Dermatofibroma protuberans: Report of a case

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Dermatofibroma protuberans is a cutaneous neoplasm that tends to recur locally after excision. The case reported here illustrates typical features of history, clinical characteristics, and histologic appearance. The local aggressiveness of the neoplasm and the lack of effectiveness of radiation makes wide local excision mandatory.

Dermatofibroma protuberans is an uncommon tumor with characteristic clinical features and a tendency for local recurrences after surgical excision. It is typically a cutaneous neoplasm that looks like an infected keloid. Unless the physician suspects the nature of the tumor, it may be misdiagnosed and inadequately excised.¹

Report of case

A 29-year-old black man was seen on an outpatient basis on October 1986 with a primary complaint of excessive burning of the right eye. The patient was evaluated and diagnosed as having Bell's palsy. Further examination revealed a 4 × 6 hyperemic growth in the abdominal region.

The patient's past medical history was essentially unremarkable. He had no known allergies, and was taking no medications. The patient stated that the growth had been present for 1 month. He denied previous abdominal trauma. His job, in a defense plant, required exposure to trichloroethene and alcohol.

The patient was treated on a trial basis, being placed on a regimen of amoxicillin, 250 mg. four times a day for 2 weeks, because of the possibility of an abscess formation in this region. The growth resembled an infected keloid. He had also been on prednisone, 5 mg. twice daily, for Bell's palsy, which was stopped prior to hospitalization.

The initial surgical treatment consisted of a biopsy. The specimen revealed histologic findings consistent with those of dermatofibroma protuberans, and surgical excision was recommended.

The patient was subsequently admitted to University General Hospital and prepared for surgery the following

day. At the time of admission, the oral temperature was 97.6 F. The pulse rate, respiratory rate, and blood pressure were normal. Results of physical examination of the heart, lungs, genitalia, extremities, and cranial nerves were within normal limits. Examination of the thoracoabdominal wall revealed a 4 × 6 cm. mass, which resembled a keloid formation, and several satellite lesions.

Routine laboratory studies on admission revealed the following hematologic values: leukocyte count, 7,000/cu.mm.; erythrocyte count, 4.61 million/cu.mm.; hemoglobin, 14.4 gm./dl.; hematocrit, 42.4 ml./dl., 35 segmented cells, 1 band form, 55 lymphocytes, 6 monocytes, and 3 eosinophils. The prothrombin time was 13 seconds (11.9 control). A partial thromboplastin time was 33.7 seconds (25.4 control). A rapid plasma reagin was non-reactive. Results of a serum profile were essentially within normal limits except for elevated phosphorus level (5.5 mg./dl.), and elevated total protein (8.0 gm./dl., with normal, 6.5 to 8.0). Serum protein electrophoresis yielded essentially normal results, as did the urinalysis.

A bone scan revealed a small amount of increased activity overlying the right hip, in the anterior projection only, but this was thought to be artifact rather than true increased activity within the bony structures. The electrocardiogram showed a normal sinus rhythm with a suggestion of incomplete right bundle branch block and nonspecific ST-T wave changes.

At surgery, after the patient was placed under general anesthesia, a large panel of tissue measuring 16 × 8 cm. was excised. The panel consisted of skin, subcutaneous fat, fascia, and underlying rectus and external oblique muscle. Specimens were prepared for pathologic examination. The resultant defect was closed by a split-thickness skin graft (Figs. 1 and 2).

The patient tolerated the operation well, and had no postoperative complications. The hospital course progressed satisfactorily. The patient was allowed to return home in 6 days, to be followed closely on an outpatient basis. He did not receive postoperative radiotherapy or chemotherapy. He was lost to follow-up.

Review of literature

Dermatofibroma protuberans occurs primarily in early adulthood or early middle age.¹⁻⁵ Men are afflicted more often than women.³⁻⁵ The most common location for this lesion is on the trunk or prox-

Figs. 1 and 2. Views of patient after excision of lesion.

imal extremities.²⁻⁵ Clinically, it is a raised, firm, multinodular tumor which often resembles an infected keloid or indurated plaque. It is often bluish and reddish, of firm consistency, and with a tendency to ulcerate as it increases in size.³ The lesion is usually slow-growing and locally invasive. A history of antecedent trauma was cited in 16.5 percent of Taylor and Helwig's³ 115 cases, but may be coincidental.² The local aggressiveness of this tumor is widely recognized.³ It may recur in up to half of cases.² Metastasis is rare, with Enzinger and Weiss² suggesting that the rate is less than 1 percent. When metastasis occurs, the lungs are the most common site.²

Diagnosis

The diagnosis should be based on the history, clinical findings, and histologic appearance.² The diagnosis can be confirmed with the use of the histologic criteria of Taylor and Helwig,³ which include the distinct storiform, or "cartwheel" pattern, low mitotic rate, and involvement of the cutis and subcutis with bulging of the epidermis. Sometimes, however, the tumor contains myxoid areas² and more mitotic activities.⁷

Dermatofibroma protuberans is uncommon, and unless there is a high index of clinical suspicion, the lesion is easily misdiagnosed.¹

It must be differentiated from dermatofibroma nonprotuberans in which the lesion does not protrude above the skin.⁸ The microscopic picture in

dermatofibroma protuberans is helpful in differentiating it from other dermatologic spindle-cell carcinomas: fibroblastic fibrosarcoma, leiomyosarcoma, schwannoma, amelanotic malignant melanoma, spindle-cell carcinoma, and dermatofibroma.

It is important to differentiate it from fibrohistiocytic tumors. First, according to Enzinger,² "the dermatofibrosarcoma protuberans has a more uniform appearance and smaller cells and displays a more distinct storiform pattern with fewer secondary elements (giant cells, inflammatory cells) than either benign or malignant fibrous histiocytoma." Biopsy should be performed. Second, dermatofibroma protuberans must be differentiated from benign neural tumors, primarily a diffuse form of neurofibroma. Third, it must be differentiated from myxoid liposarcoma.

Recurrence

Dermatofibroma protuberans is a low-grade sarcoma with a long clinical course, pronounced tendency to progression, and local recurrence. It recurs in up to half of patients.¹⁰ Prompt, wide local excision is recommended; recurrence rates of 2.05 percent¹⁰ and 33 percent¹¹ have been reported.

Obviously, a conservative approach is not recommended in cases in which an incompletely excised lesion would jeopardize a vital structure.² It is important to note that of over 400 cases documented, less than 1 percent had metastases.¹²

According to Enzinger,² "The tumor is characterized by a slow and persistent growth over an extended period of time, often several years..." He further states that "in later stages the initial plaque may eventually enter a rapid growth phase and give rise to one or more nodules, thus appearing as the typical 'protuberant lesion.'" Although the initial tumor is usually asymptomatic, as with many skin diseases, it is a change in symptoms or appearance that causes the patient to come to their physician.³

Summary

A patient suspected of having dermatofibroma protuberans should first undergo biopsy. Once the diagnosis has been made, the lesion should be excised widely and deeply. Extensive surgical excision is the best treatment, since these tumors are radioresistant. Conservative surgery is admissible only when extensive treatment is not feasible. It is important to diagnose the tumor because of the need to surgically excise for this type of locally aggressive tumor.

1. Rowsell, A.R., Poole, M.D., and Godfrey, A.M.: Dermatofibrosarcoma protuberans. The problems of surgical management. *Br J Plast Surg* 39:262-4, Apr 86

2. Enzinger, F.M., and Weiss, S.W.: *Soft tissue tumors*. C.V. Mosby Co., St. Louis, 1983

3. Taylor, H.B., and Helwig, E.B.: Dermatofibrosarcoma protuberans. A study of 115 cases. *Cancer* 15:717-25, Jul-Aug 62

4. Roses, D.F., et al.: Surgical treatment of dermatofibrosarcoma protuberans. *Surg Gynecol Obstet* 162:449-542, May 86

5. Fletcher, CDM, et al.: Dermatofibrosarcoma protuberans. A clinicopathological and immunohistochemical study with a review of the literature. *Histopathology* 9:921-38, Sep 85

6. Hess, K.A., et al.: Chemosurgical reports. Myxoid dermatofibrosarcoma protuberans. *J Dermatol Surg Oncol* 11:268-71, Mar 85

7. Chattopadhyay, T.K., Singh, M.K., and Arunabh: Dermatofibrosarcoma protuberans—a clinicopathological study of ten cases. *Jpn J Surg* 16:435-8, Nov 86

8. Lambert, W.L., et al.: Dermatofibrosarcoma non-protuberans. Description and report of five cases of a morpheaform variant of dermatofibrosarcoma. *J Surg Oncol* 28:7-11, 1985

9. Bendix-Hansen, K., Myhre-Jensen, O., and Kaae, S.: Dermatofibrosarcoma protuberans. A clinico-pathological study of nineteen cases and review of world literature. 17:247-252, 1983

10. Burkhardt, B.R., Soule, E.H., and Winkelmann, R.K.: Dermatofibrosarcoma protuberans. Study of 56 cases. *Am J Surg* 111:638, 1966

11. Penner, D.W.: Metastasizing fibrosarcoma protuberans. *Arch Surg* 62:391, 1976

12. Brenner, W., et al.: Dermatofibrosarcoma protuberans metastatic to a regional lymph node. *Cancer* 36:1897, 1975

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CONTRAINDICATIONS: FELDENE (piroxicam) should not be used in patients who have previously exhibited hypersensitivity to it, or in individuals with the syndrome comprised of bronchospasm, nasal polyps and angioedema precipitated by aspirin or other nonsteroidal anti-inflammatory drugs.

WARNINGS: Peptic ulceration, perforation and GI bleeding—sometimes severe, and, in some instances fatal—have been reported with patients receiving FELDENE. If FELDENE must be given to patients with a history of upper gastrointestinal tract disease, the patient should be under close supervision (see ADVERSE REACTIONS).

PRECAUTIONS: Renal Effects: As with other nonsteroidal anti-inflammatory drugs, long-term administration of piroxicam to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally, nephrotic syndrome.

A second form of renal toxicity has been seen in patients with preexisting conditions leading to a reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics, and the elderly.

Because of extensive renal excretion of piroxicam and its biotransformation products (less than 5% of the daily dose excreted unchanged), lower doses of piroxicam should be anticipated in patients with impaired renal function, and they should be carefully monitored.

Although other nonsteroidal anti-inflammatory drugs do not have the same direct effect on platelets that aspirin does, all drugs inhibiting prostaglandin biosynthesis do interfere with platelet function to some degree.

Because of reports of adverse eye findings with nonsteroidal anti-inflammatory agents, it is recommended that patients who develop visual complaints during treatment with FELDENE have ophthalmic evaluation.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver tests may occur in up to 15% of patients. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom abnormal liver tests have occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with FELDENE.

Severe hepatic reactions, including jaundice and cases of fatal hepatitis have been reported with FELDENE. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), FELDENE should be discontinued. (See also ADVERSE REACTIONS.)

Although at the recommended dose of 20 mg/day of FELDENE increased fecal blood loss due to gastrointestinal irritation did not occur, in about 4% of the patients treated with FELDENE alone or concomitantly with aspirin, reductions in hemoglobin and hematocrit values were observed.

Peripheral edema has been observed in approximately 2% of the patients treated with FELDENE. Therefore, FELDENE should be used with caution in patients with heart failure, hypertension or other conditions predisposing to fluid retention.

A combination of dermatological and/or allergic signs and symptoms suggestive of serum sickness have occasionally occurred in conjunction with the use of FELDENE. These include arthralgias, pruritus, fever, fatigue, and rash including vesiculo bullous reactions and exfoliative dermatitis.

DRUG INTERACTIONS: Interactions with coumarin-type anticoagulants have been reported with FELDENE since marketing. Therefore, physicians should closely monitor patients for a change in dosage requirements when administering FELDENE to patients on coumarin-type anticoagulants and other highly protein-bound drugs.

Plasma levels of piroxicam are depressed to approximately 80% of their normal values when FELDENE is administered in conjunction with aspirin (3900 mg/day), but concomitant administration of antacids has no effect on piroxicam plasma levels.

Nonsteroidal anti-inflammatory agents, including FELDENE, have been reported to increase steady state plasma lithium levels. It is recommended that plasma lithium levels be monitored when initiating, adjusting and discontinuing FELDENE.

Carcinogenesis, Chronic Animal Toxicity and Impairment of Fertility: Subacute and chronic toxicity studies have been carried out in rats, mice, dogs, and monkeys.

The pathology most often seen was that characteristically associated with the animal toxicology of anti-inflammatory agents: renal papillary necrosis (see PRECAUTIONS) and gastrointestinal lesions.

In classical studies in laboratory animals, piroxicam did not show any teratogenic potential. Reproductive studies revealed no impairment of fertility in animals.

Pregnancy and Nursing Mothers: Like other drugs which inhibit the synthesis and release of prostaglandins, piroxicam administration continued late into pregnancy increased the incidence of dystocia and delayed parturition in animals. Gastrointestinal tract toxicity was increased in pregnant females in the last trimester of pregnancy compared to non-pregnant females or females in earlier trimesters of pregnancy.

FELDENE is not recommended for use in nursing mothers or in pregnant women because of the animal findings and since safety for such use has not been established in humans.

Use in Children: Dosage recommendations and indications for use in children have not been established.

ADVERSE REACTIONS: Gastrointestinal symptoms are the most prominent side effects, occurring in approximately 20% of the patients, which in most instances did not interfere with the course of therapy. Of the patients experiencing gastrointestinal side effects, approximately 5% discontinued therapy with an overall incidence of peptic ulceration of about 1%.

Adverse reactions are listed below by body system for all patients in clinical trials with FELDENE (piroxicam) at doses of 20 mg/day.

Incidence Greater Than 1%: The following adverse reactions occurred more frequently than 1 in 100.

Gastrointestinal: stomatitis, anorexia, epigastric distress, nausea, constipation, abdominal discomfort, flatulence, diarrhea, abdominal pain, indigestion.

Hematological: decreases in hemoglobin* and hematocrit* (see PRECAUTIONS), anemia, leucopenia, eosinophilia.

Dermatologic: pruritus, rash.

Central Nervous System: dizziness, somnolence, vertigo.

Urogenital: BUN and creatinine elevations (see PRECAUTIONS).

Body as a Whole: headache, malaise.

Special Senses: tinnitus.

Cardiovascular/Respiratory: edema (see PRECAUTIONS).

*Reactions occurring in 3% to 9% of patients treated with FELDENE.

Reactions occurring in 1% to 3% of patients are unmarked.

Incidence Less Than 1% (Causal Relationship Probable): The following adverse reactions occurred less frequently than 1 in 100. The probability exists that there is a causal relationship between FELDENE and these reactions.

Gastrointestinal: liver function abnormalities, jaundice, hepatitis (see PRECAUTIONS), vomiting, hematemesis, melena, gastrointestinal bleeding, perforation and ulceration (see WARNINGS), dry mouth.

Hematological: thrombocytopenia, petechial rash, ecchymosis, bone marrow depression including aplastic anemia, epistaxis.

Dermatologic: sweating, erythema, bruising, desquamation, exfoliative dermatitis, erythema multiforme, toxic epidermal necrolysis, Stevens-Johnson syndrome, vesiculo bullous reactions, photoallergic skin reactions.

Central Nervous System: depression, insomnia, nervousness.

Urogenital: hematuria, proteinuria, interstitial nephritis, renal failure, hyperkalemia, glomerulitis, papillary necrosis, nephrotic syndrome (see PRECAUTIONS).

Body as a Whole: pain (colic), fever, flu-like syndrome (see PRECAUTIONS).

Special Senses: swollen eyes, blurred vision, eye irritations.

Cardiovascular/Respiratory: hypertension, worsening of congestive heart failure (see PRECAUTIONS), exacerbation of angina.

Metabolic: hypoglycemia, hyperglycemia, weight increase, weight decrease.

Hypersensitivity: anaphylaxis, bronchospasm, urticaria/angioedema, vasculitis, "serum sickness" (see PRECAUTIONS).

Incidence Less Than 1% (Causal Relationship Unknown): Other adverse reactions were reported with a frequency of less than 1 in 100, but a causal relationship between FELDENE and the reaction could not be determined.

Gastrointestinal: pancreatitis.

Dermatologic: onycholysis, loss of hair.

Central Nervous System: akathisia, hallucinations, mood alterations, dream abnormalities, mental confusion, paresthesias.

Urogenital System: dysuria.

Body as a Whole: weakness.

Cardiovascular/Respiratory: palpitations, dyspnea.

Hypersensitivity: positive ANA.

Special Senses: hearing impairment.

OVERDOSAGE: In the event treatment for overdosage is required, the long plasma half-life of piroxicam should be considered. The absence of experience with acute overdosage precludes characterization of sequelae and recommendations of specific antidotal efficacy at this time. It is reasonable to assume that the standard measures of gastric evacuation and general supportive therapy would apply. In addition to supportive measures, the use of activated charcoal may effectively reduce the absorption and reabsorption of piroxicam. Experiments in dogs have demonstrated that the use of multiple-dose treatments with activated charcoal could reduce the half-life of piroxicam elimination from 27 hours (without charcoal) to 11.6 hours and reduce the systemic bioavailability of piroxicam by as much as 37% when activated charcoal is given as late as 6 hours after administration of piroxicam.

ADMINISTRATION AND DOSAGE: Rheumatoid Arthritis, Osteoarthritis: It is recommended that FELDENE therapy be initiated and maintained at a single daily dose of 20 mg. If desired, the daily dose may be divided.

Dosage recommendations and indications for use in children have not been established.

More detailed professional information available on request.

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References: 1. Siegmund W. Serum concentrations of piroxicam in relation to its clinical effect in patients with chronic polyarthritides (trans). *Wien Med Wochenschr* 130:31-35, 1980. 2. Tausch: Placebo-controlled study of piroxicam in the treatment of rheumatoid arthritis. *Am J Med (report)* 72:18-22, February 16, 1982.

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