Micosis Fungoide

- **Revisión tomada de Dynamed a traves del sitio de soporte EBSCO Servicio de la Biblioteca virtual de la UCV Sicht**

Treatment overview:

- nonspecific treatment - emollients, topical steroids (discontine for several weeks prior to skin biopsy), localized orthovoltage x-ray therapy
- standard treatments for cutaneous T-cell lymphoma include topical corticosteroids, topical mechlorethamine (Mustargen), topical carmustine (BiCNU), psoralen with ultraviolet A (PUVA), electron beam radiotherapy, systemic chemotherapy in selected cases (The Medical Letter 2000 Apr 3;42(1075):31)

Medications:

- topical chemotherapy for disease limited to skin
    - topical nitrogen mustard (mechlorethamine) or carmustine (BCNU) after definitive diagnosis of MF
    - nitrogen mustard 10-20 mg%
        - continue until skin clears (often 6-12 months) then maintenance period of 6-24 months
        - 50-60% complete response rate for limited plaque disease, 30-60% complete response rate for tumorous disease
        - most common complication is contact hypersensitivity or irritant reaction, potential hazard of cutaneous cancers
        - nitrogen mustard effective for T1 or T2 disease; retrospective study of 203 patients with MF stages I-III treated initially with topical nitrogen mustard, 83% overall response rate, 50% complete response rate, median time to achieve complete response 12 months (10 months for T1, 19 months for T2), median time to relapse 12 months (Arch Dermatol 2003 Feb;139(2):165 in JAMA 2003 May 28;289(20):2630)
    - carmustine
        - a nitrosurea compound
        - in study of 143 patients, 86% complete response for T1, 48% complete response for T2, median time to complete response 11.5 weeks
        - common side effect of erythema, 10% hematologic depression
- etretinate plus PUVA may increase efficacy with decreased toxicity than single therapy
- 13-cis-retinoic acid and etretinate have been effective for selected cases
- Ontak (fusion protein of fragment of diphtheria toxin genetically fused to interleukin-2) FDA approved for persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express CD25 component of interleukin-2 receptor (Monthly Prescribing Reference 1999 Mar;A-19)

    - loss of visual acuity, usually with loss of color vision and usually persistent, reported with denileukin diftitox (Ontak) (FDA MedWatch 2006 Mar 15)
- bexarotene (Targretin) FDA approved for cutaneous manifestations of cutaneous T-cell lymphoma refractory to at least 1 prior systemic therapy; contraindicated if any risk for pancreatitis or pregnancy (Monthly Prescribing Reference 2000 Feb;A-16)
- bexarotene (Targretin) effective in some patients for early and advanced refractory cutaneous T-cell lymphoma, but use may be limited by toxicity and cost, no comparison data with other treatments; 45-67% response rates (4-17% complete response rates) in open-label trials; see literature for drug interactions; common adverse effects (mostly dose-dependent) include dyslipidemia, central hypothyroidism, headache, asthenia, leukopenia, anemia, infectin, rash, photosensitivity; available in 75 mg capsules, recommended dose 300 mg/m2 PO once daily with meal, increase to 400 mg/m2/day if no response in 8 weeks, optimal duration of treatment unknown, average cost for 30 days' treatment $2,152.50 (The Medical Letter 2000 Apr 3;42(1075):31)
- vorinostat (Zolinza)
    - FDA approved for persistent or recurrent cutaneous T-cell lymphoma; 30% response rate reported in 2 clinical trials with 107 patients, responses lasted mean 168 days (FDA Press Release 2006 Oct 6)
    - 400 mg PO once daily, swallowed whole; may reduce to 300 mg once daily or 300 mg once daily 5 days/week if not tolerated; not recommended in children < 18 years old (Monthly Prescribing Reference 2006 Dec:A-14)
    - vorinostat (Zolinza) costs $8,546.40 for 30 days, long-term safety unknown but 4.7% rate of pulmonary embolism in clinical trials (4 of 86 patients) (The Medical Letter 2007 Mar 12;49(1256):23)
- drugs of choice according to The Medical Letter (for cutaneous T cell lymphoma)
    - regimens of choice
        - topical mechlorethamine or carmustine
        - PUVA (psoralen + ultraviolet A)
        - topical steroids - clobetasol, diflorasone, halobetasol, betamethasone
        - systemic chemotherapy - methotrexate
    - alternatives
        - bexarotene
        - denileukin diftitox
        - isotretinoin
        - pentostatin
        - fludarabine
        - cladribine
        - photophoresis (extra-corporeal photochemotherapy)
    - see Toxicities of chemotherapeutic agents
    - Reference - Treatment Guidelines from The Medical Letter 2003 Mar;1(7):41
- investigational therapies
    - high doses of interferon alpha, 50% partial response rate, combination with PUVA

    - anti-T cell monoclonal antibodies

Other management:

- UVB irradiation helpful for many patients with early patch or plaque disease
- PUVA may be given for temporary improvement of pre-MF plaques that are very symptomatic
- for disease limited to skin (after definitive diagnosis of MF made) - electron-beam radiation therapy (EBRT), spot orthovoltage photon irradiation, psoralen plus long wave ultraviolet A (PUVA) irradiation
- radiation therapy
    - orthovoltage (low energy) - modest doses (15-20 Gy in 1-2 weeks) may be adequate for long-term local control
    - electrons - depth of penetration can be controlled, large field treatment with linear accelerators, technique developed for treating entire skin surface with treatments 4 days/week for 8-10 weeks, nearly 100% response rates
    - complications - skin erythema and desquamation during therapy, epilation (hair regrowth usually occurs), inability to sweat (may persist 6-12 months), skin dryness, telangiectasias, secondary skin cancers
- PUVA - 8-methoxypsoralen (8-MOP) followed by UVA irradiation 2-3 times/week during clearing phase (3-6 months or more) then taper to maintenance regimen every 1-3 weeks; major acute side effect - phototoxicity, major long-term side effect - increased risk of squamous cell carcinoma; remission prolonged by maintenance but relapses still occur
- guidelines on eye protection for PUVA patients 1999 from British Association of Dermatologists
- extracorporeal photophoresis
    - oral 8-MOP, withdraw blood 2 hours later, return RBCs, reinfuse WBCs following exposrue to long-wave UVA
    - 27 of 37 patients with otherwise resistant CTCL responded

General references used:

- CA Cancer J Clin 1993 Mar-Apr;43(2):93 PDF

Reviews:

- review of cutaneous T-cell lymphoma can be found in Am Fam Physician 1999 May 15;59(10):2809

Guidelines:

- joint British Association of Dermatologists and UK Cutaneous Lymphoma Group guidelines for management of primary cutaneous T-cell lymphomas can be found in Br J Dermatol 2003;149:1095 PDF
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