase, all consecutive children with MHE that underwent excision of osteochondroma with a minimum 2-year postoperative follow-up were identified. A control group of age-matched cases of solitary osteochondroma was subsequently identified. All patients were interviewed for wound healing problems and noncosmetic scarring. All patients with unsatisfactory scars were asked to send pictures and/or were invited for follow-up. Data were statistically analyzed.

**Results:** Eighty-three surgeries were performed in 25 patients with MHE, whereas 25 surgeries were performed in 25 patients with solitary osteochondroma. Twelve keloid scars were noted in 7 patients with MHE, and no keloids were noted in any of the patients in the solitary group. Diagnosis of MHE was a statistically significant risk factor for formation of keloids after surgery ( $P < 0.05$ ).

**Discussion:** Abnormal scarring with keloid formation after osteochondroma excision in MHE has not been previously reported. Although this study has limited numbers, the results demonstrate a statistically significant correlation between keloid formation and MHE. The risk for abnormal scarring and keloid formation should be discussed with all patients before surgery.

**Key Words:** keloid, solitary osteochondroma, multiple hereditary exostoses (MHE), excision, abnormal scar

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To our knowledge, there are no reports in the English literature of abnormal scarring with keloid formation in children with multiple hereditary exostoses (MHE) who underwent excision of osteochondromas. For many years, the senior author has been noticing an abnormal scarring pattern in children with MHE undergoing surgery for osteochondroma excision. Therefore, we hypothesized that children with MHE have an increased incidence of abnormal scarring with keloid formation. We believed that age-matched control children with solitary osteochondroma would be an appropriate control for our index group and conducted this retrospective double-cohort study to test this hypothesis.

Multiple hereditary exostoses is an inherited condition that causes the development of numerous cartilaginous osteochondromas in the growing skeleton. It is most commonly inherited as an autosomal dominant loss of function mutation of either the *EXT1* or *EXT2* genes with almost complete penetrance. These genes are believed to be tumor suppressor genes that may be related to heparan sulfate proteoglycan biosynthesis.<sup>1–5</sup>

The gross and microscopic features of individual osteochondromas in patients with MHE do not differ significantly from solitary osteochondroma.<sup>6</sup> Similar to MHE, solitary osteochondroma lesions have a predilection for growing ends of long tubular bones and affect both sexes and all races equally.<sup>6</sup> Interestingly, a large number of solitary osteochondromas are clinically silent and remain undiagnosed. Children with osteochondromas (MHE or solitary) may be symptomatic with pain and tenderness due to the irritation of adjacent muscles, tendons or neurovascular structures by the osteochondromas, skeletal deformity due to altered growth of long bones, cosmetic concerns, and, less frequently, ischemic complications due to compression of vascular structures. These essentially form the indications for surgery in both groups.

## METHODS

After obtaining institutional review board approval, all consecutive children younger than 18 years with MHE that underwent excision of osteochondromas, with a minimum 2-year postoperative follow-up, were identified from the database of our institution (a tertiary pediatric oncology regional referral center). Subsequently, patients with a

**TABLE 1.** Data Collected by Telephone Interview**Telephone Interview Questionnaire (MHE/Solitary Osteochondroma Patients)**

Investigative team
Define hypertrophic scars and keloids
Hypertrophic scar: scar widens but is limited to the confines of the original surgical wound
Keloid: abnormal healing response characterized by scar migration beyond the confines of the original incision, possibly progressive, and with/without associated pigmentation changes
Patient (family) questionnaire
What is the total number of surgeries you have had for the excision of osteochondromas/osteochondroma?
Location of lesion(s)?
Have any lesions recurred?
Have you experienced any wound healing problems?
Based on the descriptions you were given for hypertrophic scars and keloids, what category does each of your scars fit into?
If keloid
Location
Dimensions of largest width and length in centimeters
Have you had scar revision surgery?

solitary osteochondroma were randomly selected to represent an age-/sex-matched control group. In both groups, all lesions were treated by means of surgical excision by subspecialty surgeons. Technique of osteochondroma excision, trilateral closure including subcuticular skin suture, dressing, and cast application remained similar in all cases.

Two authors (H.H. and J.G.) conducted telephone interviews with all patients to solicit information regarding the healing of their surgical incisions (Table 1). All patients or parents who felt that the scars were not normal or cosmetic were asked to send digital or printed pictures and/or present for follow-up (Fig. 1). Whereas a hypertrophic scar was defined as one that is widened, but limited to the confines of the original surgical wound, abnormal scarring with keloid formation was defined as a scar that extends beyond the limits of the primary healed incision in length and/or width and that has not subsided (the scar elevation had not settled down in the plane/level of the skin) with time (12 months).<sup>7</sup> Dorland's Illustrated Medical Dictionary (27th edition) has defined

keloid as "a sharply elevated, irregularly shaped, progressively enlarging scar resulting from formation of excessive amounts of collagen in the dermis during connective tissue repair," whereas Biology-Online Dictionary defines hypertrophic scar as "a scar resembling a keloid but which does not spread into surrounding tissues, is rarely painful, and regresses spontaneously."

Genetic information was not taken into account when evaluating or comparing groups nor were groups isolated based upon their EXT1 or EXT2 status. Demographic data of both groups with regard to age, sex, race, and size of incision were statistically evaluated using Fisher exact test. A  $P < 0.05$  was considered statistically significant.

## RESULTS

The response rate for this investigation was 100%. All patients who were contacted agreed to participate by answering the questions in the questionnaire provided in Table 1. In the study group of 25 children with MHE, there were 83 surgical incisions for primary removal of osteochondromas (Table 2). There were 25 incisions for the removal of 25 osteochondromas in the age-matched control group of 25 children. The average age at the time of first surgery in the MHE group was 12.15 years (range, 4–17 years) and 13.55 years (range, 7–18 years) in the solitary osteochondroma group. The  $P$  value for comparison of both groups was  $P = 0.281$ , demonstrating that no significant difference exists between the groups in terms of age. None of the patients in either group had any evidence of wound infection, and wounds in all cases healed by primary intention.

All patients (upon chart review) had been seen in the office between 6 and 18 months before this study. For purposes of this study, 12 of the 25 MHE patients who reported having abnormal scarring submitted photographs of their scars, and 9 of these 12 came for clinical follow-up. Seven (28%) of these patients had abnormal scarring with keloid formation (Fig. 3). In those patients that had multiple keloids, all incision sites with osteochondroma excisions developed abnormal scarring with keloid formation. Six of 25 patients with solitary osteochondroma reported noncosmetic (hypertrophic) scars, and of this group, 2 sent pictures, and 4 came for follow-up. None had abnormal scarring with keloid formation. The investigative team used the aforementioned



**FIGURE 1.** A 16-year-old white boy with MHE, status postexcision of a right proximal humeral osteochondroma demonstrating abnormal scarring with keloid formation.

**TABLE 2.** Clinical Data on Cases and Controls

	MHE Group	Solitary Osteochondroma Group
Males	12	15
Females	13	10
Average age at 1st surgery	13	13
Location of exostoses removed		
Tibia	21	11
Femur	18	9
Fibula	14	1
Hand	8	0
Wrist	7	0
Humerus	4	2
Scapula	4	1
Ulna	4	0
Ankle	2	0
Rib	1	1
Total	83	25

definitions to confirm that 12 (14%) of 83 MHE-related incisions had developed keloids (Fig. 2). In all the cases of abnormal scarring with keloid formation, no child had concomitant widespread acne or a bad case of chickenpox. In other words, no child had any aggravating factors for keloid formation.

Of the 7 children who developed abnormal scarring with keloid formation, 4 were African American, 2 were white, and 1 was Hispanic. Of the 4 African American patients, 2 had a family history of keloid formation, one of which had a history of keloid formation on another scar. There was no keloid history reported by anyone else in this



**FIGURE 2.** Keloid scar in a 15-year-old MHE patient, status postexcision of exostosis.



**FIGURE 3.** A 12-year-old boy with MHE after excision of osteochondromas of the lower femur and upper tibia with abnormal scarring and keloid formation.

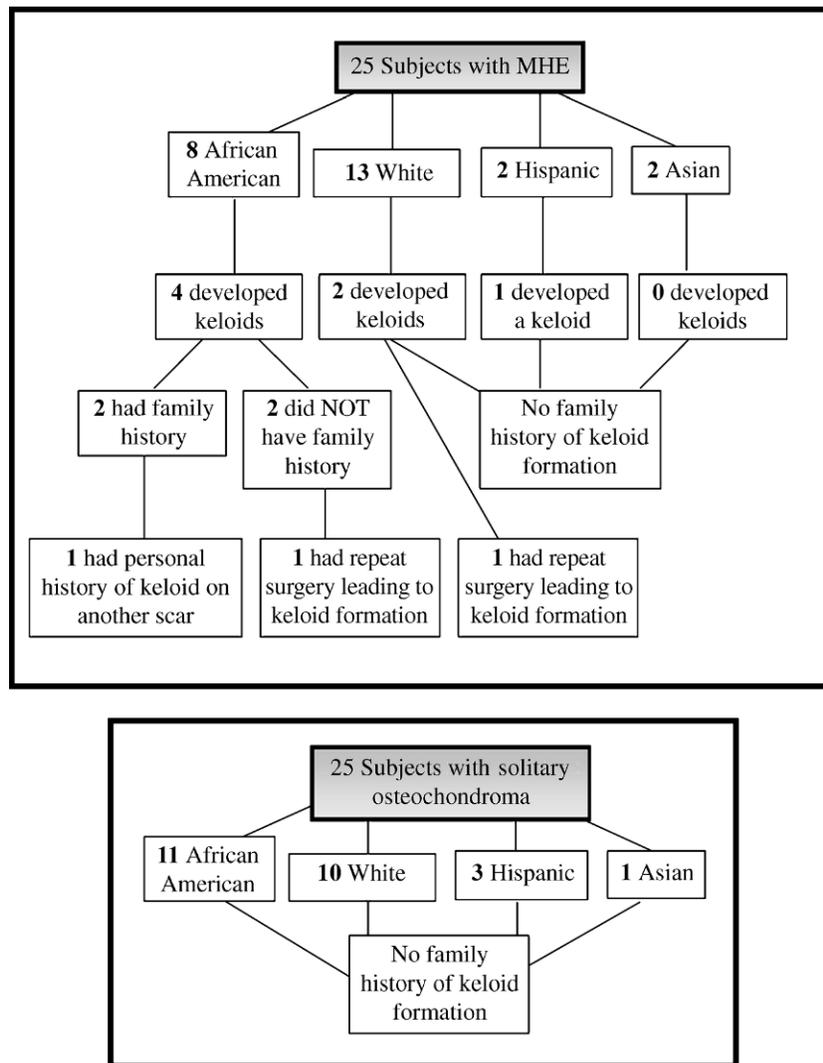
group, and no child with a solitary osteochondroma reported developing a keloid (Fig. 4). Of this solitary osteochondroma group, 11 were African American; 10, white; 3, Hispanic; and 1, Asian. None of these 25 patients had a family history of keloid formation. See Figure 5 for additional demographic information.

The keloid scars ranged in size from 3.5 to 6 cm (average, 4.5 cm) at its longest dimension. The keloid scar was located on the shoulder in 3 cases, the calf in 3 cases, the thigh in 2 cases, the knee in 2 cases, upper arm in 1 case, and the medial ankle in 1 case.

Using Fisher exact test, the diagnosis of MHE was found to be a statistically significant risk factor for the development of abnormal scarring with keloid formation after surgery ( $P < 0.05$ ). A family history of keloid formation was also found to be a statistically significant risk factor at the level of  $P < 0.05$ . However, race/ethnicity was not found



**FIGURE 4.** Lower third solitary fibular osteochondroma in a 13-year-old patient with normal scar after surgical excision.



**FIGURE 5.** Demographic information displaying presence or absence of abnormal scarring and keloid formation, race/ethnicity, and family or personal history in both the MHE and solitary osteochondroma group.

to be a risk factor for the development of abnormal scarring with keloid formation nor was a personal history of keloid formation. Scar revision surgery was performed in 4 of the 6 children with keloid formation, 2 of whom required additional scar revision procedures.

**DISCUSSION**

In this retrospective, double-cohort study, we identified a statistically significant association between children with MHE and abnormal scarring with keloid formation, after excision of osteochondromas.

Wound healing can take varied courses in different patients. Although complete wound healing occurs within the first 3 months, scar formation and remodeling can take up to 1 year. Therefore, patients may be required to follow-up for a minimum period of 12 months as far as wound healing is concerned. The reason to consider, in this study, a minimum 2-year follow-up was not out of regard to the

recurrence of osteochondromas, but to adhere to the definition of a keloid, scarring that continues to progress beyond 1 year and does not resolve. Operative notes of all cases revealed a similar trilayered surgical technique in which the subcutaneous tissue was sutured with Vicryl sutures, with a cosmetic running subcuticular closure, thereby likely minimizing surgical technique as a contributing risk factor (confounding factor) for abnormal scarring with keloid formation.

As far as the general population is concerned, patients of all ages may develop abnormal scarring with keloids, with a higher incidence being found between the ages of 10 and 30 years. Males and females are affected equally.<sup>8</sup> Most studies assessing keloid formation to date have focused predominately on black and Hispanic populations,<sup>8</sup> given that keloid scars are more common in the darker pigmented skin of individuals from these populations. The incidence of keloid formation in these populations has been reported to be between 4.5% and

16%.<sup>9</sup> At present, there are no data that report the incidence and prevalence of keloids in the general population, although it is believed that African Americans and Asians are 5 to 15 times more likely than white to develop keloids.<sup>8</sup> This study, although not specifically focused on the differences between these populations, does not demonstrate a statistically significant correlation between keloid formation and African American or Hispanic patients with MHE, or between light skin and dark skin.

Although this study is limited by numbers, the diagnosis of MHE was found to be a statistically significant risk factor for the development of abnormal scarring with keloid formation after surgical excision of osteochondromas. Based on the findings in this study, it is important to discuss with MHE children as part of informed consent the risk of abnormal scarring with keloid formation after excision of osteochondromas. In addition, given the higher rates of keloid formation in these patients, modalities for prevention of abnormal scarring could be likely considered.

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