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LABORATOIRE CMNN MONASTIR

Constitutional asprin-like defect: about a case

PN°: 220

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BACKGROUND

- ✓ With their exceptional structural and functional features, platelets play critical roles in hemostasis.
- ✓ Qualitative platelet dysfunctions result in thrombocytopathies variously characterized by defects of their adhesive and procoagulant activation endpoints.
- ✓ These disorders present with mucocutaneous bleeding and excessive bruising with an adequate platelet count, PT, and aPTT and normal screening tests for vWD.
- ✓ Amongst these disorders, we distinguish aspirin-like defect (ALD) which is a rare dysfunction of the intraplatelet arachidonic acid (AA) pathway leading to impaired thromboxane A2 signaling.

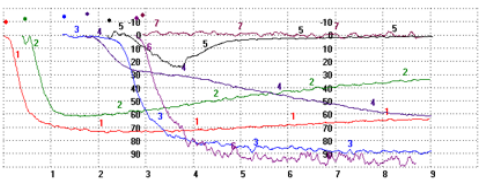
CASE REPORT

- 9 years old boy of a 2nd degree consanguineous marriage.
- **Medical history:** hypertrophic cardiopathy, a sub-valvular aortic stenosis, **recurrent epistaxis** since the age of two and no current or previous intake of any non-steroidal anti-inflammatory drugs.
- **Reason for consultation** : exploration of a prolonged PFA-200 closure times (Col/EPI = 187s > 182s and COL/ADP > 162 s).

Laboratory findings :

1. **CBC :** normal **platelet count** (178 G/L) and **MPV** (10,2 fl).
2. **Hemostasis global tests** : **PT** = 70% , **kCTT** = 31s/33s (ratio =0,9), **Fg** = 3,16 g/L.
3. **Specialized coagulation testing** : **vWF:Rco** = 79%, **vWF:Ag** = 139.1%, **F VIII activity** = 161%
4. **Light transmission aggregometry** → platelet aggregation response (PAR) to AA, adenosine diphosphate (ADP), collagen, epinephrine and ristocetin → **impaired PAR to AA** and platelet **disaggregation** following their stimulation with 2 different concentration of **ADP** (**Figure 1**).

→ **Constitutional asprin-like defect**



ID Number	Date	Test Type	Details	PA	PS	SA	SS	ADC*	LP	DA	MA	FA
07052024	07/05/2024	ADP	10	73	64	0	0	595	0	9	73	64
07052024	07/05/2024	ADP	5	61	56	0	0	394	0	28	61	34
07052024	07/05/2024	Collagen		89	52	0	0	525	55	0	89	89
07052024	07/05/2024	Epinephrine		61	19	0	0	298	0	0	61	61
07052024	07/05/2024	AA		23	13	0	0	38	28	23	23	0
07052024	07/05/2024	RIPA		97	54	0	0	493	0	0	97	95
07052024	07/05/2024	Spontaneous Agg		1	0	0	0	4	0	0	1	0

Figure 1 : Patient's platelets in vitro function with impaired PAR to AA

DISCUSSION

- ✓ ALD is a rare, mostly autosomal dominant inherited dysfunction of the intraplatelet AA.
- ✓ Most reported mutations affects the prostaglandin endoperoxide synthase 1(PTGS1) which reproduces the selective anti-platelet effect of aspirin **[1].**
- ✓ To confirm the diagnosis of ALD, it is suggested to measure the serum TXB2 as mandatory for ALD diagnosis and phenotypic classification because it selectively and specifically reflects the activities of all the enzymes involved in the AA pathway (PLA2, COX-1,TX synthase) **[2].**
- ✓ AA induced aggregation is suggested as an optional method and he PFA and ADP aggregometry are excluded diagnostic criteria **[2].**

CONCLUSION

- ALDs are a group of heterogeneous and poorly defined disorders
- The lack of definition and reference assays for ALDs, leads to the underdiagnosis of this condition.

REFERENCES

[1] : Chan and al, Identification of a homozygous recessive variant in *PTGS1* resulting in a congenital aspirin-like defect in platelet function, 2021
[2] : Dragani and al, Clinical and laboratory phenotype associated with the aspirin-like defect. 2010