Table 1 Summary of eight cutaneous melanoma cases in genetically confirmed Li-Fraumeni syndrome (LFS)

	Sex	Age at diagnosis of cutaneous melanoma	Age at diagnosis of LFS	Other malignancies	Note
Pötzsch *et al.*[8]	F	26	32	Leiomyosarcoma (age 22), Breast cancer (age 30)	—
Curiel-Lewandrowski *et al.*[5]	F	32	32	Osteosarcoma (age 28)	Five melanomas, One within prior radiotherapy field
Kollipara *et al.*[7]	M	3	4 months	Choroid plexus carcinoma (age 4 months), MDS (age 3)	Spitzoid melanoma within prior radiotherapy field
Villani *et al.*[2]	M	40	40	None	—
	F	57	52	MDS (age 52)	
Giavedoni *et al.*[6]	F	26, 35	28	Breast cancer, Adrenal cancer, Osteosarcoma (before melanoma, exact age N/A), BCC (age 29, 33), Pancreatic cancer (age 35)	Identical twin
	F	31	28	Breast cancer (age 25)	
Present case	M	16	16	None	—

BCC, basal cell carcinoma; MDS, myelodysplastic syndrome.

of cutaneous melanoma in LFS patients are rare[1,5–8] (Table 1). In addition to cases in the table, there were eight patients (six females, two males, mean age 40) who developed melanoma within a cohort of 322 LFS patients followed between 1993 and 2013.[2] In most cases, the patients had been diagnosed with brain tumour, sarcoma or adrenocortical carcinoma in their early age before the development of cutaneous melanoma.[5–8] To our knowledge, this is the first paediatric case in which cutaneous melanoma preceded all other common tumour components associated with LFS. This case further strengthens the association between melanoma and LFS and need for surveillance of cutaneous melanoma in LFS patients starting from early age. Furthermore, it reinforces the need for comprehensive family history work-up for paediatric melanoma patients.

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Polymorphisms associated with anti-TNF drugs response in patients with psoriasis and psoriatic arthritis

Editor

Psoriatic arthritis (PsA) has been classified as an inflammatory musculoskeletal disease with a strong genetic background.[1] Although anti-TNF drugs are effective for PsA and moderate-to-severe psoriasis, up to 30%–40% of patients do not respond to them.[2] We evaluated the possible association between 13

single nucleotide polymorphisms (SNPs) and anti-TNF drug response in psoriasis and PsA patients. We recruited 20 patients from the Dermatology Department of 'Hospital Universitario La Princesa' in Madrid diagnosed of moderate-to-severe plaque psoriasis[3] and of PsA by rheumatologists based on CASPAR criteria.[4] PsA severity was measured with a Numeric Rating Scale for Pain (NRS-Pain, 0–10).[5] Only patients with a baseline NRS-Pain higher than three and older than 18 years were included. NRS-Pain50 (a decrease of 50% with respect to baseline NRS-Pain) was considered a criteria of anti-TNF drugs response in PsA. Quality of life was measured by the European Quality of life Visual Analog Scale (EQ-VAS).[6] Percentage improvement of EQ-VAS (%EQ-VAS) and NRS-Pain after drug administration was measured at 3 and 6 months.[6] PASI75 (a 75% improvement over their baseline Psoriasis Area and Severity Index) was set as a criteria of psoriasis response. The protocol fulfilled Spanish law on biomedical research.

Table 1 Clinical and demographic data and response to treatment of patients with psoriasis and psoriatic arthritis included in the study

Variable	Patients (N = 20)
Age at the beginning of the treatment (years)	46.25 ± 12.81
Duration of psoriatic arthritis (years)	10.75 ± 8.55
NRS-Pain	
Baseline NRS-Pain	5.80 ± 1.99
Duration of psoriasis (years)	23.95 ± 11.19
50% improvement of NRS-Pain at 3 months (%)	65.0% (n = 13)
50% improvement of NRS-Pain at 6 months (%)	60.0% (n = 12)
EQ VAS	
Baseline EQ VAS	63.00 ± 13.80
EQ VAS at 3 months	81.25 ± 10.50
EQ VAS at 6 months	80.00 ± 12.46
% EQ VAS improvement at 3 months	18.25 ± 12.70
% EQ VAS improvement at 6 months	80.00 ± 12.46
PASI	
Baseline PASI	24.32 ± 11.42
PASI at 3 months	3.07 ± 3.13
PASI at 6 months	3.50 ± 5.49
PASI75 at 3 months	90.0 % (n = 18)
PASI75 at 6 months	90.0% (n = 18)

DNA was obtained from 3 mL of peripheral blood using the MagNa Pure® System (Roche Applied Science, Penzberg, Germany). Ten polymorphisms were analysed with Illumina Veracode genotyping platform (Human Genotyping Unit; CeGen, Madrid, Spain): rs1061622 and rs1061624 (*TNFRSF1B*); rs767455 (*TNFRSF1A*), rs610604 and rs6920220 (*TNFAIP3*); rs17728338 (*TNIP1*); rs361525 (*TNF*(*-238*)); and rs240993, rs33980500 and rs13210247 (*TRAF3IP2*). Furthermore, three SNPs, rs1800629 (*TNF*(*-308*)), rs1799724 (*TNF*(*-857*)) and rs1799964 (*TNF*(*-1301*)), were genotyped as described previously in.[7] Linkage disequilibrium, Hardy–Weinberg equilibrium (HWE), allele and genotype frequencies were calculated with SNPStats. Every SNP was tested to determine which logistic regression model had the best adjustment thus exhibiting the lowest Akaike information criterion (AIC). Significant SNPs in the univariate analysis ($P \leq 0.05$) were included in a multivariate logistic regression model (SPSS v19).

Our population included 20 patients with moderate-to-severe plaque psoriasis and PsA treated with anti-TNF drugs (Table 1). Initially, we tested whether the genotyped SNPs were associated with an improvement in PsA based on NRS-Pain50. At 3 months, univariate analysis showed a significant association of NRS-Pain50 with rs1061624 (*TNFRSF1B*) and rs6920220 (*TNFAIP3*) and with rs6920220 (*TNFAIP3*) at 6 months. However, these associations were lost in the multivariate analysis. Furthermore, we searched for biomarkers of patients' quality of life improvement after treatment. Two SNPs: rs610604 and rs6920220 (*TNFAIP3*) were significantly associated with %EQ-VAS at 3 months both in the univariate and multivariate analysis. rs610604 (*TNFAIP3*) was also significantly associated with %EQ-VAS at 6 months in the univariate analysis (Table 2). Although we also searched for biomarkers of psoriasis improvement, no significant association was found between PASI75 and the genotyped SNPs at 3 months. In contrast, significant association of PASI75 with polymorphisms of four genes as follows: *TNFRSF1B*,

Table 2 Summary of the results of univariate and multivariate logistic regression for the percentage of improvement in the EQ-VAS at 3 and 6 months (n = 20)

Months	SNP	Gene	Model	Risk genotype (mean of the difference of EQ-VAS)	Univariate analysis		Multivariate analysis	
					Difference (95% CI)	P	Difference (95% CI)	P
3	rs610604	*TNFAIP3*	D	AC/CC (13.85)	−12.58 (−23.07 to −2.10)	0.030*	−10.60 (−20.71 to −0.48)	0.041*
3	rs6920220	*TNFAIP3*	R	AA (−10.00)	−29.74 (−52.09 to −7.39)	0.018*	−25.83 (−47.969 to −3.698)	0.025*
6	rs6920220	*TNFAIP3*	R	AA (−30.00)	−49.47 (−70.91 to 28.04)	0.000*	–	–

*$P \leq 0.05$.

Only polymorphisms significant for the univariate analysis ($P < 0.05$) are shown and were included in the multivariate analysis. Only one SNP was significant in the univariate analysis for the percentage of improvement in the EQ-VAS at 6 months (rs6920220). Thus, multivariate analysis could not be performed.

CI, confidence interval; D, dominant; Difference, difference of the baseline EQ-VAS with respect to EQ-VAS at 3 months of treatment; R, recessive; SNP, single nucleotide polymorphism; *TNFAIP3*, TNF alpha-induced protein.

TNFAIP3, *TNF[(-238)*, (*-857*) and (*-1031*)], and *TRAF3IP2* was found at 6 months only in the univariate analysis.

There are few pharmacogenetic studies in PsA.[8,9] Our results agree with a previous study showing an association of rs610604 (*TNFAIP3*) with etanercept response in psoriasis.[10] We did not find an association between polymorphism located on *TNF* [(*-238*) and (*-308*)] and response to anti-TNF drugs, in agreement with a previous publication[9] (n = 57).The main limitation of this study is the sample size. Furthermore, in daily practice, the parameters used to evaluate the severity of PsA (NRS-Pain and EQ-VAS) have some limitations.

In conclusion, our findings suggest that rs6920220 and rs610604 (*TNFAIP3*) are associated with an improvement in the quality of life of PsA patients receiving anti-TNFs. Further studies should be performed to confirm these results.

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Cervical cutaneous sclerosis: the stomach is not far from the skin

Editor

Here in, we report a particular case presenting an erythematous and indurated plaque of the neck that has revealed gastric linitis plastic (GLP).

An 80-year-old man presented to the Department of Dermatology in November 2015 with a 2-month history of a sclerotic inflammatory infiltration of the skin located on the anterior cervical region (Fig. 1a,b) associated with a general impaired condition. Medical history revealed a partial gastrectomy for peptic ulcer 30 years ago. A punch biopsy specimen was performed, and the associated histologic findings are shown in Fig. 2a,b,c.

Histological examination of the skin showed an interstitial infiltrate dissociating collagen fibres in the dermis consisting of independent, atypical and mucus-secreting cells – signet ring cells (SRCs). Immunochemistry revealed a $CK7^{+}$ $CK20^{-}$, $CK19^{+}$, thyroid transcription factor (TTF) 1- phenotype profile evocative of dermo-hypodermic cutaneous metastasis of a poorly differentiated adenocarcinoma within dependent mucus-secreting cells or GLP (Fig. 2c). These findings were similar with those found on the gastric biopsy. CT scan showed gastric diffuse circumferential wall thickening (Fig. 1c). Gastric endoscopy revealed diffuse and intense erythematous stiff gastric mucosa with several superficial erosions; biopsy-confirmed diagnosis of GLP. The patient also presented bone metastasis and peritoneal carcinomatosis. The first-line treatment of 5-fluorouracil (5FU) with oxaliplatin (10 cycles) followed by 5FU maintenance resulted in both rapid radiological and clinical response. However, the patient died due to sepsis 9 months later.

This case reports an erythematous and indurated plaque of the neck that has revealed GLP. GLP represents 3%–19% of gastric cancers.[1] It is a macroscopic entity characterized by a whitish

