
CASE REPORTS

SQUAMOUS CELL CARCINOMA OF THE CERVIX METASTATIC TO THE UMBILICUS

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A patient with umbilical metastasis from a primary squamous carcinoma of the cervix is presented and the literature is reviewed.

Metastasis to unusual sites occurs in a significant number of patients with malignant disease. Metastasis to the skin from internal malignancies is generally considered to be a preterminal event, and occurs in 1 to 5 percent of cases. Umbilical metastases account for 10 percent of the lesions involving the abdominal wall, and are generally adenocarcinomas. Metastases from a squamous cell carcinoma of the cervix are extremely rare, and only a few cases are reported.

CASE REPORT

An 86-year-old, gravida 2, para 2, black woman was admitted to the tumor service with a three-month history of rectovaginal bleeding. General examination revealed a firm, solid 3 to 4 cm mass encircling the umbilicus (Figure 1). Gynecological examination revealed 3 to 4 mL of clotted blood in the vagina. An exophytic, friable lesion arising from the cervix involved the upper half of the vagina, extended onto

the pelvic sidewalls, and involved the bladder. Biopsies of the cervix, umbilical mass, and the bladder wall revealed moderately differentiated squamous cell carcinoma (Figures 2, 3, and 4). The patient was staged as IVB, treated palliatively with external irradiation, and discharged for follow-up by the oncology clinic. She did well during the interval, but was readmitted to the hospital about four months later with recurrent vaginal bleeding and increased growth and hemorrhage of the umbilical mass. Treatment at this time consisted of an additional 1,000 rad to the pelvis and 2,000 rad to the umbilical mass. She died a few weeks after completion of therapy, six months after diagnosis.

DISCUSSION

Because of the embryological and anatomical communications of the umbilicus with the intraabdominal organs, the umbilicus may harbor a variety of tumors. Tumors may arise from the attachments of the round and falciform ligaments, the urachus, and vestiges of the omphalomesenteric duct. Lymphatic and venous communications with the umbilicus may carry tumor from the upper and lower portions of the body. Direct extension from the peritoneal surfaces may occur, and tumor may lodge in the umbilicus via the arterial system.

Many adenocarcinomas metastasize to the umbilicus.¹ More common are lesions from the gastrointestinal tract and the gynecological system. Of the lesions of known origin, the most common metastatic tumors to the umbilicus in women are carcinoma of

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UMBILICAL METASTASIS

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ZANTAC® 150 Tablets
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

BRIEF SUMMARY

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:

1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease (GERD)**. Symptomatic relief commonly occurs within one or two weeks after starting therapy. Therapy for longer than six weeks has not been studied.

In active duodenal ulcer, active, benign gastric ulcer, hypersecretory states, and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.

2. Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy, and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although ZANTAC has been reported to bind weakly to cytochrome P-450 in vitro, recommended doses of the drug do not inhibit the action of the cytochrome P-450-linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in lifespan studies in mice and rats at doses up to 2,000 mg/kg/day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella*, *E. coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg to male rats was without effect on the outcome of two matings per week for the next nine weeks.

Pregnancy: Teratogenic Effects: Pregnancy Category B: Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ZANTAC. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: ZANTAC is secreted in human milk. Caution should be exercised when ZANTAC is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Use in Elderly Patients: Ulcer healing rates in elderly patients (65 to 82 years of age) were no different from those in younger age groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with oral ZANTAC®. The relationship to ZANTAC therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to ZANTAC administration.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported.

Cardiovascular: Rare reports of tachycardia, bradycardia, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain.

Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid IV for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

Musculoskeletal: Rare reports of arthralgias.

Hematologic: Reversible blood count changes (leukopenia, granulocytopenia, thrombocytopenia) have occurred in a few patients. Rare cases of agranulocytosis or of pancytopenia, sometimes with marrow hypoplasia, have been reported.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by ZANTAC (ranitidine hydrochloride) and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when ZANTAC has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Integumentary: Rash, including rare cases suggestive of mild erythema multiforme, and rarely, alopecia.

Other: Rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC® 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

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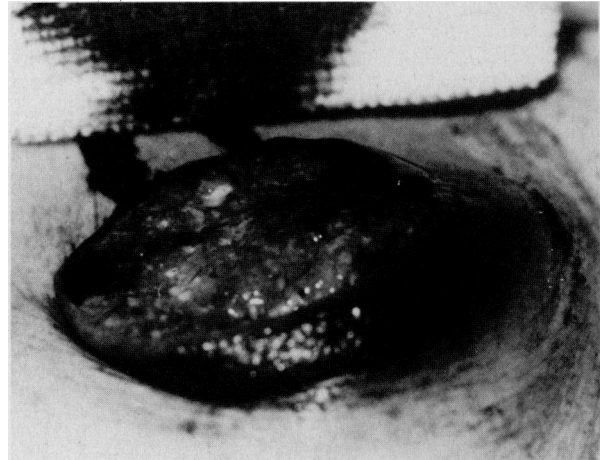


Figure 1. Squamous carcinoma metastatic to umbilicus.

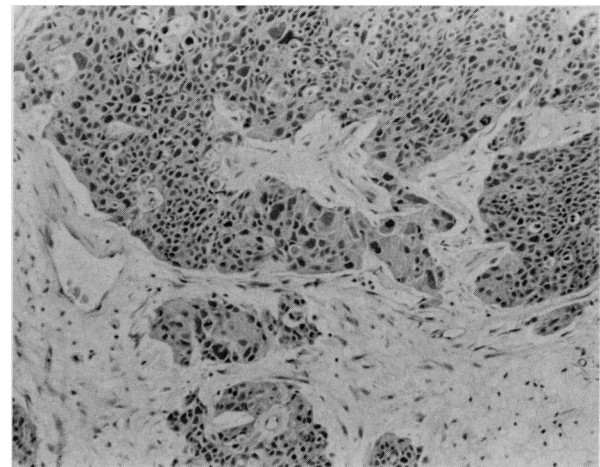


Figure 2. Cervical stroma with fragments of infiltrating moderately differentiated squamous cell carcinoma

the colon and ovaries. Lesions may, however, arise from the small bowel, appendix, rectum, liver, gallbladder, fallopian tubes, uterus, kidney, and breast. Notably absent are reports of lymphoma, leukemia, recticuloendothelial and bladder and genitourinary tract tumors metastasizing to the umbilicus.

In general, metastasis to the skin from internal organs occurs in about 1 to 5 percent of cases, but umbilical metastasis from a cervical carcinoma is extremely rare, and only a few cases have been reported. Squamous lesions metastasizing from the cervix to the skin have previously been reported.²⁻⁴ In review-

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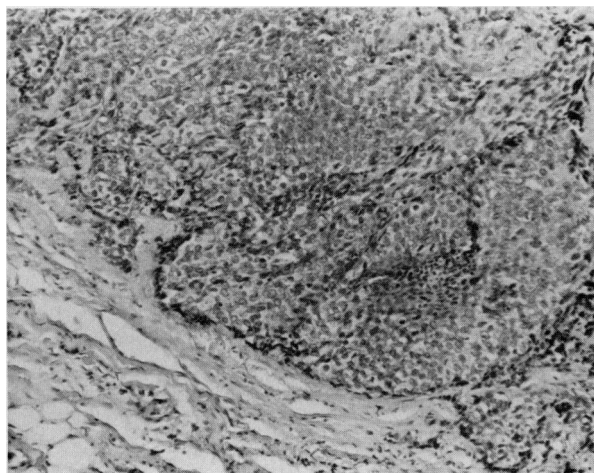


Figure 3. Nests of poorly differentiated squamous cell carcinoma infiltrating the soft fibroadipose connective tissue of the umbilicus and periumbilical region

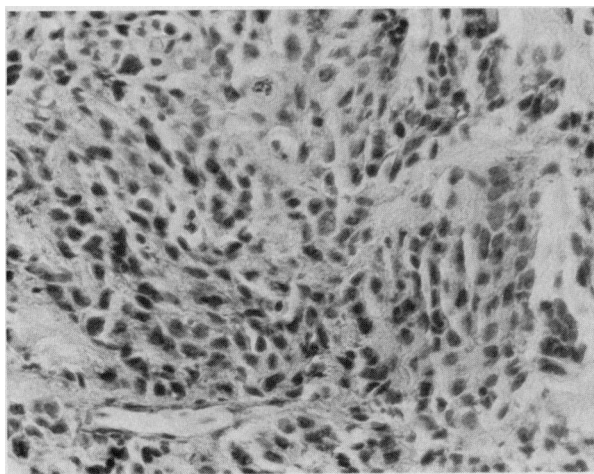


Figure 4. Squamous cell carcinoma infiltrating the bladder wall

ing 112 cases of umbilical metastases from the Armed Forces Institute of Pathology, Steck and Helwig⁵ found only one case arising from the cervix. Daw and Riley⁶ reported an additional case. The case reported here constitutes the third report.

Metastasis to the skin portends a poor prognosis with the average survival being approximately three months from discovery of the lesion. Patients with ovarian cancers, however, tend to survive for longer periods, up to approximately seven months. Steck and Helwig⁵ recommended wide excision of the lesion with provision for abdominal exploration pending results of a frozen-section examination, particularly when the primary site is unknown. Because of the size of the lesion in the case report by Daw and Riley,⁶ excision was not possible, and treatment was not given. In reports by others^{7,8} dealing with different primaries, wide local excision of the umbilicus has been utilized as the method of treatment.

Because of the rarity of these tumors, the best treatment is not known. A wide local excision with removal of the lesion is the recommended treatment at the present time.

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