

The patient is still alive with stable disease and on regular follow up after 8 cycles of chemotherapy.

The estimated prevalence of secondary breast ANSA after conserving therapy for breast adenocarcinoma ranges from 0.9 to 1.59 cases per 1000 patients, with an estimated relative risk of 15.9 of developing breast ANSA after breast-conserving therapy plus RT vs. breast-conserving therapy alone [1,2]. In Italy, the total number of all ANSAs (any site, primary and secondary) recorded from 1976 to 2007 was 414.

It has been hypothesized that there may be an association between the onset of primary liver ANSA and certain carcinogens such as vinyl chloride (VCM), arsenic and thorotrast [3,4].

ANSA has the worst prognosis of all types of sarcomas in terms of overall and disease-free survival [5]. Whatever the histological type, surgery is the treatment of choice. Breast ANSA is frequently advanced at diagnosis and has a tendency for locoregional recurrence. A significant number of responses to chemotherapy was observed in the metastatic setting. These data suggest that a multidisciplinary therapeutic approach should be employed in high-risk patients with large primary tumors.

It is certain that further studies are necessary to determine whether there are genetic factors predisposing to the disease and also to evaluate the effects of some carcinogens and other risk factors that may contribute to ANSA genesis.

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## Epidemiological characteristics of acrochordons

Dear Editor,

Skin tag (ST, acrochordon, fibroepithelial polyp) is the most common fibrous lesion of the skin and presents as a soft, pedunculated, skin-colored papule (1-2 mm). Epidermis has a papillomatous acanthotic pattern while the dermis is normal. Close to 50% of all individuals in the population at large have at least one skin tag [1]. Multiple acrochordons may reflect obesity and endocrine disease, whereas solitary and larger lesions may occasionally represent dermal melanocytic nevi in regression. Occasionally larger tags may be admixed with small lesions.

Results were obtained from two independent series of the dermatologic clinic of a general state hospital in Athens.

At first, data from an 8-year cross sectional study (1995-2002) regarding lifetime detection rates of ST as presenting complaint were analyzed, considered closer to incidence trends. The diagnosis was based on clinical findings. The overall denominator and reference population consisted of 50,237 self-referred Greek dermatologic outpatients, aged from 35 days to 96 years, consecutively examined by dermatologists (males 20,909; 41.6% and females 29,328; 58.4%; Table 1). All cases entered in the study were first-time referrals. Mantel-Haenszel chi-square stratified analysis was used to compare detection rates by age and gender without confounding effects [2,3].

In the second series (n=787) of consecutively examined dermatologic outpatients irrespective of the presenting complaint, 204 total cases of ST (25.9%) were diagnosed and possible associations with body mass index (BMI, for obesity) and diabetes mellitus were investigated [1,4].

In the first series, that is skin tags as presenting complaint (n=832, relative frequency 1.6%) median age was 43 years for men

(range 7-92) and 47 years for women (range 7-87). In accordance with a previous study [3], overall both sexes were equally affected. This occurred also by age groups (Table 1).

Within both sexes detection rates did not differ between childhood (0-10 years) and adolescence (11-20 years), whereas from adolescence up to 40 years a significant increment by age was noted (Table 1). From 41 to 70 years highest detection rates were detected. Thereafter, diagnoses began to decline, probably because in the elderly aesthetic concerns are overlooked. For both sexes

**Table 1.** Detection rates of skin tags as presenting complaint by gender and age

Age (y)	Men		Women	
	Exam.	STn (‰)	Exam.	STn (‰)
0-10	2326	2 (0.8)	2194	4 (1.8)
11-20	4171	15 (3.6) ¶	5491	23 (4.2) †
21-30	3184	34 (10.7) ¶‡	4616	36 (7.8) †‡
31-40	2287	67 (29.3) ‡	3980	93 (23.3) ≠
41-50	2148	79 (36.8)	3761	112 (29.7)
51-60	1975	69 (34.9)	3165	77 (24.3)
61-70	2671	64 (24.2)	3587	102 (28.4)
71-80	1630	20 (12.2)	1977	30 (15.2)
> 80	517	2 (3.9)	557	2 (3.6)
Total	20909	353 (16.9)	29328	479 (16.3)

Exam: number of patients examined, STn (‰): number of skin tag cases (per thousand).

Significant comparisons within the groups:

Males: ¶p=0.0003, OR 3.0 (1.6-5.8), ‡p<10<sup>-6</sup>, OR 2.8 (1.8-4.3)

Females: †p=0.02, OR 1.9 (1.1-3.3), ≠p<10<sup>-9</sup>, OR 3.0 (2.0-4.6)

peak prevalence was observed in the age group from 41 to 50 years.

In the second series, BMI did not differ between ST cases and the remaining without ST patient population (mean±SEM, unpaired t-test, n=204, 27.7±0.35 and n=583, 29.4±3.03), contrary to “classic” opinions [1].

In ST cases a positive history of diabetes was reported from 7.8% (16/204) vs. 9.1% (53/583) from the remaining non-ST population. The lack of difference as regards diabetes mellitus frequency (chi-square) opposes a previously held opinion [4] and reinforces another report that has not confirmed this association [5].

The problem seems that is often overlooked, since perceived disease duration differed significantly between ST cases and the remaining skin diseases [mean±SEM; unpaired t-test, n=202, 5.8±0.35 years (range 1 month-30 years) vs. n=580, 4.06±0.26 years (range 0.0 month-65 years), p=0.0004]. Moreover, skin tags as presenting complaint accounted for 24.0% of ST diagnoses (n=49/204). Lesions were localized on the neck (43.1%), multiple sites (21.5%), other intertriginous area (axilla and groin 15.2%), eyelids (10.1%) and trunk (8.8%).

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## Imatinib-induced anasarca without heart failure: capillary leakage?

Dear Editor,

Imatinib mesylate, a selective tyrosine kinase receptor inhibitor of KIT and platelet derived growth factor receptor  $\alpha$  (PDGFR $\alpha$ ), is currently licensed for the treatment of chronic myelogenous leukemia (CML) and unresectable or metastatic gastrointestinal stromal tumors (GISTs), which are KIT-positive [1]. Treatment with imatinib is generally well tolerated with a low incidence of severe side effects, muscle cramps, diarrhea, nausea, skin rashes, and myelosuppression. Superficial edema and fluid retention occurs in nearly 10% of the patients on imatinib monotherapy but the anasarca type edema was not reported until today [2]. This letter presents a case of anasarca type edema without heart failure with imatinib treatment.

A 69-year-old man presented with nausea and right upper quadrant pain. On physical examination the patient was asthenic and had hepatomegaly. Laboratory evaluation revealed mild anemia with mild hypoalbuminemia. Abdominal computed tomography revealed multiple metastatic lesions in the liver and a 158×145×90 mm mass extending from the subhepatic area to the pelvis. A tru-cut biopsy of the mass showed KIT-positive GIST. The cardiac function was normal. The patient was put on imatinib 400 mg/day for metastatic GIST. After the 15th day of imatinib monotherapy the patient was readmitted with superficial leg edema. The laboratory evaluation showed mild anemia with normal renal and thyroid functions. He was treated with salt restriction and furosemide 40 mg twice a day. One week later the patient was readmitted with minimal improvement although imatinib dose had been reduced to 300 mg/day. After the 35th day of treatment the patient was readmitted again with anasarca type edema without heart failure. Imatinib was stopped. Doppler ultrasonography of the lower extremities and the pelvic region revealed massive subcutaneous edema without pressure of iliac veins. The patient was treated with salt restriction and intensive diuretic treatment with 80 mg/day i.v. furosemide. After the 14th day of intensive treatment with diuretics and salt restric-

tion the anasarca type edema disappeared and the patient was doing well. Imatinib was readministered at 400 mg per day. After 15 days of imatinib treatment the patient was readmitted again with anasarca type edema. The drug was stopped and intensive diuretic treatment was repeated. After one week of intensive diuretic treatment the anasarca type edema was resolved and then sunitinib 50 mg/day was started. The patient is still on follow-up without any complication.

Edema and fluid retention are characteristic side effects of imatinib. The edema is usually mild, localized at the periorbital region or legs and may respond to diuretics. The periorbital edema is the most common site occurring in 47-70% of patients taking imatinib [3,4]. Very severe periorbital edema, cerebral edema and intramuscular edema was also reported with imatinib [5]. Anasarca type edema has not been reported so far. The mechanism of fluid retention and edema remains largely unknown. One possible mechanism is that imatinib-derived inhibition of PDGFR $\alpha$  on dermal dendrocytes may cause interstitial edema. In rats, the regulation of interstitial pressure between cells in the connective tissue is disturbed. As a result of increase of the interstitial fluid pressure in patients may similarly result in increased capillary permeability and fluid extravasation. Localized edema may not be explained by this hypothesis, but this theory may explain the cause of anasarca type edema. The optimal treatment of localized and anasarca type edema is still not known. As in all cases of edema, other causes should be carefully considered. Because of the risk of relapse, it is currently recommended that imatinib therapy be continued indefinitely in patients with CML and metastatic GIST. Repeated edema should be kept in mind with imatinib treatment.

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