

DESMOID TUMORS IN FAMILIAL ADENOMATOUS POLYPOSIS

- Definition
 - Desmoids are benign mesenchymal tumors
 - Characterized by mature, highly differentiated fibroblasts and myofibroblasts with abundant collagen matrix
- Epidemiology
 - 8 to 17 percent of patients with FAP will develop desmoids
 - Rate of almost 1000 times that in the general population.
 - Desmoid locations in patients with FAP
 - Up to 80 percent of desmoids in the mesentery
 - 20 to 30 percent are in the abdominal wall or extremities
 - Second leading cause of death in patients with FAP
- Appearance
 - Early desmoids (desmoid precursor lesion or desmoid reaction) appear as flat, white plaques
 - Larger lesions tend to form non-encapsulated, lobulated masses
- Clinical Presentation
 - Ranges from asymptomatic plaques or masses discovered incidentally on imaging or during prophylactic surgery to many non-specific symptoms
 - Symptomatic desmoids may cause
 - abdominal pain
 - bowel obstruction or ischemia
 - deep venous thrombosis from venous compression
 - sensory and motor deficits from nerve compression
 - ureteric obstruction
 - sepsis from enteric fistula
 - upper gastrointestinal hemorrhage
 - pouch failure
- Risk Factors
 - Surgical trauma
 - Interval between surgery and the diagnosis usually less than 5 years, but may extend well beyond this interval
 - Estrogens
 - Regression has been reported following natural or surgical menopause
 - Genotype-phenotype correlations
 - Mutations towards the 3' end of the APC gene have a higher incidence

- Preoperative Diagnosis
 - Computed tomography (CT)
 - Although CT findings correlate poorly with symptoms, poor prognostic features include size greater than 10 centimeters, multiple lesions, bilateral hydronephrosis, and extensive small bowel involvement
 - Magnetic resonance imaging (MRI)
 - Most useful for extremity and abdominal wall desmoids, but can also be used to evaluate intra-abdominal lesions
 - Radionuclide scans
 - May differentiate scar from recurrent desmoid tumor post-resection

- Non-Surgical Treatment
 - Non-cytotoxic Agents
 - Non-steroidal anti-inflammatory drugs (NSAIDs)
 - Sulindac, indomethacin, and celecoxib are considered first line therapy
 - ❖ Response rates of up to 57%
 - ❖ Most patients respond to NSAIDs within 3 months, but delayed response over 24 months rarely occur
 - Antiestrogens
 - Tamoxifen, raloxifene, and toremifene
 - ❖ Reported to produce response rates comparable to those of NSAIDs
 - ❖ Combination regimens containing both NSAIDs and tamoxifen may result in improved response rates
 - Modifiers of cyclic AMP metabolism (ascorbic acid, theophylline, testolactone, and chlorothiazide), corticosteroids, colchicine, interferon-alpha, and warfarin)
 - Cytotoxic Agents
 - Anti-sarcoma agents
 - Doxorubicin with dacarbazine or cyclophosphamide and vincristine
 - ❖ Response rates range from 17 to 100%, with a median of 50%
 - ❖ Severe early and late toxicity are major concerns
 - ❖ Use limited to extensive life-threatening disease resistant to other therapy or when alternative approaches are contraindicated.
 - Regional chemotherapy with isolated limb perfusion
 - Radiotherapy in doses of 36 to 65 Gy
 - ❖ Local control following surgical resection (80%) and as primary therapy for unresectable tumors (81%)
 - Pre-clinical research with gene transfer

- Surgical Treatment
 - Reserved for select cases of symptomatic disease
 - Infiltrating growth pattern often makes complete resection impossible without extensive small bowel resection
 - Local control rates following resection
 - Positive margins: 41%
 - Negative margins: 72%
 - Postoperative radiation therapy may improve local control to as high as 94% when negative pathologic margins are achieved
 - Bypass procedures may be required to treat select cases of non-resolving bowel obstruction.
 - Major complications have been reported in up to 50% of patients with intra-abdominal desmoids treated with surgical resection
 - Extensive resection may lead to short bowel syndrome
 - High recurrence rate (up to 85% in some series)
 - Abdominal wall desmoids may be treated with surgical resection with margins of 2 centimeters
 - Reconstruction with prosthetic mesh or a myocutaneous flap may be required
 - Recurrence rates for extra-abdominal desmoids treated with surgical resection
 - Primary tumors: 76%
 - Recurrent tumors: 59%

- Treatment Algorithm
 - Begin with NSAIDs such as sulindac (150 milligrams twice per day)
 - If the tumor does not respond or progresses following 6 or more months of therapy, an anti-estrogen such as tamoxifen (30 milligrams per day) may be added
 - If the tumor responds, therapy can be gradually withdrawn over 6 months
 - Cytotoxic chemotherapy extensive or life-threatening tumors that do not respond to non-cytotoxic pharmacologic regimens and are not amenable to surgery
 - Surgery should be reserved for localized desmoids of the limbs or abdominal wall or intra-abdominal desmoids causing symptoms or complications.

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