

# Multiple Eruptive Dermatofibromas Associated With Down Syndrome

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## PRACTICE POINTS

- Although dermatofibromas are common and benign skin lesions, multiple eruptive dermatofibromas have been associated with a number of underlying conditions, particularly those associated with immune dysregulation.
- The immune dysregulation reported in Down syndrome may explain the appearance of multiple dermatofibromas.

To the Editor:

Dermatofibromas (also known as fibrous histiocytomas) are benign fibrous nodules that most often arise as solitary lesions on the lower extremities. Multiple eruptive dermatofibromas (MEDFs) are uncommon and have been defined as more than 15 in number<sup>1</sup> or 5 to 8 dermatofibromas appearing within 4 months.<sup>2</sup> They have been reported in association with a number of conditions of immune dysregulation such as systemic lupus erythematosus, Sjögren syndrome, HIV infection, and leukemia.<sup>3</sup> Multiple eruptive dermatofibromas also have been described in patients with Down syndrome (DS).<sup>4-7</sup> We report a case of MEDFs in a patient with DS and review the literature on the association between MEDFs and DS.

A 38-year-old woman with DS, hidradenitis suppurativa, and hypothyroidism presented with multiple cutaneous lesions developing over the last year. The lesions continued to increase in number but were otherwise

asymptomatic. Physical examination revealed approximately 20 rubbery, pink-tan papules measuring less than 1 cm in diameter that were scattered along the trunk (Figure, A), arms, and legs (Figure, B).

The patient had no known history of immunosuppression or rheumatologic disease and was otherwise healthy. Basic laboratory tests including a complete blood cell count and antinuclear antibody titer were within reference range. The lesions were clinically consistent with dermatofibromas, but due to their increasing number within a short period of time, a biopsy of a representative lesion was performed to confirm the diagnosis.

The exact incidence of MEDFs is unknown, but they are rare, with one review finding only 50 cases reported from 1960 to 2002.<sup>8</sup> They are increasingly recognized as a sign of potential immune dysregulation. Approximately 56% to 70% of cases are seen in patients with an underlying disease state; 80% are immune mediated.<sup>8,9</sup> Interestingly, DS has long been associated with notable immune dysfunction,<sup>10,11</sup> with evidence suggesting that trisomy 21 may result in widespread changes in gene expression that can lead to interferon activation.<sup>12</sup>

A PubMed search of articles indexed for MEDLINE using the terms *dermatofibroma* and *Down*, *dermatofibroma* and *Down syndrome*, *eruptive dermatofibroma* and *Down syndrome*, and *multiple dermatofibroma* and *Down syndrome* revealed 6 cases of MEDFs in patients with DS that have been reported since 2005.<sup>4-7</sup> An additional report by Honda et al<sup>13</sup> described a patient with DS who developed 7 dermatofibromas, but no time frame of development was specified. We

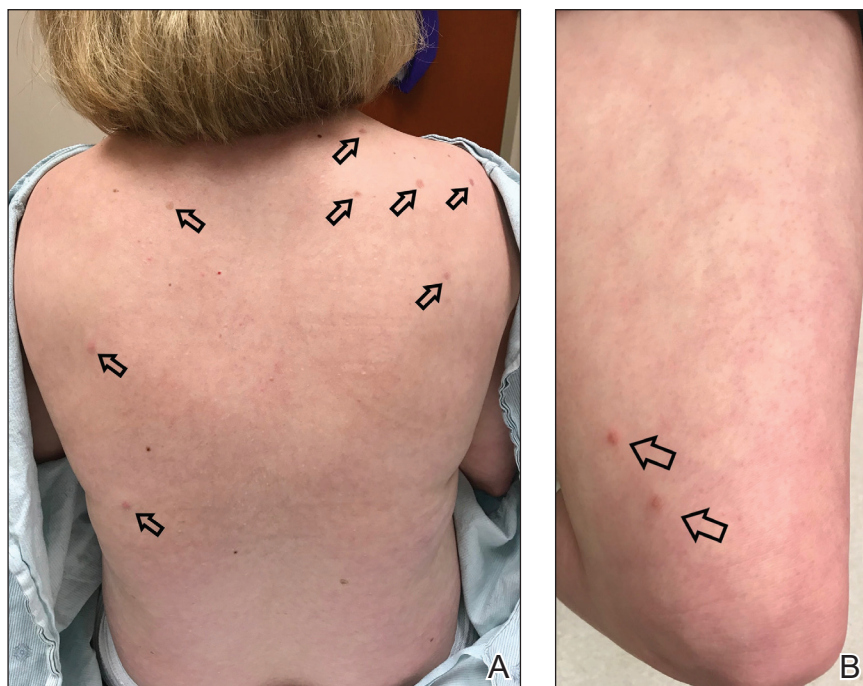
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The authors report no conflict of interest.

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A and B, Numerous sclerotic papules (arrows) consistent with dermatofibromas on the upper back and left leg, respectively.



### Multiple Eruptive Dermatofibromas in Patients With Down Syndrome

| Reference (year)                     | Gender | Age, y | No. of DFs       | Location                     | Timeline <sup>a</sup>      | Comorbidities                                |
|--------------------------------------|--------|--------|------------------|------------------------------|----------------------------|--|
| Monteagudo et al <sup>5</sup> (2005) | F      | 37     | 39               | Trunk, arm, leg              | 2 y                        | N/A  |
| Monteagudo et al <sup>6</sup> (2009) | F      | 45     | 7                | Trunk, arm, leg              | 3 mo                       | Psoriatic arthritis (on methotrexate)        |
|                                      | F      | 47     | 31               | Trunk, arm, leg              | 6 mo                       | Graves disease                               |
|                                      | F      | 42     | 44               | Trunk, arm, leg              | 3 y                        | Hypercholesterolemia                         |
| Lamb et al <sup>4</sup> (2014)       | M      | 65     | 20–30            | Arm, leg                     | Several months             | Mild lymphopenia                             |
| Honda et al <sup>13</sup> (2016)     | M      | 26     | 7                | Trunk, leg <sup>b</sup>      | Not specified <sup>c</sup> | Acute megakaryoblastic leukemia <sup>d</sup> |
| Tanaka et al <sup>7</sup> (2017)     | F      | 15     | 6                | Trunk, arm, leg <sup>e</sup> | 6 mo                       | N/A  |
| Current report                       | F      | 38     | ~20 <sup>f</sup> | Trunk, arm, leg              | 1 y                        | Hidradenitis suppurativa, hypothyroidism     |

Abbreviations: DF, dermatofibroma; F, female; M, male; N/A, not available.

<sup>a</sup>Time period in which DFs appeared as given in months or years.

<sup>b</sup>Unknown if DFs were present on the arms. Authors reported lesions on limbs and trunk but only showed pictures of DFs on the legs.

<sup>c</sup>This report was included in the analysis of this review even though no time frame was reported.

<sup>d</sup>Patient was treated with chemotherapy (agent unknown) from 3 months of age until 4 years of age. The first DFs were reported at 19 years of age.

<sup>e</sup>Lesions were reported as unilateral on the right side of the body.

<sup>f</sup>Number of DFs was estimated in the patient's medical record. Clinical images of the anterior limbs and posterior trunk revealed at least 17 DFs.

reviewed the characteristics of 8 patients with DS with MEDFs, which included our patient (Table). The average age at time of presentation was 39 years (median age, 40 years). Six patients (75%) were female and 2 (25%) were male. Dermatofibromas were reported to appear over the course of months to years. Comorbidities included psoriatic arthritis (treated with methotrexate),<sup>6</sup> thyroid disorders (ie, Graves disease),<sup>6</sup> hypercholesterolemia,<sup>6</sup> hidradenitis suppurativa, long-standing mild lymphopenia ( $1.4 \times 10^9/L$  [reference range,  $1.5 - 4.0 \times 10^9/L$ ]),<sup>4</sup> and acute megakaryoblastic leukemia<sup>13</sup> treated 15 years before the appearance of dermatofibromas.

Many dermatologic conditions have been reported at increased rates in individuals with DS, including seborrheic dermatitis, alopecia areata, syringomas, elastosis perforans serpiginosa, cutis marmorata, xerosis, and palmoplantar hyperkeratosis.<sup>14,15</sup> Although drawing conclusions about associations between MEDFs and DS is limited by our small sample size, we have reported this case and reviewed existing cases of MEDFs in DS to highlight a potential association that may be underrecognized or underreported. More evidence is needed to determine the strength of the association between MEDFs and DS, but dermatologists should be aware that MEDFs may be an additional skin finding associated with DS that is related to the syndrome's immune dysregulation.

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