



Synchronic Systemic Aggressive Mastocytosis and Langerhans Cell Histiocytosis with BRAF p.N486_P490del

André Abdo, MD¹

Jean Francois Emile, PhD²

Philip Bachour, MD¹

Otávio Baiocchi, PhD¹

1- Lymphoma Center, Hospital Alemão Oswaldo Cruz, São Paulo, Brazil

2- University of Bologna, France

Agenda

- Case presentation (part 1) – ASM
- Case presentation (part 2)- LCH
- Points do discussion
- Conclusion

Case Presentation

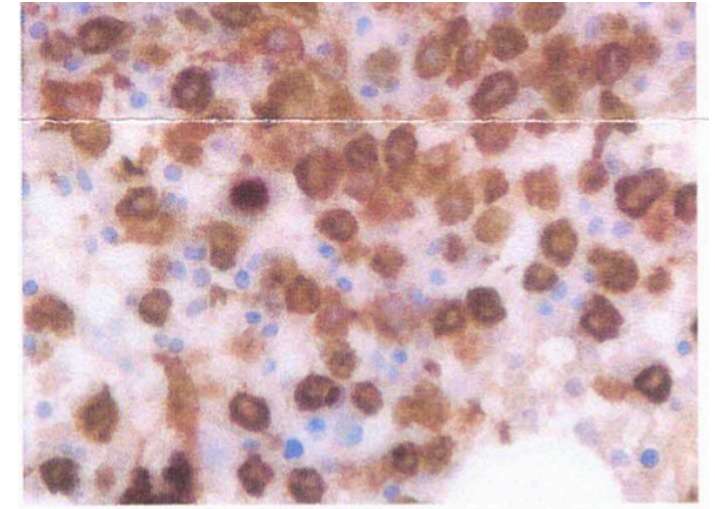
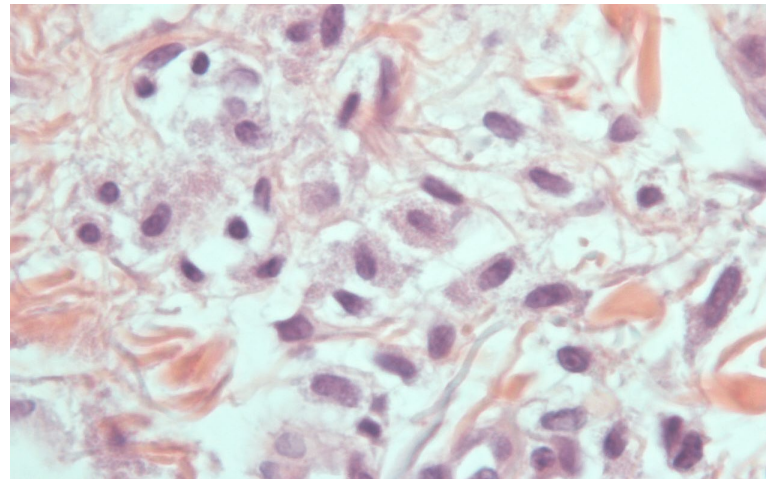
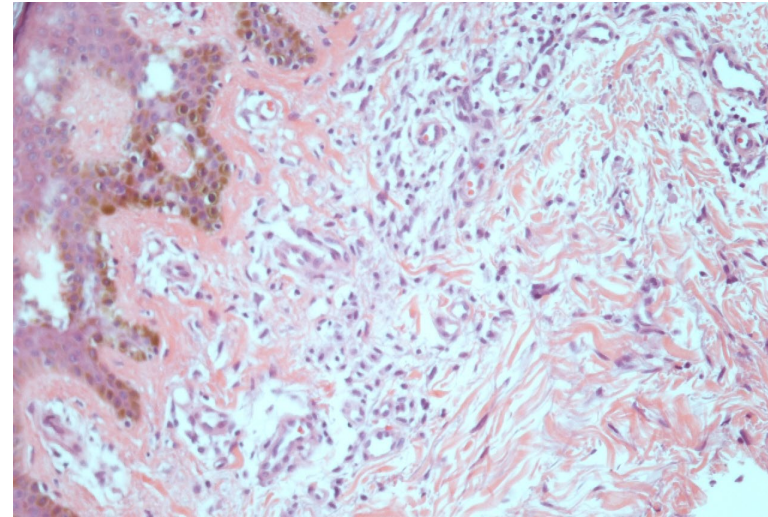
52 yof, born in Barretos-SP, married, catholic, G2P2A0

- No comorbidities

In Feb/2018 started to note some 'little spots' in the skin, with fast evolution, with pruritus and worsening after exposure to hot water

No other symptoms, and only after 1 year searching almost 10 dermatologists a biopsy was performed, and the diagnosis of Cutaneous Mastocytosis (UP) was done.

Case Presentation

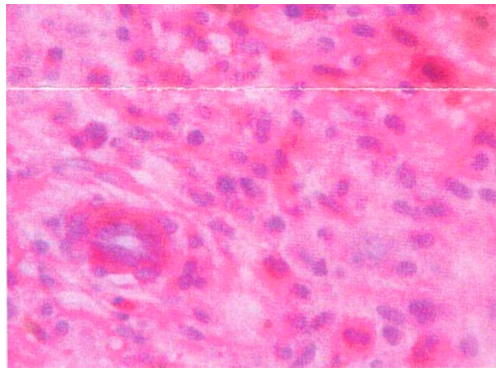


Diagnosis: Urticaria Pigmentosa

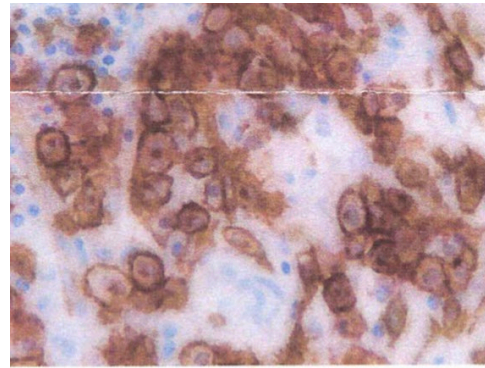
Case Presentation

Next 4 months patient got worsening with fatigue, fever, bone pain, weight loss and diarrhea.

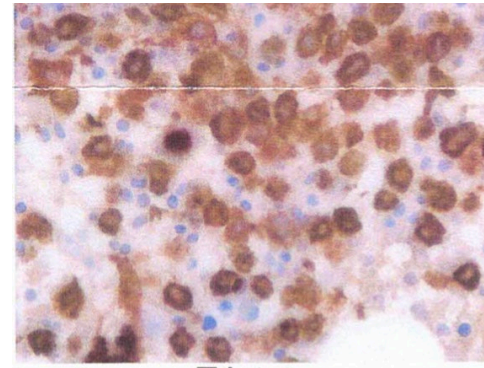
She was referred to a Hematologist and after a full investigation Aggressive Systemic Mastocytosis was concluded with involvement of bone marrow (and cytopenias), GI (with diarrhea) , disseminated lytic bone lesions and high tryptase levels.



HE



cKIT

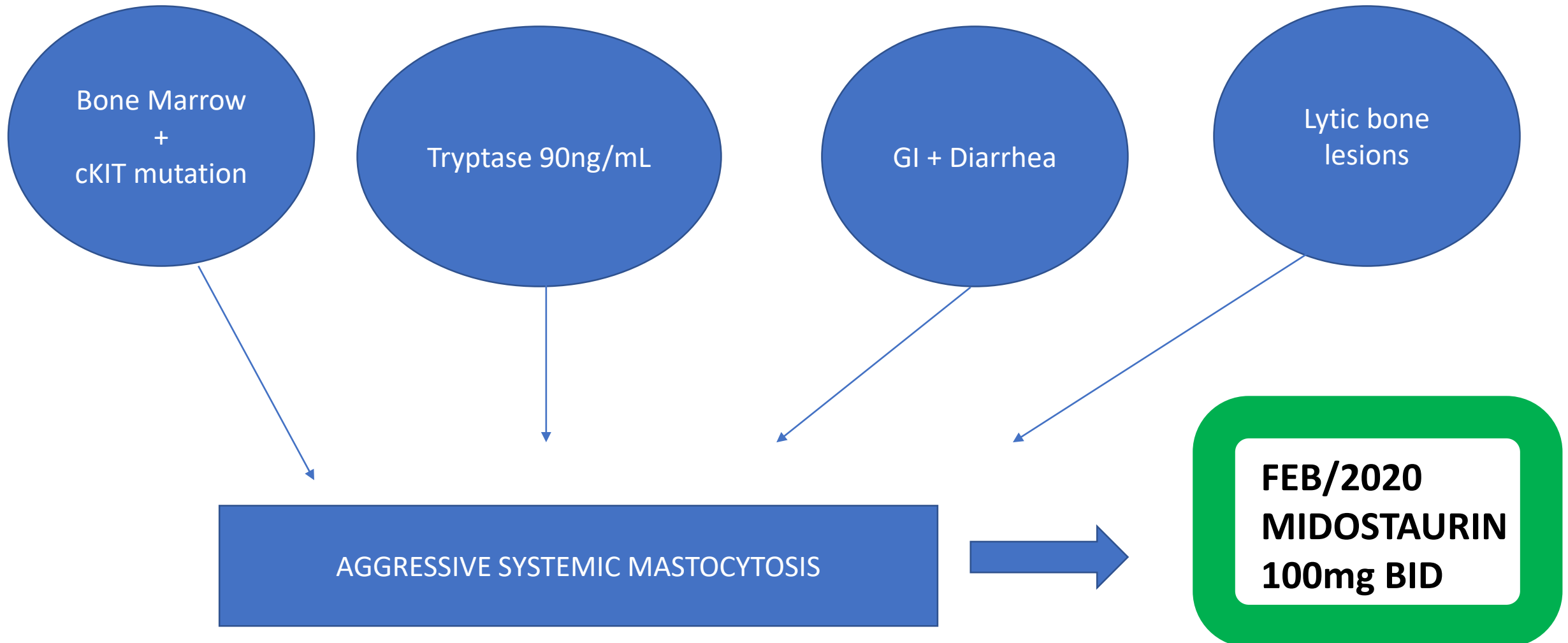


Tryptase

NGS Bone Marrow

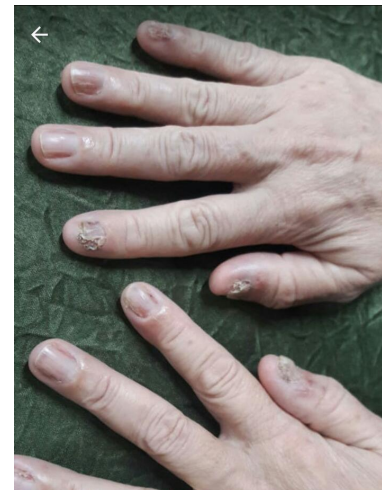
Gene	Variante	Medicamentos com potencial beneficio clínico
KIT	D816V	Midostaurin
TET2	V1395_C1396insL	-
TET2	c.4044+1>T	-

Case Presentation



Case Presentation

After 3 months on Midostaurin the patient started to present new skin lesions, including scalp (seborrheic dermatitis), onycholysis and deafness with otorrhea. No one of these new symptoms were due to Midostaurin toxicity and at this point her tryptase levels was 60ng/mL.



Case Presentation

AGGRESSIVE
SYSTEMIC
MASTOCYTOSIS

OTORRHEA AND
DEAFNESS

SCALP
DERMATITIS

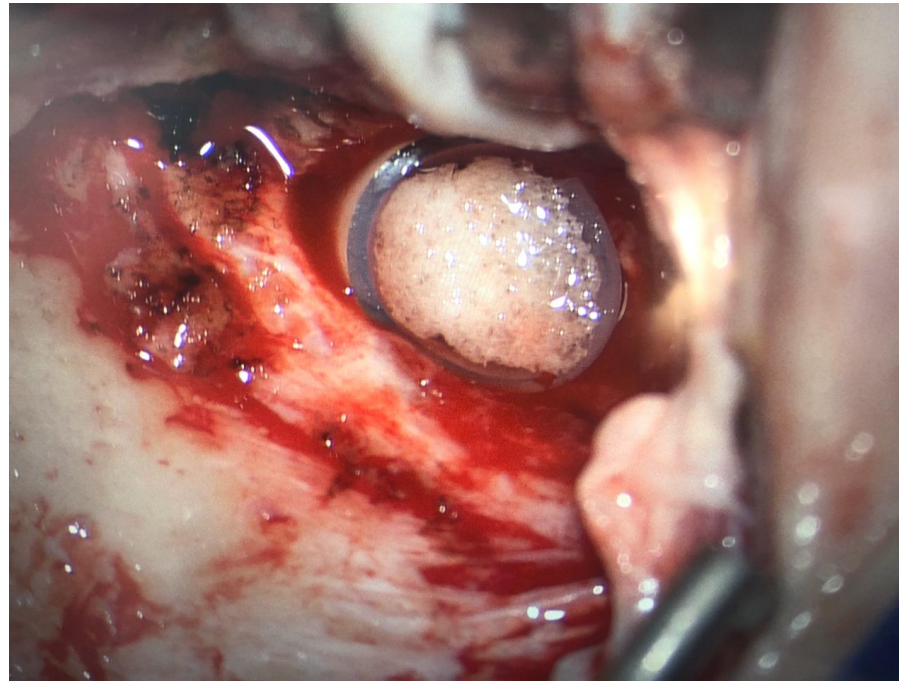
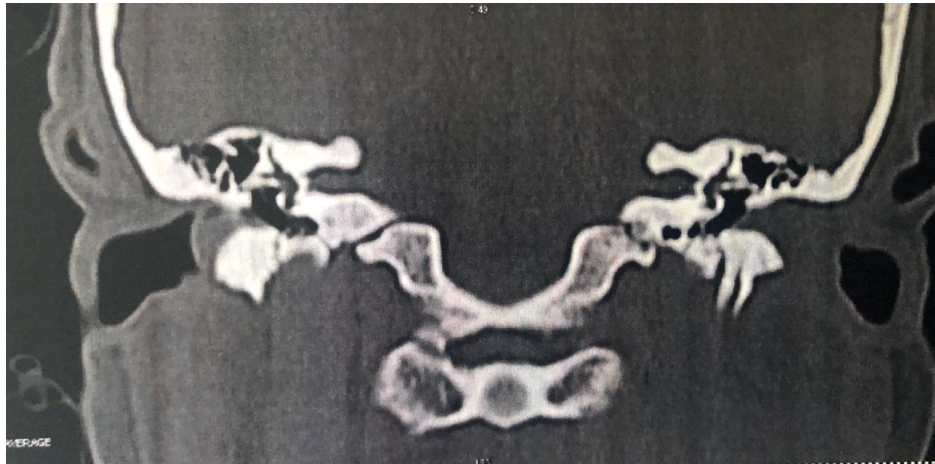
ONYCHOLYSIS

NEW IDEAS ARE WELCOME !!!



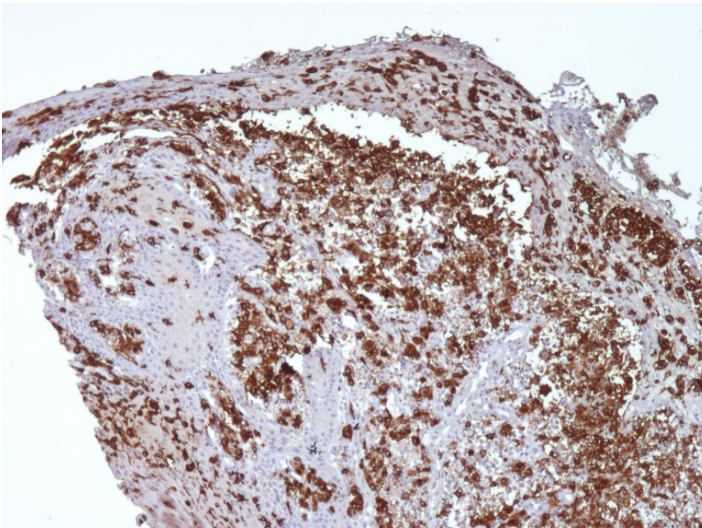
Case Presentation

In Aug/2019 a Video Otoscopy was performed with surgical biopsy and curettage and the soft mass was sent to pathology.

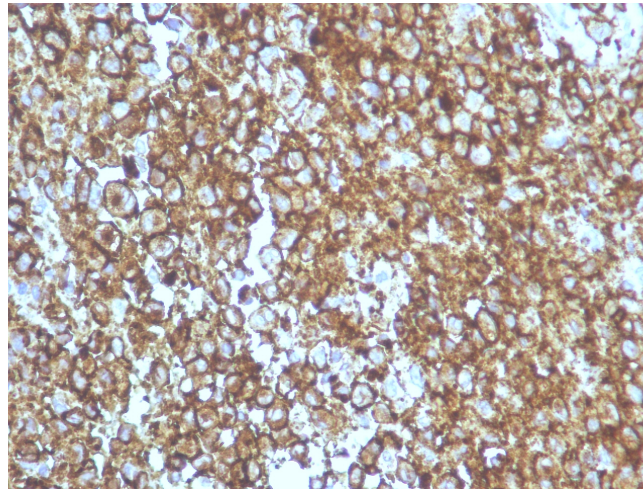


Case Presentation

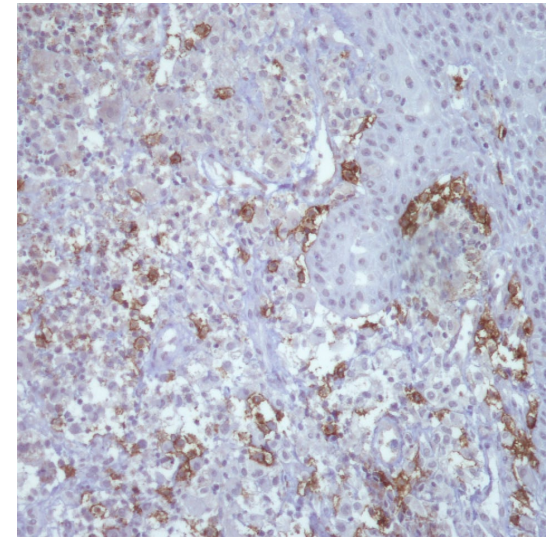
And the diagnosis was...



CD1a



CD1a 400x



CD117

***** BRAF V600E/K by PCR was NEGATIVE**

Case Presentation

We sent those samples do JFE for review and NGS...

... at this point the patient was extremely symptomatic with absolutely no response to Midostaurin for up to 7 months...

--- and so far we had ... Aggressive Systemic Mastocytosis AND Langerhans Cell Histiocytosis

In Nov/2020 after discussion with patient and Family, we started Cladribine 0.14mg/kg D1-D5 for 6 cycles.

Searching...

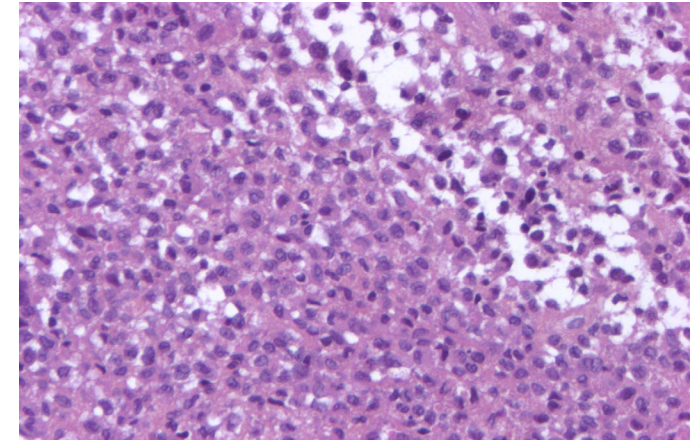
POL J PATHOL 2011; 2: 101-104

SYSTEMIC MASTOCYTOSIS (SM) AND ASSOCIATED MALIGNANT BONE MARROW HISTIOCYTOSIS – A HITHERTO UNDESCRIBED FORM OF SM-AHNMD

ZBIGNIEW RUDZKI¹, KARL SOTLAR², ANDRZEJ KUDELA³, JOLANTA STARZAK-GWÓŹDŹ³,
HANS-PETER HORNY⁴

Case Presentation

Prof JFE review and NGS... (ear soft tissue)

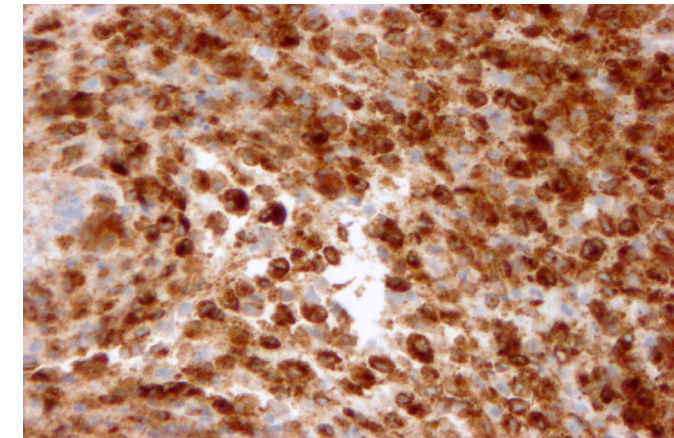


HE

Conclusion :

Altération() génétique(s) détectée(s) :

BRAF mutation de type : **c.1457_1471del, p.(486_490del)**, VAF* : 38.2%,
Séquences de référence *BRAF* : NM_004333.4



CD207

Langerhans Cell Histiocytosis with BRAF c.1457_1471del

Courtesy Prof JFE

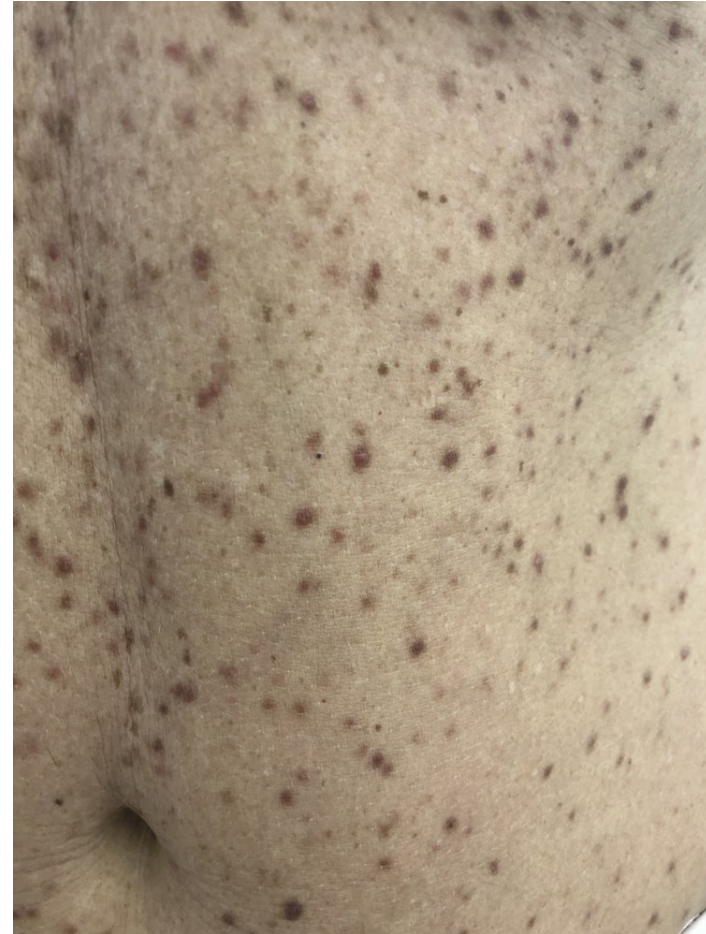
Case Presentation

After 6 cycles of Cladribine...

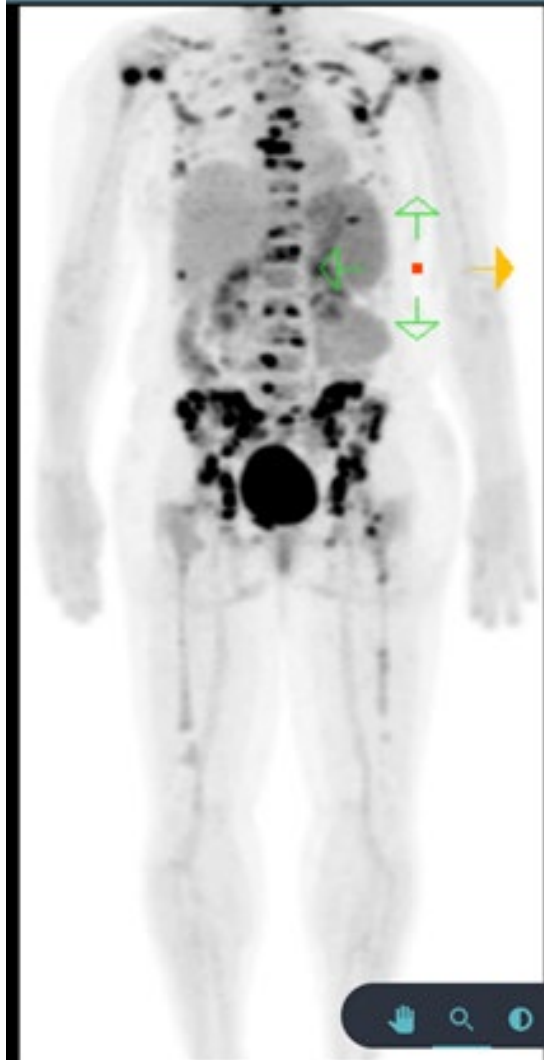
Tryptase <20ng/mL (normal range)

Improvement UP

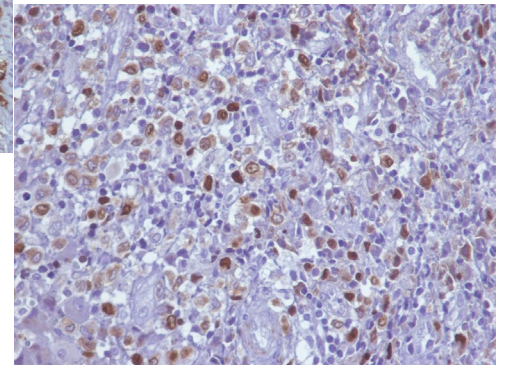
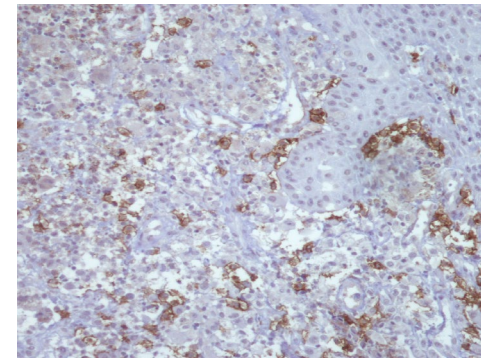
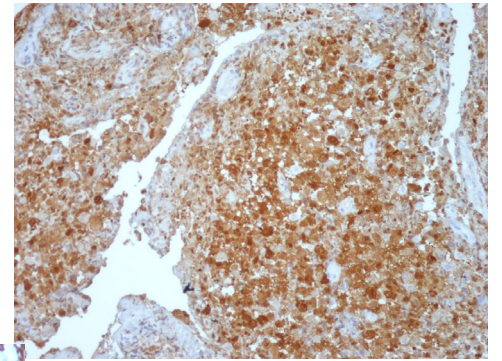
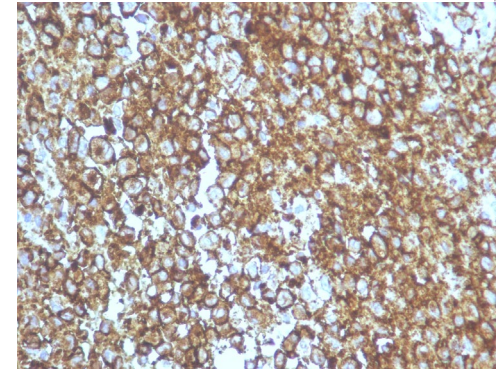
No more diarrhea



BUT



BONE MARROW BIOPSY



Case presentation – May/2021

Aggressive Systemic Mastocytosis in CR Mulisystemic Langerhans Cell Histiocytosis Refractory



Received: 27 July 2020 | Revised: 15 August 2020 | Accepted: 3 September 2020

DOI: 10.1002/pbc.28712

ONCOLOGY: BRIEF REPORT


Pediatric
Blood &
Cancer



aspho
The American Society of
Pediatric Hematology/Oncology

WILEY

Langerhans cell histiocytosis with *BRAF* p.N486_P490del or *MAP2K1* p.K57_G61del treated by the MEK inhibitor trametinib

Yoav H. Messinger¹  | Bruce C. Bostrom¹  | Damon R. Olson² | Nathan P. Gossai¹ |
Lane H. Miller¹  | Michael K. Richards¹

Case presentation

In June/2021 we started Trametinib 1mg daily

1 month after: No more fatigue, No more dermatitis, Recovery almost all hearing, No more bone pain... Went to GYM...

- Keep no sign (clinical and tryptase) of Mastocytosis

Have developed grade 2 acneiform eruption on face (good response to topical steroids)

Last follow up ... Sep/2021



3 months Trametinib



Last follow up ... Oct/2021



Some points to discussion, more doubts

- this is the first (in our knowledge) case with Synchronic ASM and MS-LCH
- ASM : TET-2 and KIT mut + MS-LCH : BRAF non V600E/K mut
- Are they spectrum from a common myeloid progenitor?
- Is MS-LCH in this case a SM-AHNMD?

Conclusions

- Rare presentation on rare diseases... We need to share data
- and Probably BEM (Clinical trial) would be replaced for precision medicine
- Genomic/molecular information was the turning point in this case
- Partnership is indisputably important for low income countries

Thank you

Special thanks to:

CGP (the patient) and her Family

Jessi and Kathy (ECDGA)



Lymphoma and Myeloma Center



Prof JF Emile



Prof Otavio Baiocchi



Dr Philp Bachour

