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Pleomorphic Hyalinizing Angiectatic Tumor: A Clinicopathologic Characterization

Vincent M. Moretti, MD[1]
John S. Brooks, MD[1]
Richard D. Lackman, MD[1]

[1] Department of Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA

Pleomorphic hyalinizing angiectatic tumor (PHAT) is a rare and only recently described soft-tissue neoplasm of unknown histogenesis. This case report describes a PHAT which developed in the forearm of a 55 year-old male. PHAT predominately develops in the subcutaneous tissue of middle-aged adults. The most common site is the lower extremity, where 63% of the lesions arise. On MRI, it typically appears as a soft-tissue mass with decreased T1 signal, high T2 signal with scattered areas of low signal, and homogenous enhancement. Grossly, all lesions are non-encapsulated and 41% are well-circumscribed. Histologically, the tumor is characterized by sheet-like proliferations of mitotically inactive spindled and pleomorphic cells and scattered clusters of ectatic vessels with circumferential hyalinization. PHAT have the potential to be locally aggressive, and 27% of the patients in the literature experienced recurrence after excision. Forty-three percent of patients initially treated by marginal excision experienced a recurrence, while no patient initially treated by wide excision experienced a recurrence. There are no reports of any metastases to date. Our patient was treated by marginal resection. He remains disease-free 22 months after resection.

Pleomorphic hyalinizing angiectatic tumor (PHAT) is a rare soft-tissue neoplasm that was only recently added to the World Health Organization (WHO) Classification of Tumours[1]. Smith et al[2] were the first to describe the tumor in 1996. Most cases have been primarily published in pathology journals[2-22]. There are no prior reports of PHAT in any of the orthopaedic or oncologic literature.

PHAT is generally considered a locally aggressive low-grade mesenchymal tumor of unknown histogenesis. PHAT predominately develops in the lower extremity of middle-aged adults, although cases occurring in the upper extremity, chest/breast, groin/perineum, buttock, and back have also been reported[2-22]. Treatment is usually wide or local excision. To date, there have been no reports of metastases, but the rate of local recurrence has been high[2-22].

To add to the minimal body of data on PHAT, we describe an uncommon case of this rare neoplasm arising in the forearm. We also study the literature to date on PHAT and attempt to characterize its clinical, imaging, and histologic patterns.

Case Report

A 55-year-old male was referred to our orthopaedic oncology service for a six-month history of a left forearm mass. The patient first noticed the mass after injuring his arm while golfing. He denied any current pain, fevers/chills, night sweats, or weight loss. His medical and family histories were unremarkable.

Physical examination revealed a soft and non-tender mass in the anterior forearm. There was no swelling, erythema, or increased warmth. Strength, range of motion, neurologic examination, and vascular examination were unremarkable. No lymphadenopathy was found.

MRI revealed a 3.0 x 4.0 x 3.0 cm lesion in the fat between the brachioradialis and pronator muscles (Figure 1A-D). The lesion was homogenously low in signal intensity on T1-weighted sequences (Figure 1A-B). It was generally high in signal on T2-weighted sequences, with scattered areas of low-signal and fibrous-appearing septae (Figure 1C). There was intense and homogenous enhancement with contrast (Figure 1D)

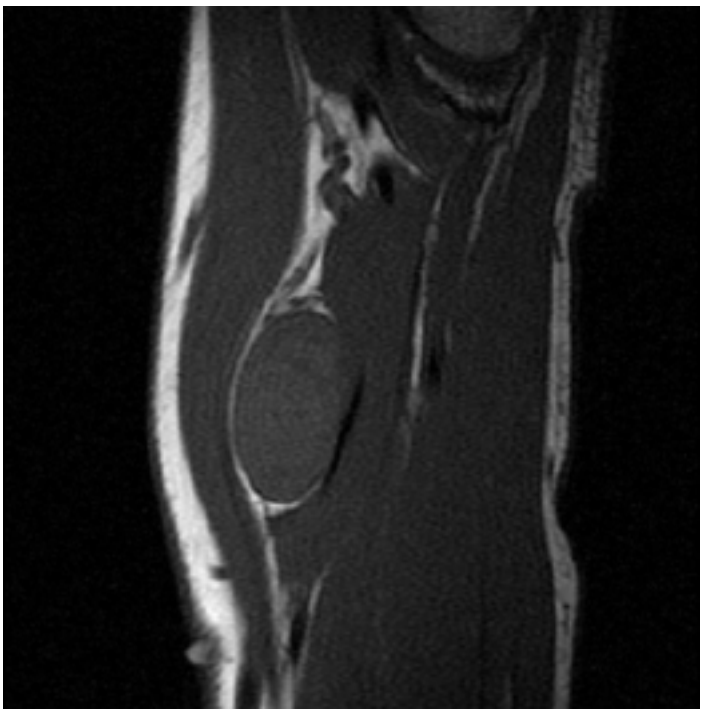
An open biopsy was subsequently performed. Initial review of frozen-section slides suggested an organizing hematoma. The remainder of the lesion was then immediately removed by marginal excision. Subsequent pathologic analysis revealed a circumscribed tumor with a sclerotic collagenized stroma (Figure 2A). Widely scattered spindle cells were found with enlarged pleomorphic cells and ectatic blood vessels (Figure 2B-C). Hemosiderin deposits were also found in spindled and pleomorphic cells (Figure 2D). Lesional spindle cells and giant cells were focally positive for smooth muscle actin and negative for CD31, CD34, desmin, and S-100. These results were diagnostic for PHAT.

There were no peri-operative complications. Repeat exams and imaging, last completed at postoperative month 22, found the patient well and without evidence of recurrence.

Discussion

PHAT is a rare soft-tissue neoplasm[1, 2]. The WHO Classification of Tumours lists it as a benign soft-tissue tumor of unknown differentiation[1]. Smith et al[2] first described these tumors in 1996 and distinguished them histologically by their sheet-like proliferations of mitotically inactive spindled and pleomorphic cells and their scattered clusters of ectatic vessels with circumferential hyalinization. They also were

Corresponding Author:
Richard D. Lackman, MD
Pennsylvania Hospital
Garfield Duncan Building, Suite 2C
301 South 8th Street
Philadelphia, PA 19106
rilack@pahosp.com



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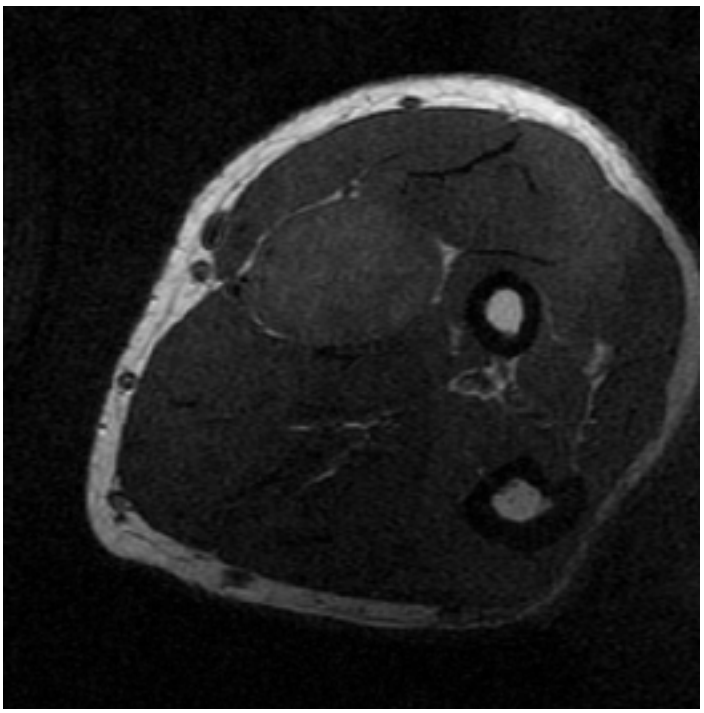

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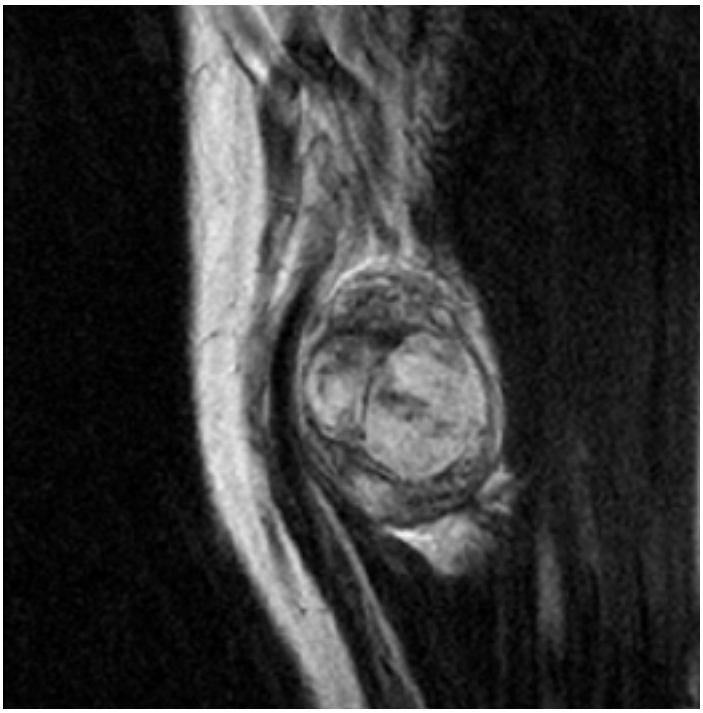

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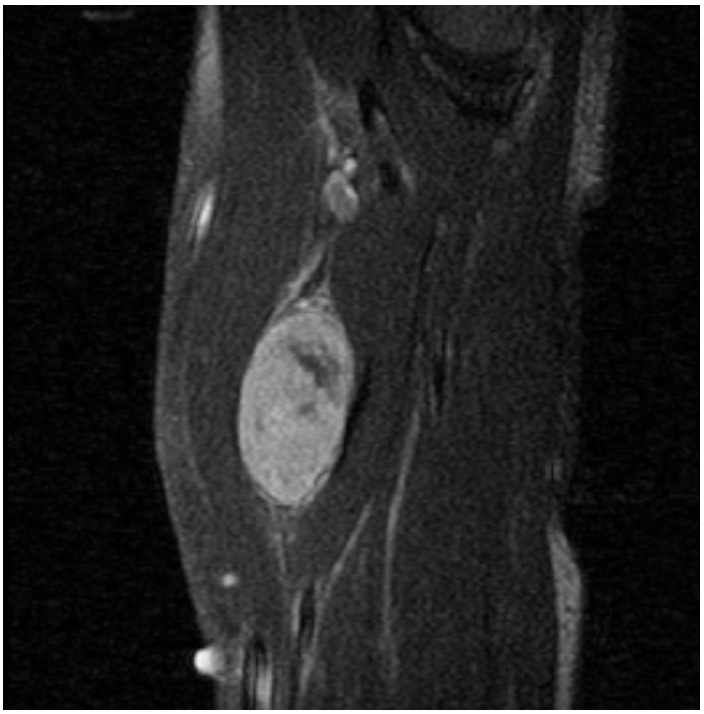

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Figure 1. (A) Coronal and (B) axial T1-weighted MR images demonstrate a homogenously low-signal lesion, only slightly brighter than muscle, within the fat between the brachioradialis and pronator muscles. (C) A coronal T2-weighted MR images demonstrates a generally high-signal lesion containing scattered areas of low-signal and fibrous-appearing septae. (D) A coronal fat-saturated T1-weighted MR image demonstrates intense and homogenous enhancement of the lesion after gadolinium administration, with small central areas of non-enhancement.

found to contain intranuclear inclusions and intracytoplasmic hemosiderin deposits[2]. Since this initial description, few cases with similar histologic features have been published in the scientific literature[2-22]. This number includes several cases of so called "early-PHAT," a lesion with many identical features that some propose is a precursor to classic PHAT[3,6].

Our review suggests that PHAT predominately occurs in the fifth to eighth decades, with an average age of 55 years at diagnosis[2-22]. However, cases of PHAT have occurred in patients as young as 10 years and as old as 89 years[6]. There is a slight female predilection of 4:3[2-22]. The lesion typically presents as a slow-growing painless mass in the subcutaneous

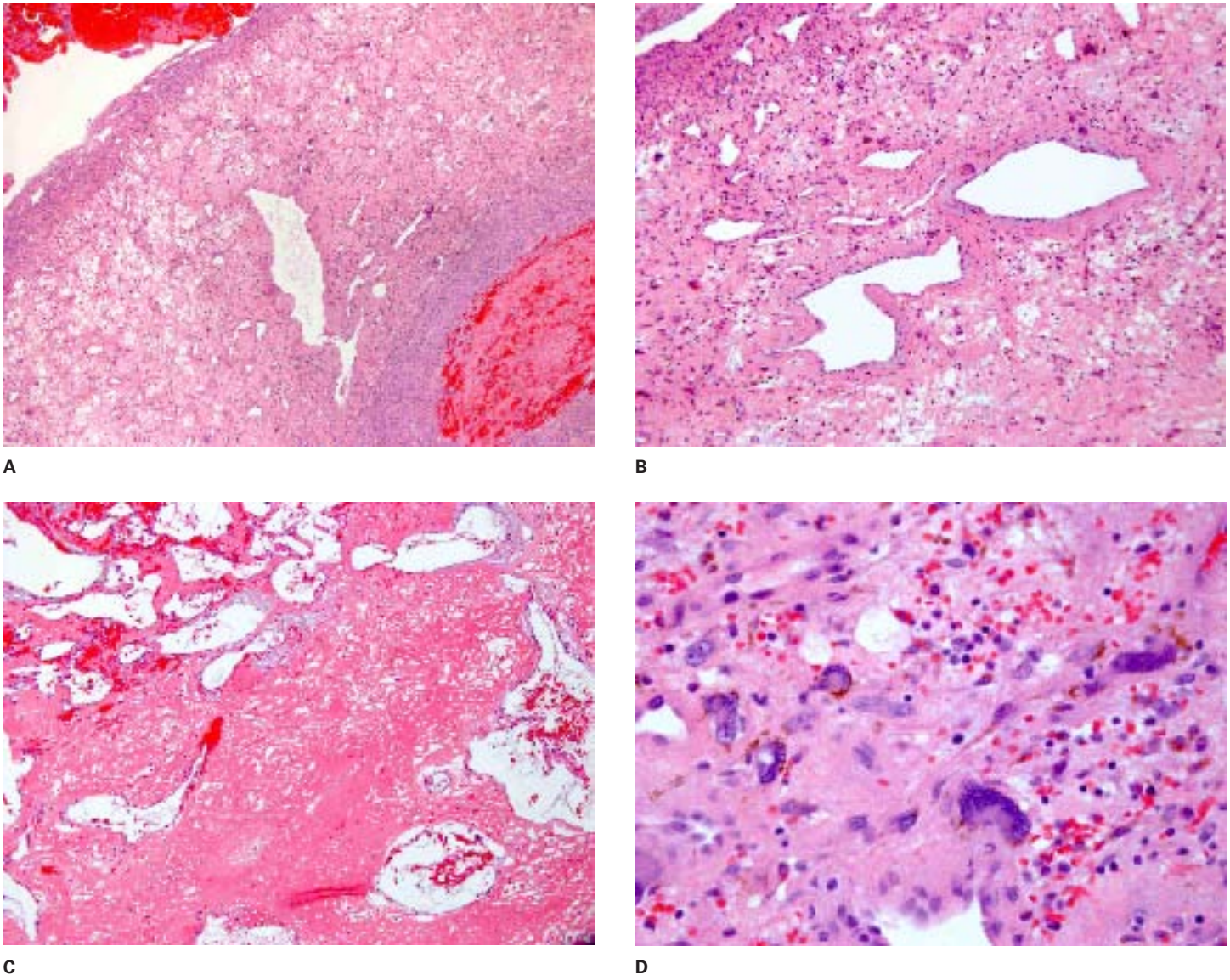

Figure 2. (A) At low power, a circumscribed tumor is seen with a sclerotic collagenized stroma, dilated vessels, and areas of hemorrhage. (B) At medium power, widely scattered spindle cells are found along with enlarged pleomorphic cells and ectatic blood vessels. (C) In other areas, a fibrinous rim encircles the ectatic vessels. (D) At high power, hemosiderin is found in spindled and pleomorphic cells.

tissue[2-17, 21]. It most frequently occurs in the lower extremity (63%), particularly in the foot/ankle (27%). Less common sites include the upper extremity (10%), chest/breast (8%), groin/perineum (8%), buttock (6%), and back (2%)[2-22]. There are also singular reports of PHAT occurring in the oral cavity and mesorectal tissue[11, 20]. The average size at diagnosis of these tumors is 5.4 cm, with values ranging from 0.3 cm to 19.7 cm[2-7, 10-13, 15-18, 21]. Grossly, all PHAT have been non-encapsulated and 14 (41%) of the 34 cases with gross details available were well-circumscribed[2, 5, 7-11, 13, 15, 17, 18,]

Imaging studies are very rarely reported in the PHAT literature and are not diagnostically specific. Lin & Crapanzano[21] presented a case of PHAT appearing similar to ours on MRI – a soft tissue mass with decreased T1 signal intensity, heterogeneously increased T2 signal intensity, and moderate enhancement with contrast. Another author described a predominately cystic appearance on MRI that similarly contained an enhancing soft tissue component[16]. Tallarigo et al[18] presented descriptions of PHAT by both mammography and ultrasound. Mammography revealed a high-density, well circumscribed mass with a marginal halo and no calcification. Ultrasound revealed a hypoechoic lesion with ill-defined margins and a non-homogeneous hyperechogenic internal structure. This internal structure was separated by hypoechoic bands suggestive of blood vessels. Based on these few cases, as well as our own, the typical appearance of PHAT by MRI seems to be that of a soft-tissue mass with decreased T1 signal, high T2 signal with scattered areas of low signal, and homogenous enhancement.

PHAT is commonly confused clinically with hematoma, Baker's cyst, desmoid, Kaposi's sarcoma, lipoma, and other malignant or benign tumors[2, 13, 14, 21]. Tissue samples are therefore necessary for accurate diagnosis, although PHAT can still microscopically be confused for other processes. Its

high degree of pleomorphism can suggest a malignant process like malignant fibrous histiocytoma (MFH) and its hyalinized vasculature can suggest neurilemoma[2]. In-depth histological evaluation and immunohistochemistry are thus typically necessary to arrive at the true diagnosis. The remarkably low degree of proliferation, implied by the lack of mitotic figures and low MIB1 counts, argues against a high-grade malignancy like MFH[2]. MIB1 values are typically below 3% for these lesions, with 8% being the highest reported[2, 3, 5, 7, 10, 12, 13, 15, 18]. Lack of a lesion capsule and universally negative S-100 protein reactivity also virtually rule out neurilemoma[2, 3, 5-7, 10-13, 15, 17, 18, 21]. From our review, CD34 reactivity was seen in 73% of cases and both Vimentin and CD99 reactivities were universally positive[2, 3, 5, 7, 10-13, 15, 17, 18, 21]. This reactivity to CD34, vimentin, and CD99 suggests that PHAT is an undifferentiated primitive mesenchymal tumor.

Although the small number of PHAT cases makes it difficult to establish consensus, the prognosis for these tumors is generally considered good due to their slow proliferation and low histologic grade. The lack of any metastases to date further supports this benign presumption[2-22]. However, the two largest studies on PHAT revealed local recurrences occurring at rates of 33-50% and at time-intervals as great as 35 years after initial excision[2, 6]. From our review of the 44 cases with follow-up information available, we found 17+ recurrences in 12 patients (27%) through an average follow-up of 64 months (median 42, range 6-420)[2, 4, 6, 9, 10, 12-16, 20]. On average, recurrences occurred at 56 months (median 47, range 3-120). Several of these patients experienced multiple recurrences and 2 patients required subsequent amputation for control. There is also one report of PHAT recurring as a myxoid sarcoma and another case of a PHAT-like lesion, differing only by increased mitotic activity, recurring as high-grade myxofibrosarcoma[6, 23]. Based on this high recurrence rate, risk of significant morbidity, and reports of possible progression to sarcoma, several authors recommend that this tumor be considered an intermediate or borderline malignancy[6, 15, 18].

We suggest these tumors be treated by wide excision instead of marginal excision whenever possible. Of cases with treatment details and follow-up information available, 10 patients (43%) out of 23 initially treated by marginal excision experienced recurrence through an average 85 months (median 50, range 13-420) of follow-up[2, 6, 10, 15]. In comparison, 0 patients out of 9 initially treated by wide excision experienced recurrence through an average 49 months (median 36, range 8-120) of follow-up[2, 4, 6, 13, 15, 16]. Adjuvant radiotherapy has sporadically been used with excision in the treatment of PHAT, with 12 cases documenting its use[2, 6, 15]. It is not known whether this has an impact on cure or recurrence rate though. Of 11 radiotherapy cases with follow-up information available, 2 patients (18%) experienced a recurrence, but it is not clear whether radiotherapy was used before or after the recurrence[2, 6, 15]. To our knowledge, chemotherapeutic agents have never been used against PHAT.

In summary, PHAT is a rare soft-tissue neoplasm with unique histologic features and unknown histogenesis. The tumors typically develop in the subcutaneous tissue of the lower extremity in middle-aged adults, but an array of other sites and ages have also been reported. Physical exam and imaging are not specific for these lesions, so microscopic and immunohistochemical analyses are required for accurate diagnosis. Although there are no cases of metastases in the literature, we suggest PHAT be treated by wide excision whenever possible to minimize the risk of recurrence, morbidity, and potential malignant progression.

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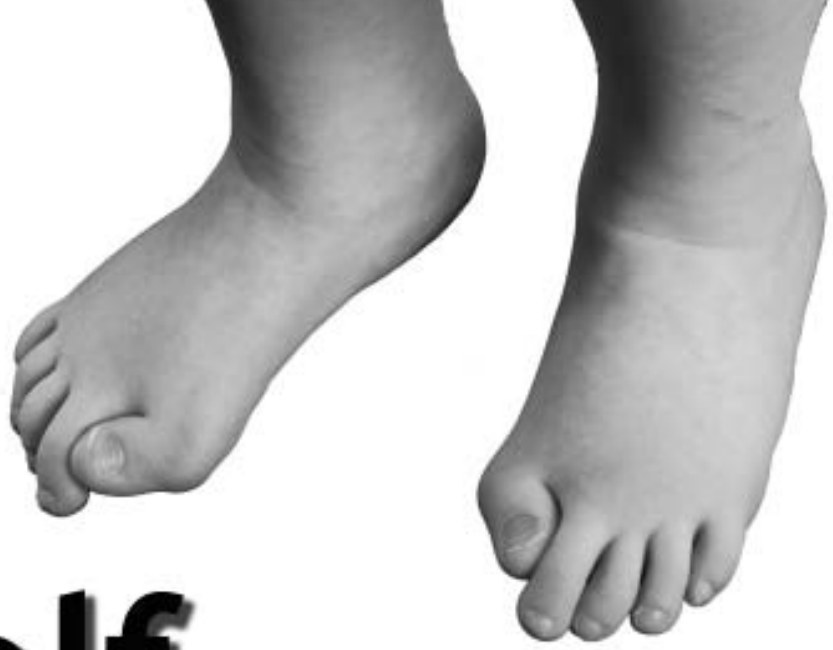

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