Referral patterns, prognostic models and treatment in soft tissue sarcomas

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Chapter 10

Desmoid type fibromatosis

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Desmoid type fibromatosis (DF) is part of a group of disorders characterized by excessive proliferation of spindle-shaped mesenchymal cells, e.g. Dupuytren's and Peyronie's diseases [1]. Deep DF is even more rare than superficial DF. Its hallmark is infiltrative growth without the potential to metastasize and the inability to dedifferentiate into a high grade malignancy in case of recurrence. Therefore DF is considered to be an intermediate tumor according to the World Health Organization. [1]

Pediatric and adult DF have an equal incidence between genders, but the peak incidence is at 30 years of age and is more common in women. The overall incidence of DF is low and only makes up for 0.03% of all types of cancer. [2] There are several distinctive patient groups in which the prevalence of DF is transcending the prevalence in the normal population; pregnant women, post surgery patients, and patients with Gardner disease (familial colorectal polyposis) or familial adenomatous polyposis (FAP). The latter genetic syndromes known to be autosomal dominantly inherited with mutations located in the adenomatous polyposis coli (APC) gene on chromosome 5q21–22. [3-5] APC in turn helps to regulate the β-catenin, which has a key role in wound healing and fibroproliferative disorders. [6] Patients with FAP have a nearly 100% chance of developing a colorectal malignancy, therefore, most patients are offered a preventive proctocolectomy. As a consequence, more patients survive and the incidence of DF has increased within this group. The prevalence of DF in this group is 7-12%, with a lifetime risk of about 20%. [7] The other associated conditions as pregnancy and trauma suggest that there are also endocrine and physical factors underlying the pathogenesis of DF.

Because DF is a heterogeneous tumor with a variety of locations, it has an unpredictable clinical course. For clinical utility DF is usually classified according to anatomical location - intra-abdominal, abdominal wall and extra abdominal. The clinical presentation is like other soft tissue sarcomas usually with a painless mass that grows insidiously. Sometimes they cause neurological symptoms and, when located at the extremities, they can cause decreased functional mobility. Intra-abdominal fibromatosis is often asymptomatic, but can lead to gastro intestinal bleeding or acute abdomen secondary to bowel perforation.

Differential diagnosis of DF is: scar tissue, proliferative myositis, nodular fasciitis, other types of fibromatosis and other types of soft tissue sarcomas. The preferred imaging is magnetic resonance imaging (MRI), except for intra abdominal DF, in which computomography (CT) scan is more valuable. But final diagnosis is based on histology.

The treatment for DF has evolved over time and an aggressive first approach is now debated. In the beginning of the 21th century imatinib was reported as an active agent against DF. [8] Later also pazopanib [9] and sorafenib [10] have been found active against AF. However, none of these targeted therapies are standardized first line therapy. And ongoing studies are trying to validate earlier findings. [11,12]

Another type of treatment is antihormonal treatment. The rationale behind the use of antihormonal therapy, mainly tamoxifen, is based on observations of the natural history of the disease. Higher incidences of desmoids during and after pregnancy and reports of spontaneous tumor regression after menopause, form the basis for antihormonal therapy. However, although several studies have shown that almost all DF express nuclear estrogen receptor-β, only a small subset of patients respond to antihormonal therapy.

In 2003, a systematic review about the pharmalogical treatment was published (anti estrogen therapy n = 37, other hormonal treatment n = 31, anti inflammatory therapy n = 29, interferon therapy n = 9, chemotherapy n = 148) showing that systemic treatment is affective against DF.[4] The rational behind an endocrine approach is logic regarding the role of cyclooxygenase-2 (COX-2), fibroblast derived growth factor and the receptor for hyaluronan-mediated motility (Rham) in the pathogenesis of DF. [6] Yet, the included studies that were analyzing the effects of non cytotoxic treatment were consisting for a large part out of case reports.

None of the abovementioned systematic or targeted therapy is standard, and as an alternative to invasive treatment with surgery a new approach towards DF has been investigated; a wait-and-see policy. The next chapter reviewed literature about standard surgery, radiotherapy and the new conservative approach.

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