

## **Supplementary material**

We collect in Table S1 the most relevant personal history and comorbidities of the patients and controls included in the study. Personal history was recorded in healthy controls; however, no complementary tests or examinations were carried out to confirm the existence of complementary associations since this was not one of the objectives of this investigation. Therefore, we only analyze statistically significant associations between dermatological findings and comorbidities with a higher than expected prevalence in the pediatric population not affected by NF1.

### **Analysis of statistically significant associations of NA.**

For NA, a statistically significant association was found with FASI in cerebral MRI ( $p$  0.025). The value of the Odds ratio (OR) = 4.5 ( $p$  0.036), showing an increase of 4.5 times the probability of presenting hypersignals in the patients in whom we observed NA (Table S2). The associations between NA and HM ( $p$  0.004), atopic dermatitis ( $p$  0.003), and epilepsy (0.013) were statistically significant. However, in the three variables the direction of the association was negative (OR <1). The presence of NA is associated with a lower probability of developing HM, atopic dermatitis, or epilepsy. (Table S3).

### **Analysis of statistically significant associations of the JXG**

In none of the patients with JXG, there were alterations in the hemogram or physical findings suggesting an associated hematological neoplastic process. None of the patients in our series, nor the controls, had been diagnosed with leukemia or any other lymphoproliferative process before, or during the study period. No statistical association could be established between NF1, JXG, and leukemia. However, a statistically significant association was found with CNS malformations ( $p$  0.025). The OR value = 4.24 ( $p$  0.038), demonstrating a 4.24-fold increase in the probability of presenting CNS malformations in patients. patients in whom we observed JXG (Table S4).

The associations between the JXG and the hyperintense signals ( $p$  0.037) were statistically significant. However, the direction of the association was negative ( $OR < 1$ ), so the presence of JXG is associated with a lower probability of FASI in the cerebral MRI. The association between JXG and attention deficit hyperactivity disorder (ADHD) was statistically significant ( $p$  0.04). The OR and the direction of the association could not be calculated as there was a value of 0 in one of the cells. The analysis of the contingency table suggests a lower probability of presenting ADHD among patients with JXG (Table S5)

Using the Pearson  $\chi^2$  test, the existence of an association between the JXG and the phototype was noted ( $p$  0.025), however, the OR value (0.51) of this association was not significant ( $p$  0.191).

# Tables Supplementary

Table S1. Personal history of patients and controls

Non Dermatological Background		NF1 patients n, (%)	Controls n, (%)
<b>Digestive</b>	Celiac Disease	4, (3,7)	2, (1,46)
<b>Cardiovascular</b>	High blood pressure	6, (5,6)	NV
	Cardiac Malformations	7, (6,5)	1, (0,73)
<b>Neurological</b>	Tumors	5, (4,6)	0
	CNS Malformations (arachnoid cysts, Malf. Chiari, etc)	13, (12)	0
	Vascular tumors	3, (2,8)	0
	Epilepsy	11, (10,2)	0
	Headache	11, (10,2)	3, (2,2)
<b>Musculoskeletal</b>	Scoliosis	12, (11,1)	NV
	Pectus excavatum/carinate	9, (8,3)	0
<b>Size</b>	Down	34, (31,5)	NV
	Elevated	10, (9,3)	NV
<b>Macrocephaly</b>	Relative	12, (11,1)	NV
	> p90	30, (27,8)	NV
<b>Psychomotor-learning deficit</b>	Attention Déficit hyperactivity disorder (ADHD)	24, (22,2)	NV
	Language deficit	5, (4,6)	NV
	Learning deficit	9, (8,3)	NV
	Motor Deficit - Gear	4, (3,7)	NV

NV: Not valued.

Table S2 Table contingency NA / FASI in cerebral MRI

		FASI		
		No	Yes	totals
NA	No	5	20	25
	Yes	4	72	76
	totals	9	92	
Pearson chi <sup>2</sup> = 5.0333 p = 0.025, OR = 4.5 (p = 0.036).				

Table S3 Other statistically significant associations of NA

Hypopigmented macules					Atopic dermatitis				Epilepsy			
NA	No	18	8	26	No	19	7	26	No	20	6	26
	Yes	75	7	82	Yes	77	5	82	Yes	77	5	82
	totals	93	15	108	totals	96	12	108	totals	97	11	108
	Pearson chi <sup>2</sup> = 8,1587. p = 0.004, OR = 0,21 (p = 0.007).				Pearson chi <sup>2</sup> = 8,6686. p = 0.003, OR = 0,17 (p = 0.007).				Pearson chi <sup>2</sup> = 6,2214. p = 0.013, OR = 0,22 (p = 0.020).			

Table S4 Table JXG / CNS malformations.

CNS malformations				
		No	Yes	totals
JXG	No	86	9	95
	Yes	9	4	13
	totals	95	13	108
Pearson $\chi^2 = 4,8975$ <b>p = 0.027, OR = 4.24 (p = 0.038).</b>				

Table S5. Other statistically significant associations of the JXG

FASI in cerebral MRI					ADHD			
JXG		No	Yes	totals		No	Yes	Totals
	No	6	83	89	No	71	24	95
	Yes	3	9	12	Yes	13	0	13
	totals	9	92	108	totals	84	24	108
Pearson $\chi^2 = 4,3430$ . p = 0.017, <b>OR = 0,21 (p = 0.049).</b>					Pearson $\chi^2 = 4,2226$ . p = 0.04, <b>OR =NV).</b>			