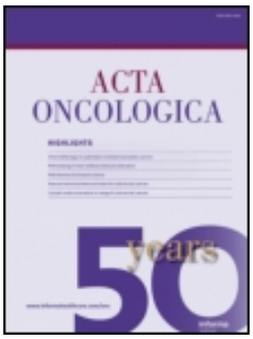

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ORIGINAL ARTICLE

Rare skin cancer: A population-based cancer registry descriptive study of 151 consecutive cases diagnosed between 1980 and 2004

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Abstract

Background. There are few epidemiological data available on rare skin cancer, including Merkel cell carcinoma, Paget's disease, adnexal carcinoma, and sarcoma. We conducted this study to investigate the epidemiological of rare skin cancer diagnosed in the *département* of Doubs from 1980 to 2004. *Methods.* Data were collected from a population-based cancer registry from 1980 to 2004. Diagnosis was based on the 3rd edition of the International Classification of Diseases for Oncology. The incidence rates were standardized on world population. *Results.* One hundred and fifty one patients were investigated (88 women and 63 men). Median age for the diagnosed disease was 63 years. The standardized incidence rate was 0.82/100 000 person-year (95% CI = 0.68–0.96) and increased from 0.25 in 1980–1984 to 1.50 in 2000–2004. Fifty nine cases (39%) were sarcomas, 35 (23%) adnexal carcinomas, 27 (18%) Merkel cell carcinoma and 27 (18%) Paget's disease. The standardized incidence rates were 0.37/100 000 (0.27–0.47) for sarcomas, 0.16 (0.10–0.22) for adnexal tumors, 0.13 (0.08–0.18) for Merkel cell carcinoma, and 0.15 (0.09–0.21) for Paget's disease. *Conclusions.* Our results based on a population-based cancer registry showed an increase of the standardized incidence rate for all types of rare skin tumors. These results may be useful when considering the growing interest in rare diseases in identifying risk factors and planning scientific research programmes.

Set aside for a long time by physicians, scientists and politicians, there were no adequate political and scientific research programmes in the field of rare diseases until a few years ago. There is now a growing interest from pharmaceutical companies and governments to target these "orphan" diseases. Knowledge on natural history of rare diseases is improved by the set up of cancer registries. There is a paucity of data available describing epidemiology of rare skin cancers and most of them involve patients attending a single institution with a specific histologic type. Using data from the Doubs cancer registry, we recently analyzed the epidemiological, cytological and clinical features, the type of treatment and the outcome of consecutive pathologically proved cases of primary cutaneous lymphoma [1]. We then wished to investigate the epidemiological features of the remaining other rare skin cancers which include Merkel cell carcinoma, Paget's disease, adnexal carcinoma and sarcoma.

Patients and methods

Patients selection

The *département* of Doubs (505 557 inhabitants as of January 1, 2003) is a well-defined administrative area located in eastern France. The Doubs Cancer Registry was established in 1976 and has received international recognition as demonstrated by its inclusion in the International Agency for Research on Cancer (IARC) series entitled 'Cancer Incidence in Five Continents'. Accreditation and legal authorization are renewed every 4 years by a national committee that assess the completeness and quality of data as well as the scientific production of the

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registry. The Doubs cancer registry belongs to the Francim association (French Network of cancer registries) that gathers qualified registries following standard rules in accordance with the recommendations of the IARC and the European Network of Cancer Registries. These registries include all incident invasive tumor cases diagnosed in patients residing in the *départements* they cover. The main data sources are public and private pathology and cytology laboratories and hospital and clinical records. Although the Doubs Cancer Registry was established in 1976, only cases registered between 1980 and 2003 were included in our study to minimize the risk of under-registration in the early years. All the patients with rare skin cancers recorded between 1980 and 2003 by the Doubs Cancer Registry were included in our study. Selection of cases from the registry was based on the topographical code of the tumour (C44 for cutaneous tumours; for Paget's disease, the topographic code C50 was used) and the morphological code (8000, 8003, 8010, 8020, 8021, 8022, 8031, 8033, 8100, 8110, 8140, 8190, 8200, 8246, 8247, 8310, 8390, 8400, 8401, 8402, 8409, 8410, 8413, 8430, 8481, 8540, 8541, 8542, 8543, 8800, 8804, 8810, 8830, 8832, 8833, 8850, 8851, 8852, 8853, 8854, 8855, 8857, 8858, 8890, 8891, 8896, 8900, 9040, 9041, 9042, 9043, 9044, 9120, 9150, 9540) as defined by the International Classification of Diseases for Oncology-3rd edition [2]. Patients with Kaposi sarcoma were excluded since, in the setting of acquired immunodeficiency syndrome, it constitutes a major subset of cases. Thus, it would have introduced a major bias to the study. In addition, it must be pointed out that in our study as in previous studies, we did not review histological slides (except when histologic diagnostic was unspecified: 6 cases) and the diagnosis of rare skin cancers was only based on pathology reports.

Statistical analysis

The standardized incidence rates were calculated for the whole period 1980–2004 by the method of direct standardization. The number of person-years is based on the data of the population census in the *département* of Doubs made by the National Institute for Economic and Statistical Information (INSEE, Paris, France). The reference population in use is the world population [3]. The standardized incidence and its 95% confidence interval were calculated with the software Stata v8.2® (Stata Corporation, College Station, Texas, USA). The development of the incidence for a time-span was estimated by calculation of incidence rates over periods of 5 years and their confidence interval (CI). Five periods were defined (1980–1984, 1985–1989, 1990–1994, 1995–1999, 2000–2003).

Results

Demographic data

Between 1980 and 2004, 151 cases of rare skin cancers were diagnosed in the *département* of Doubs (88 men and 63 women). The age at the time of the diagnosis varied from 10 to 99 years with a median age of 63 years without any significant difference in sex (men: 64 and women: 70). Three cutaneous sarcomas were diagnosed in children less than 15 years old and 63% of all cases were diagnosed after the age of 60 years.

Histological types

Nine cases over 154 (5.8%) were histologically verified. For 3 patients, no accurate diagnosis could be made even after re-examination. These cases were excluded from the study. In addition, 6 additional cases were unspecified and required histological re-examination for specific diagnosis. Final diagnosis included 1 trichilemmal carcinoma, 2 pilomatrical carcinomas, and 3 sebaceous carcinomas. Among the remaining 151 cases of rare skin cancers, 59 cases (39%) were sarcomas, 35 (23%) adnexal carcinomas, 27 (18%) Merkel cell carcinomas and 27 (18%) Paget's disease (1 man and 26 women). The different pathological types of sarcomas are reported in the following table (Table I). Sweat gland carcinomas were classified into recognizable histologic patterns (2 hidradenocarcinomas, 4 porocarcinomas, 1 microcystic adnexal carcinoma, 5 adenoid cystic carcinomas, and 4 apocrine carcinomas). Other adnexal carcinomas included 2 trichilemmal carcinomas, 4 pilomatrical carcinomas and 13 sebaceous carcinomas.

Incidence rate

The standardized incidence rate (SIR) and the crude incidence rate of rare skin cancers are reported in Table II. SIR was 0.82 for 100 000 persons per year [95% confidence interval (Ci) of 0.68–0.96] and increased from 0.25 in 1980–1984 to 1.50 in 2000–2004. The standardized incidence rate and the crude incidence rate of the different histological types of rare skin cancers are reported in Table III. However, the number of cases was not large enough to compare the evolution of incidence rate during the different periods of 5 years.

Table I. Histological types of cutaneous sarcomas in the Doubs between 1980 and 2004.

Type of sarcomas	N	(%)	Localization
Dermatofibrosarcoma	31	52.5	Tr: 12; UL: 6; LL: 4; H: 7; UK: 2
Malignant fibrous histiocytoma	7	11.9	Tr: 2, UL: 2, H: 3
Atypical fibroxanthoma	1	1.7	H
Leiomyosarcoma	8	13.6	Tr: 3; LL: 3; UL: 1; H: 1
Liposarcoma	5	8.5	UL: 2; LL: 3
Epithelioid sarcoma	2	3.3	H: 2
Angiosarcoma	4	6.8	UL: 2; Tr: 2
Clear cell sarcoma	1	1.7	H

H: head; Tr: Trunk; UL: upper limb; LL: lower limb; UK: unknown.

Discussion

The focus on rare diseases is a relatively new phenomenon in Europe. Until recently, public health authorities and policy makers largely ignored them. The European Commission on Public Health defines rare diseases as "life-threatening or chronically debilitating diseases which are of such low prevalence that special combined efforts are needed to address them. As a guide, low prevalence is taken as prevalence of less than 5 per 10 000 in the Community." This would calculate into 0.05% of the overall population. The USA definition is very similar to the European one. In the USA an orphan or rare disease is generally considered to have a prevalence of fewer than 200 000 affected individuals. Rare skin cancers are recognized as a heterogeneous group of cutaneous tumours including primary cutaneous lymphoma, Merkel carcinoma, adnexal carcinoma, sarcoma and Paget's disease. All these tumors demonstrate an aggressive local growth, a high recurrence rate, and a low metastatic potential. Surgery alone or combined with radiotherapy is used for initial lesions, and chemotherapy is indicated for disseminated tumors. Five-year survival rates ranged between 15% for angiosarcomas to about 50% for sebaceous carcinomas and Merkel cell carcinomas and 99% for adnexal tumors [4].

Table II. New cases and standardized incidence rate (SIR) and crude incidence (CI) of rare skin cancers; Ci: 95% confidence interval 95% per 100 000 persons per year in the Doubs from 1980 to 2004.

Periods	New cases	SIR	Ci min	Ci max	CI
1980–1984	8	0.25	0.07	0.43	0.33
1985–1989	10	0.32	0.11	0.53	0.41
1990–1994	28	0.83	0.50	1.15	1.14
1995–1999	40	1.03	0.69	1.38	1.61
2000–2004	65	1.50	1.09	1.91	2.56
1980–2004	151	0.82	0.68	0.96	1.23

As in primary cutaneous lymphoma [1], there are few epidemiological data available on the remaining rare skin cancer, including Merkel cell carcinoma, Paget's disease, adnexal carcinoma, and sarcomas. Most of them are provided by large database from population-based cancer registries [5–7], or patients attending a single institution [8,9]. In addition, most of epidemiological studies on soft tissue sarcoma [10–14] selected all cases regardless of primary site and skin site was not specifically investigated.

The SIR of Merkel cell carcinoma was lower in our population-based cancer registry (0.13 per 100 000 person-year, 95% CI: 0.08–0.18) as compared with other population-based series of cases. The annual incidence of Merkel cell carcinoma based on patients included in 13 population-based cancer registries in the US (SEER) was 0.23 per 100 000 person-year [15,16], which was similar to the estimates using the defined patient population of the Mayo Clinic [17] and of South East Scotland [18]. Updated data from the SEER program [16,19] demonstrated an increase of the annual incidence over time between 1973 and 2001.

The SIR of cutaneous sarcoma was 0.37 per 100 000 persons per year (95% Ci: 0.27–0.47). The incidence of skin sarcomas was previously calculated by Toro et al. [7] on the basis of 26 758 cases diagnosed from 1978 to 2001 among USA patients (SEER data). The age-adjusted incidence rate to the 2 000 USA population was 0.69 per 100 000 person-year for skin sarcomas. As in our

Table III. Standardized incidence rate (SIR) and crude incidence (CI) of rare skin cancers; Ci: 95% confidence interval per 100 000 persons per year in the Doubs from 1980 to 2004.

Types of tumours (n)	SIR	Ci min	Ci max	CI
Sarcoma (59)	0.37	0.27	0.47	0.48
Adnexal carcinoma (35)	0.16	0.10	0.22	0.28
Merkel cell carcinoma (27)	0.13	0.08	0.18	0.22
Paget's disease (27)	0.15	0.09	0.21	0.22

study, Kaposi sarcoma was excluded. The distribution of histologic types of soft tissue sarcoma was also different, since dermatofibrosarcoma accounted for only 10.5% as compared to 52% in our study. As previously reported [7], we observed a considerable variation in distribution of sarcomas by histologic type and subtypes, supporting the notion that these tumors are etiologically distinct and that they should be considered separately in studies of potential risk factors.

The SIR of Paget's disease was 0.15 per 100 000 persons per year (95% Ci: 0.09–0.21). This was much lower than the European Standardized Rate of 0.78 per 100 000 person-years found in a recent study [5] based on the Netherlands Cancer Registry. This later rate was similar to those calculated in female between 1988 and 2002 by the 9 USA registries of the Surveillance, Epidemiology, and End Results (SEER) Program [6].

The SIR for adnexal carcinoma was 0.16 per 100 000 persons per year (95% Ci: 0.10–0.22). One recent population-based cancer registry study [20] calculated an overall population-matched rate of sebaceous carcinoma of 0.2 cases per 100 000 persons per year. To our knowledge, there is no epidemiological data from population-based cancer registries for other types of adnexal carcinoma, and only large series of patients attending a single institution have been described [17,21–23].

We do not have any clear explanation for the low incidence of cutaneous sarcomas and Paget's disease found in our study. The discrepancy between these results may be explained by the different reference populations used to calculate the age-adjusted incidence rates. Although most of the epidemiological data are adjusted to the 2 000 USA population [6,7], European population or world population as in our study are used by other authors. Furthermore, prior studies of SEER registry data before 1987 showed that the incidence of Paget's disease increased during that time as for the incidence of breast cancer and the use of mammography in asymptomatic women [24]. By contrast, the incidence of Paget's disease decreased by 45% between 1988 and 2002 whereas the incidence of breast cancer still increased. This decreasing incidence of Paget's disease suggests the role of early detection of breast cancer and underlying ductal carcinoma in situ prior to the development of Pagetoid changes. These data are thus consistent with the epidermotropic theory, which maintains that Paget's disease develops as an extension of an underlying invasive or noninvasive cancer.

Although the number of cases was not large enough to compare the evolution of the incidence rate for each tumor type, we observed an overall increase from 0.25 in 1980–1984 to 1.50 in 2000–2004 (Table II). This increase can be explained by several hypotheses. The increased diversity of the notification sources and information received by the cancer registry, which contributed consequently to the exhaustivity of recording, could explain this increase. The increase of the incidence rates may reflect the improvement in diagnosis, which has seen the recent introduction and diffusion of new diagnostic procedures, techniques and biomarkers. In our study, selection of the tumors was based on the morphological code and topographical code as defined by the International Classification of Diseases for Oncology-3rd edition [2]. However, changes made in the classification (2nd and 3rd edition) with the introduction of new morphology code (like Merkel cell carcinoma) could influence the correct registration of the cases leading to an underestimation of incidence. Furthermore, improvements in detection and access to specialised medical care have also been suggested [25]. The rate increase of sarcomas observed in the USA [8] may be a result of recent shifts in the diagnostic criteria and classification of sarcomas [26]. However, it was remarkable to note that previous other population-based series from USA [12], Iceland [13], northwest England [14], and Switzerland [10] showed overall stable rates for soft tissues sarcomas between 1985 and 1994. Recent histogenetic studies have shown genetic aberrations [27–29] which may be induced by still unknown predisposing factors. Angiosarcomas can be induced by ionizing radiation and the number of radiation treatments has increased since 1980 [30]. Among other potential risk factors for sarcomas are environmental or occupational exposure to chemical agents including pesticides, herbicides and dioxin [31,32]. Population ageing and ultraviolet exposure may also contribute to the increasing incidence since most of adnexal and Merkel cell carcinomas develop on sun-exposed sites in the elderly. However, it is possible that several more years of follow-up will be required to ascertain the steady incidence rate increase of rare skin cancers and to evaluate if better diagnosis and recognition of these tumors may hide the presence of a true increase.

In conclusion, our population-based study provides updated data on the incidence of rare skin cancers in France. These results may be useful when considering the growing interest in rare diseases in identifying risk factors and planning scientific research programmes.

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References

[1] Riou-Gotta MO, Fournier E, Mermet I, Pelletier F, Humbert P, Danzon A, et al. Primary cutaneous lymphomas: A population-based cancer registry descriptive study of 71 consecutive cases diagnosed between 1980 and 2003. Leukaemia Lymphoma 2008;49:1537–44.

[2] Fritz A, Percy C, Jack A, Kanagaratnam S, Sobin L, Parkin DM. International classification of diseases for oncology. 3rd ed. Geneva: World Health Organisation; 2001.

[3] Waterhouse J, Muir C, Correa P, Powell J. Cancer incidence in five continents. In: IARC scientific publication editor. (editors), Volume 3, Number 15. Lyon: International Agency for Research on Cancer; 1976.

[4] Dixon A. Rare skin cancers in general practice. Aust Fam Physician 2007;36:141–3.

[5] Siesling S, Elferink MA, van Dijck JA, Pierie JP, Blokx WA. Epidemiology and treatment of extramammary Paget disease in the Netherlands. Eur J Surg Oncol 2007;33:951–5.

[6] Chen CY, Sun LM, Anderson BO. Paget disease of the breast: Changing patterns of incidence, clinical presentation, and treatment in the U.S. Cancer 2006;107:1448–58.

[7] Toro JR, Travis LB, Wu HJ, Zhu K, Fletcher CD, Devesa SS. Incidence patterns of soft tissue sarcomas, regardless of primary site, in the surveillance, epidemiology and end results program, 1978–2001: An analysis of 26,758 cases. Int J Cancer 2006;119:2922–30.

[8] Kransdorf MJ. Malignant soft-tissue tumors in a large referral population: Distribution of diagnoses by age, sex, and location. AJR Am J Roentgenol 1995;164:129–34.

[9] Mark RJ, Poen JC, Tran LM, Fu YS, Juillard GF. Angiosarcoma. A report of 67 patients and a review of the literature. Cancer 1996;77:2400–6.

[10] Levi F, La Vecchia C, Randimbison L, Te VC. Descriptive epidemiology of soft tissue sarcomas in Vaud, Switzerland. Eur J Cancer 1999;35:1711–6.

[11] Nijhuis PH, Schaapveld M, Otter R, Molenaar WM, van der Graaf WT, Hoekstra HJ. Epidemiological aspects of soft tissue sarcomas (STS)–consequences for the design of clinical STS trials. Eur J Cancer 1999;35:1705–10.

[12] Ross JA, Severson RK, Davis S, Brooks JJ. Trends in the incidence of soft tissue sarcomas in the United States from 1973 through 1987. Cancer 1993;72:486–90.

[13] Baldursson G, Agnarsson BA, Benediktsdóttir KR, Hrafnkelsson J. Soft tissue sarcomas in Iceland 1955-1988. Analysis of survival and prognostic factors. Acta Oncol 1991;30:563–8.

[14] Hartley AL, Blair V, Harris M, Birch JM, Banerjee SS, Freemont AJ, et al. Sarcomas in north west England: II. Incidence. Br J Cancer 1991;64:1145–50.

[15] Miller RW, Rabkin CS. Merkel cell carcinoma and melanoma: Etiological similarities and differences. Cancer Epidemiol Biomarkers Prev 1999;8:153–8.

[16] Agelli M, Clegg LX. Epidemiology of the primary Merkel cell carcinoma in the United States. J Am Acad Dermatol 2003;49:832–41.

[17] Chuang TY, Su D WP, Muller SA. Incidence of cutaneous T cell lymphoma and other rare skin cancers in a defined population. J Am Acad Dermatol 1990;23:254–6.

[18] Mills LA, Durrani AJ, Watson JD. Merkel cell carcinoma in South East Scotland, 1993-2003. Surgeon 2006;4:133–8.

[19] Hodgson NC. Merkel cell carcinoma: Changing incidence trends. J Surg Oncol 2005;89:1–4.

[20] Dasgupta T, Wilson LD, Yu JB. A retropective review of 1349 cases of sebaceous carcinoma. Cancer 2008 (in press).

[21] Urso C, Bondi R, Paglierani M, Salvadori A, Anichini C, Giannini A. Carcinomas of sweat glands: Report of 60 cases. Arch Pathol Lab Med 2001;125:498–505.

[22] Saito A, Tsutsumida A, Furukawa H, Saito N, Yamamoto Y. Sebaceous carcinoma of the eyelids: A review of 21 cases. J Plast Reconstr Aesthet Surg 2007 (in press)

[23] Robson A, Lazar AJ, Ben Nagi J, Hanby A, Grayson W, Feinmesser M, et al. Primary cutaneous apocrine carcinoma: A clinico-pathologic analysis of 24 cases. Am J Surg Pathol 2008;32:682–90.

[24] Berg JW, Hutter RV. Breast cancer. Cancer 1995;75(1 Suppl):257–69.

[25] Higginbotham JC, Moulder J, Currier M. Rural v. urban aspects of cancer: First-year data from the Mississippi Central Cancer Registry. Fam Community Health 2001; 24:1–9.

[26] Fletcher CDM, Unni KK, Mertens F, editors. WHO Classification of tumors: Pathology and genetics of tumors of soft tissue and bone. Lyon: IARC Press; 2002.

[27] Simon MP, Pedeutour F, Sirvent N, Grosgeorge J, Minoletti F, Coindre JM, et al. Deregulation of the platelet-derived growth factor B-chain gene via fusion with collagen gene COL1A1 in dermatofibrosarcoma protuberans and giant-cell fibroblastoma. Nat Genet 1997;15:95–8.

[28] Crozat A, Aman P, Mandahl N, Ron D. Fusion of CHOP to a novel RNA-binding protein in human myxoid liposarcoma. Nature 1993;363:640–4.

[29] Pedeutour F, Forus A, Coindre JM, Berner JM, Nicolo G, Michiels JF, et al. Structure of the supernumerary ring and giant rod chromosomes in adipose tissue tumors. Genes Chromosomes Cancer 1999;24:30–41.

[30] Penel N, Grosjean J, Robin YM, Vanseymortier L, Clisant S, Adenis A. Frequency of certain established risk factors in soft tissue sarcomas in adults: A prospective descriptive study of 658 cases. Sarcoma 2008;2008:459386.

[31] Hardell L. Pesticides, soft-tissue sarcoma and non-Hodgkin lymphoma – historical aspects on the precautionary principle in cancer prevention. Acta Oncol 2008;47:347–54.

[32] Zambon P, Ricci P, Bovo E, Casula A, Gattolin M, Fiore AR, et al. Sarcoma risk and dioxin emissions from incinerators and industrial plants: A population-based case-control study (Italy). Environ Health 2007;6:19–28.