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Desmoid Tumors: A Review of Their Natural History, Imaging, and Treatment

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A B S T R A C T

Desmoid tumors are uncommon neoplasms that are also termed desmoid-type fibromatosis and aggressive fibromatosis. Although desmoids lack metastatic potential, they often exhibit aggressive local invasion. Desmoid tumors have a typical but nonspecific appearance on multiple imaging modalities, including computed tomography, magnetic resonance imaging, and ultrasound. Radiology plays an integral role with imaging and intervention in the management of these tumors as their location and relationship to adjacent structures determines the optimal treatment pathway. Currently, the standard of care for the management of desmoid tumors begins with a conservative observational approach, with additional interventions, such as surgery, radiation, systemic therapy, or alternative therapies used depending on the behavior of the individual desmoid tumor. Although not malignant, desmoid tumors can have serious medical and psychological implications for patients.

Introduction

Fibromatosis is a broad term that can be further divided into two specific categories: superficial fibromatosis and deep fibromatosis (Robbins, Kumar, & Cotran, 2010). The superficial fibromatoses consist of palmar, plantar, and penile variants. The palmar and penile fibromatoses are commonly called Dupuytren contracture and Peyronie disease, respectively. Conversely, deep fibromatosis is a single entity that goes by a number of names, including aggressive fibromatosis, desmoid-type fibromatosis, or simply desmoid tumor. MacFarlane (1832) first described desmoid-type fibromatosis in 1832, but the term desmoid tumor was not used until 1838 by Mueller (1838). Mueller derived this term from the Greek word *desmos*, meaning band-like, because of the tumors' tendon-like consistency (Rosen & Kimball, 1966; Skubitz, 2017). Desmoid tumors are uncommon locally aggressive tumors that lack metastatic potential. Desmoids arise from myofibroblasts and most commonly occur sporadically but can be associated with heritable genetic conditions, including familial adenomatous polyposis (FAP) syndrome (Howard & Pollock, 2016). They can occur almost anywhere in the body but have a predilection for the abdomen, either intra-abdominally or within the abdominal wall (Escobar, Munker, Thomas, Li, & Burton, 2012). Desmoids typically present as indolent soft tissue masses that demonstrate slow growth over time, but they can be painful for some patients. Because of the difficulty in achieving definitive treatment in many cases, this disease can become chronic and potentially debilitating.

Epidemiology and pathophysiology

Desmoid tumors are uncommon, comprising approximately 3% of all soft tissue tumors and only 0.03% of all neoplasms (Sakorafas, Nissotakis, & Peros, 2007). Desmoids have a female-to-male predominance of about 2:1 and usually affect patients between the ages of 15 and 60 years (Eastley, Hennig, Esler, & Ashford, 2015; Fallen, Wilson, Morlan, & Lindor, 2006). However, they most commonly occur in the young adult population ages 25 to 35 years and are usually more aggressive in these patients.

Most desmoids arise sporadically, but 5% to 15% occur in the setting of FAP (Nieuwenhuis et al., 2011). FAP is typically characterized by extensive intestinal polyposis, osteomas, fibromas, and sebaceous cysts (Smith, 1958). When desmoid tumors are also present, it is more specifically called Gardner syndrome, a

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subtype of FAP. In all patients with FAP, 7.5% to 10% will develop a desmoid tumor, putting them at a relative risk 800 times greater than the general population (Gurbuz et al., 1994; Nieuwenhuis et al., 2011). The desmoid tumors associated with FAP most commonly occur in the mesentery and can often be multifocal. These intra-abdominal desmoids can often present with more serious complications, including small bowel obstruction or bowel ischemia. Aside from FAP, other risk factors for development of desmoids include pregnancy, prior surgery, and trauma. Specifically, the most common site for pregnancy-associated desmoid tumors is the abdominal wall (Robinson, McMillan, Kendall, & Pearlman, 2012).

Pathologically, desmoids are grossly firm, rubbery, gray-white soft tissue masses that resemble fibrotic scar tissue (Braschi-Amirfarzan et al., 2016; Robbins et al., 2010). At a cellular level, these tumors appear as poorly circumscribed proliferations of monoclonal myofibroblasts that lack a capsule (Escobar et al., 2012; Skubitz, 2017). The fascicles of bland spindle cells are usually relatively low in cellularity but are set in a collagenous stroma. These cells lack the typical histologic findings of malignancy, including nuclear atypia, increased mitotic activity, and necrosis. Often, the tumor cells will infiltrate into the adjacent soft tissue, at times precluding accurate assessment of the margins at surgery, before final pathology of the resection margins. FAP-associated desmoid tumors are histologically identical to sporadic desmoids (Burke, Sobin, Shekitka, Federspiel, & Helwig, 1990). The composition of desmoid tumors is usually heterogeneous, with the relative amounts of the cellular, fibrotic, and collagenous portions being highly variable, both within a single tumor and between separate tumors.

Genetically, there are multiple pathways that probably play a role in the pathogenesis of desmoid tumors. However, the Wnt (beta-catenin) signaling pathway plays a central role in the cascade of genetic events that usually lead to desmoid tumor formation (Amary et al., 2007). This was first hinted at by the early observation that desmoids had a strong association with FAP, which is caused by an underlying mutation in the *adenomatous polyposis coli* gene that regulates beta-catenin protein degradation (Giardiello et al., 1997; Gurbuz et al., 1994). One study reported that a mutation in the beta-catenin gene was present in 88% of sporadic cases of desmoid tumors (Le Guellec et al., 2012). Beta-catenin protein levels are abnormally high in desmoid tumor cells because of uncontrolled activation of the beta-catenin gene or malfunction of the adenomatous polyposis coli protein degradation complex (Minde, Anvarian, Rudiger, & Maurice, 2011). These high beta-catenin protein levels result in increased translocation of beta-catenin to the nucleus, resulting in a prosurvival signal and the proliferation that can result in eventual tumor formation.

Imaging characteristics

Although desmoid tumors can have a variety of appearances on ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI), cross-sectional imaging plays a vital role in determining the optimal course of treatment for a patient (Braschi-Amirfarzan et al., 2016). In general, CT and MRI are more commonly used to evaluate desmoids, given their greater ability to visualize deeper structures when compared with US. CT and MRI can also be more useful for evaluating the relation of the desmoids to adjacent anatomic structures. For all modalities, the appearance of these tumors will vary based on the tissue composition of the desmoid, which can have varying degrees of collagen, fibrotic, vascular, and cellular components (Francis et al., 1986; Mantello, Haller, & Marquis, 1989; Sundaram, McGuire, & Schajowicz, 1987).

Computed Tomography

Desmoid tumors typically appear as a well-circumscribed soft tissue mass (Brant & Helms, 2007; Braschi-Amirfarzan et al., 2016; Casillas, Sais, Greve, Iparraguirre, & Morillo, 1991; Sheth et al., 2016). However, depending on the degree of local invasion and location of the tumor, the margins can be less well defined. This is particularly true for desmoids occurring at sites outside the abdomen or for more infiltrative abdominal tumors. Desmoids occurring within the abdominal mesentery will often have spiculations that extend into the neighboring mesenteric fat (Sinha et al., 2012). This is often described as a whorled appearance. They can have a homogenous or a more heterogeneous appearance. The overall attenuation of desmoid tumors can vary, but most are isodense to slightly hyperdense when compared with skeletal muscle (Murphey et al., 2009). The amount of enhancement that desmoids demonstrate is also variable, but usually they demonstrate a mild to moderate amount of enhancement with iodinated intravenous contrast. Larger lesions may demonstrate areas of lower attenuation, corresponding to regions of necrotic tumor (Sheth et al., 2016). Calcifications are very uncommon but can occasionally be present (Rhim et al., 2013). Figure 1 demonstrates the typical CT appearance of a desmoid.

Desmoid tumors that are associated with FAP, or more specifically the Gardner syndrome variant of FAP, have identical characteristics on CT imaging as the tumors that are not associated with a genetic condition (Kawashima et al., 1994). Kawashima et al. observed that there were no CT characteristics, including attenuation, margins, or contrast enhancement characteristics, which would allow reliable differentiation between desmoids that were or were not associated with FAP. However, desmoid tumors associated with FAP are more likely to occur in the mesentery or in the abdominal wall, whereas sporadic desmoids have a predilection for the pelvis, retroperitoneum, and other extra-abdominal sites.

Magnetic Resonance Imaging

Compared with CT, MRI provides greater characterization and resolution of the soft tissue components of a desmoid tumor (Lee, Thomas, Phillips, Fisher, & Moskovic, 2006). Most commonly, desmoids will appear as heterogeneous soft tissue masses with isointense to hyperintense T2 signal and isointense T1 signal, when compared with skeletal muscle, as demonstrated in Figure 2 (Braschi-Amirfarzan et al., 2016; Dinauer, Brixey, Moncur, Fanburg-Smith, & Murphey, 2007). The heterogeneous signal intensity across all MRI sequences is likely reflective of the variable composition of the tumor and should correspond to the separate collagenous, fibrotic, and cellular components. Most desmoid tumors undergo moderate to marked enhancement on contrast-enhanced sequences, although areas of nonenhancement can be present.

A large majority of lesions will demonstrate hypointense bands across all sequences that represent dense collections of collagen bundles, sometimes known as the band sign. These bands do not enhance after gadolinium-based contrast administration given their acellular nature. However, greater enhancement in a portion of the tumor is usually indicative of a more cellular composition (Robbin, Murphey, Temple, Kransdorf, & Choi, 2001).

Over time, the relative histologic composition of desmoid tumors will undergo a general trend of increasing collagen and decreasing cellularity, which can be identified on MRI (McCarville et al., 2007; Vandevenne et al., 1997).