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Review

Pediatric aggressive fibromatosis of the head and neck: a 20-year retrospective review

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Abstract Aggressive fibromatosis in children is a rare, benign condition that is locally infiltrative and destructive. It often presents as a rapidly growing, painless lump in the head and neck region. To date, only small series and case reports have been reported, and the management of the condition remains unclear. Recently, nuclear β-catenin expression has been suggested as a tumor-specific marker for aggressive fibromatosis (desmoid).

Aim: The aims of the study were to review our experience of the presentation, management, and treatment outcome of pediatric aggressive fibromatosis in the head and neck and to identify the presence of the desmoid tumor marker β-catenin within this population.

Method: The study was conducted as a retrospective case review of children diagnosed with aggressive fibromatosis in the head and neck for a period of 20 years and a review of the literature. Pathologic review of the original tumor specimens was undertaken for evidence of positive tumor margins and presence of nuclear β-catenin expression.

Results: A total of 10 patients (6 males, 4 females) were identified. The age at presentation ranged from 12 months to 14 years. In total, 8 patients were treated with surgery alone. This included 7 patients with extension of the tumor to the resection margin; all had good long-term outcomes with no disease progression. Two patients received chemoradiotherapy, one as primary treatment, and the other as adjuvant treatment after gross incomplete resection. Both resulted in poor outcomes requiring further treatments.Within our series of pediatric fibromatosis, only 4 cases (40%) had positive results for any nuclear β-catenin expression, and 6 (60%) of 10 patients had negative results for β-catenin.

Conclusion: Our experience is that total gross resection and preservation of form and function is of higher priority than achieving a negative resection margin. Pediatric fibromatosis though aggressive is still a benign condition, and careful thought should be taken before considering adjuvant chemoradiotherapy. Nuclear β-catenin expression should not be considered a specific tumor marker for pediatric aggressive fibromatosis of the head and neck. Pediatric aggressive fibromatosis in this region may be a distinct subtype of desmoid tumor from its adult form.

Aggressive fibromatosis is a benign tumor arising from connective tissue, the fascial sheaths, and musculoaponeurotic structures of muscle [1,2]. The tumor consists of dense masses of fibroblasts with a poorly defined margin

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and tends to interdigitate with muscle fibers making complete surgical excision difficult. Although aggressive fibromatosis is a nonmetastasizing tumor, it has significant potential for local invasion and recurrence [3,4] and may be fatal because of its size and location [5].

The overall incidence has been reported as 2 to 5 cases per 1 million per year [1,6,7]. Head and neck lesions represent about 12% to 15% of aggressive fibromatosis [8,9] where the tumors appear to infiltrate more widely and rapidly [10]. The incidence of childhood aggressive fibromatosis peaks at about 8 years of age [11] with a range of birth to 19 years. Other series have suggested that several age peaks occur throughout life, with a bimodal age of incidence in childhood and adolescence; an early peak around 4.5 years (0-10 years) and a second peak in 29s (15-35 years) [6].

Aggressive fibromatosis presents as a rapidly growing painless lump in the head and neck region in children. It is often fixed to underlying structures such as muscle and bone. The tumor may cause secondary symptoms such as trismus, airway obstruction, dysphagia, and proptosis depending on its site. Pain is rarely a symptom though can occur as the tumor grows. The tumor may infiltrate around nerves causing pain and dysfunction [12].

The etiology of aggressive fibromatosis is unknown. However, a genetic predisposition [13,14], association with familiar adenomatous polyposis and Gardner's syndrome [6], trauma [15-17] including surgical trauma [18,19], and endocrine factors [20] have all been implicated. Interestingly, the progression of the tumor appears to be hormonally based with regression occurring in females in menarche and menopause [6,21].

Aggressive fibromatosis may involve a deregulation of connective tissue growth. It has been suggested that the process is neoplastic rather than reactive based on X-chromosome analysis and is a monoclonal disorder [22]. Abnormal expression of c-sis and platelet-derived growth factor has been identified, which can act as a mitogen for fibrocytes [23]. It has been suggested that deep fibromatosis have somatic β-catenin or adenomatous polyposis coli (APC) gene mutations [24] leading to increased intranuclear accumulation of β-catenin that may explain the proliferative advantage of these cells [25]. Conversely, the tumor suppressor gene Rb1 has been shown to have decreased expression and may also play a role in tumor progression [26].

The clinical behavior of aggressive fibromatosis is very unpredictable, and the natural history remains unknown. There are documented cases of spontaneous regression without treatment [2,4,27,28], but because of the aggressive nature of the tumor, many clinicians are reluctant to adopt an expectant policy [11,17]. It is accepted that the most successful treatment, defined as least chance of recurrence, is primary surgical excision with a clear margin [17]. Nonsurgical treatment with radiotherapy, chemotherapy, hormonal therapy, and nonsteroidal antiinflammatory drugs (NSAIDs) are adjuvant treatments for residual tumor or recurrence. There is little evidence to support the need for aggressive adjuvant treatment of aggressive fibromatosis [11]. The side effects of treatments are well documented, and particular concern may be raised in the potential iatrogenic morbidity or mortality in a child, who may survive the benign disease for many more years than their adult counterpart. Because of the rarity of the disease, the management of the condition remains unclear and general recommendations for clinical management of residual or recurrent disease are lacking.

1. Method

A retrospective chart review was performed to identify all patients with a diagnosis of aggressive fibromatosis of the head and neck region treated at The Hospital for Sick Children, Toronto, Canada, from to January 1, 1987, to December 31, 2006.

Patients were identified from an institutional pathology database. A senior pathologist reviewed the original histologic and tumor specimens to confirm the diagnosis of aggressive fibromatosis. The original specimens were reexamined for positivity of the surgical resection margin.

Specimens were stained for β-catenin to determine its usefulness as a specific tumor marker for aggressive fibromatosis [24,29,30]. A representative formalin-fixed, paraffin-embedded tumor tissue section form each of the patients was subjected to immunohistochemical staining with commercially available biotinylated mouse monoclonal antibody to β-catenin (1/200 dilution; BD Transduction Laboratories, Lexington, Ky). Sections were deparaffinized and subjected to antigen retrieval procedures. Immunostaining was performed with an automated stainer (Ventanna, Tucson, Ariz). Antibody reaction was detected by the biotin-avidin/immunoperoxidase amplification procedures with the appropriate reagents and methods recommended and supplied by the staining equipment supplier (Ventanna, Tucson, Ariz). Nuclear staining/expression of β-catenin was assessed by microscopy and recorded as percent positive-stained nuclei in the areas within the tissue that showed the highest staining intensities.

The medical records of identified cases were closely reviewed to follow the progress and outcomes of each individual. The age, mode, and duration of presentation, site, and size of the lesion were all noted. Initial management (surgical or nonsurgical) was noted, as was any subsequent management if any, for residual or recurrent disease. The disease progression was monitored both clinically and radiologically.

A literature review was performed using Medline. "Aggressive fibromatosis" and "desmoid tumors" were the keywords used for the search. The review included pediatric case series and series that included both adults and children.