CONJUNCTIVOCORNEAL INTRAEPITHELIAL NEOPLASIA (CIN)

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Introduction:

Conjunctivocorneal intraepitheial neoplasia replaces such previously used terms as Bowen's disease, ocular surface intraepithelial neoplasia, intrepithelioma, tyloma,keratosis or callosities. Most primary epithelial carcinomas are identical to those of the cervix from which this terminology is derived.

Case History:

We report a case of a 50 year old married lady, a farmer by occupation, residing in the interior of Maharashtra, who presented with progressively increasing paralimbal swelling in the right eye, since seven months. There was no history suggestive of an inflammatory or infective focus or of systemic malignancy elsewhere in the body.

Her visual acuity was hand movements in the right eye, with good projection of light. An elevated well defined, scaly, crusty, limbal growth, with a gelatinous surface was seen encircling the cornea, with conjunctival leucoplakia and vascularization.The anterior and posterior segment examined radiologically was normal.The extraocular movements were full. The left eye was entirely normal and there was no evidence of lymphadenopathy. Medical and gynecological examination clinically and radiologically, revealed no evidence of septic focus or internal malignanncy. The erythrocyte sedimentation rate was 30 mm at the end of one hour. The complete hemogram, bleeding profile,liver and renal profiles were normal and HIV and VDRL were negative.

Excisional biopsy of the lesion was performed for therapeputic amd diagnostic purposes. Topical ocular anesthetic was instilled and the conjunctiva under and around the lesion was elevated with the subconjunctival injection of 2 % lidocaine with epinephrine.This ruled out the possibility of an infiltrating squamous cell carcinoma. Multiple conjunctival cautery applications 1.5 to 2.0 mm from the suspected tumour margin were used to outline the area to be excised. An incision was then made through these marks down to bare sclera. The conjunctival and episcleral tissues were then surgically dissected to the limbus. Multiple applications of local anesthetic were used to soften the corneal epithelium. Using a 15 No. bard Parker blade, 1 mm of normal epithelium and the involved corneal epithelium were removed by simply "bulldozing" the epithelium to the limbus. A 4 mm liquid nitrogen probe tip was used to freeze the dissected area. The probe was completely frozen before ocular application and then applied for one second, causing a white circular imprint of the probe tip on the eye. Multiple overlapping imprints were done to cover the entire surgical limbus twice. A topical antibiotic-corticosteroid preparation was instilled three times daily for three days.

The tissue was fixed in 10% neutral buffered formalin and subjected to histopathological examination. The study revealed hyperkeratosis, parakeratosis,and dyskeratosis. The entire thickness of the epithelium revealed disorderly cellular atypia showing marked pleomorphism, nuclear cytoplasmic dissociation, hyperchromatic nuclei,and increased mitotic figures. The most common cellular type was the spindle cell - an atypical keratinocyte. The epithelial basement membrane was intact with no evidence of micrometastasis.

The diagnosis of conjunctivocorneal intraepithelial neoplasia was established.

Differential diagnosis:

The different stages of ocular surface intraepithelial neoplasia are difficult to distinguish clinically with a accuracy of diagnosis by experienced clinicians of approximately 40%. The differential diagnoses are:

1) Malignant Melanoma.
2) Papilloma.
3) Pterygium
4) Pinguecula.
5) Amelanotic benign nevi.
6) Pseudoepitheliomatous hyperplasia (PEH)

This entity is associated with diseases such as:

1) Bowen's disease of the skin.
2) Chronic lymphocytic leukemia
3) Non Hodgkin's lymphoma
4) Multiple basal cell carcinoma/ squamous cell

carcinoma.
5) Xeroderma Pigmentosa
6) HIV: squamous cell carcinoma is the third most commonly described malignancy associated with HIV - especially involving the mucosa of the oral cavity and anus.

Discussion:
Conjunctivocorneal intraepithelial neoplasia has a distinctive clinical course. It is predominantly a disease of the sixth and seventh decade. The lesions are almost always unilateral and they are primarily located at the limbus. The predisposing factors are ultraviolet light, exposure to petroleum products, heavy cigarette smoking, light hair, ocular pigmentation and soft contact lens wear.
The possible etiologies are:
1) Limbal transition zone/stem cell abnormality
2) Ultraviolet damage
3) HPV (type 16) infection.

It is believed that benign lesions can gradually transform into more malignant ones over a few years. The spectrum of degree of malignancy is
1) Benign
2) Dysplasia/ premalignant depending on the thickness occupied by the atypical cells as:
i. Mild (a third thickness is occupied by the atypical cells)
ii. Moderate (three quarters thickness is occupied by the atypical cells)
iii.Severe (nearly full thickness is occupied by atypical cells)
3) Carcinoma in situ/ locally malignant as above with loss of the normal surface layer.
4) Invasive squamous cell carcinoma: as above with breach in the basement membrane of the basal epithelial layer and invasion of the substantia propria.

Treatment:
All lesions resulting from CIN are treated because at least 5 % harbour an invasive squamous cell carcinoma. Complete excisional biopsy with supplemental cryotherapy is the only treatment required.
If neglected carcinomatous CIN may eventually invade the subepithelial tissues requiring lamellar keratectomy and sclerectomy. Intraocular extension is treated with iridocyclectomy or orbital exenteration. Involvement of the trabecular meshwork provides the tumour access to the sytemic circulation. If the individual is a poor surgical candidate, immunotherapy and chemotherapy is an effective alternative treatment modality.
Complications include intraocular invasion though limbal perforating vessels or Schlemm's canal, affecting structures like the anterior chamber, trabecular meshwork, uvea and suprachoroidal space, associated with complications like inflammation, iritis, glaucoma, retinal detachment, scleral thinning with globe rupture. Metastasis is usually seen with lesions which are more than 2 square cm. It may be regional or distant. The sites of metastasis are the preauricular, submandibular and cervical lymph nodes and the parotid gland, lungs and bone.

The patient was evaluated periodically. No recurrence was noted. The first two years postoperatively are however critical for recurrence since the lesion involved more than two thirds of the limbus. Carcinoma of the ocular surface is generally regarded as a low grade malignancy with a recurrence rate of 30%. The other risk factors for recurrence being irritation as a presenting symptom, corneal location, inadequacy of excisional margins and invasive CIN. Interstingly local invasion is related to tumour related mortality rather than development of regional metastases. Prevention of this disease through the use of UV protective devices such as sunglasses and hats has been emphasized.
The use of 193 nm Argon Fluoride excimer laser has recently been reported for recurrent CINS. The photoablation achieved with this technique is sharply defined and it is simpler and safer. The adequacy of the excisional margins however are impossible to determine, and also no histopathological examination is possible on the ablated tissue.

Conclusion:
CIN poses a diagnostic challenge met with histopathological evaluation, meticulous excisional biopsy, supplemental cryotherapy and close follow

The lives of great men all remind us,
We can make our lives sublime;
And departing leave behind us,
Footprints on the sands of time.

HW Longfellow