"Activated PI3K Delta Syndrome in a Pediatric Patient: A Case Report on Diagnosis and Management"

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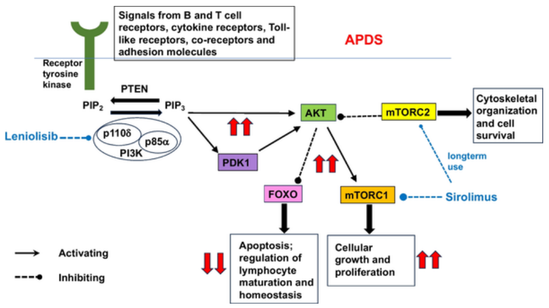
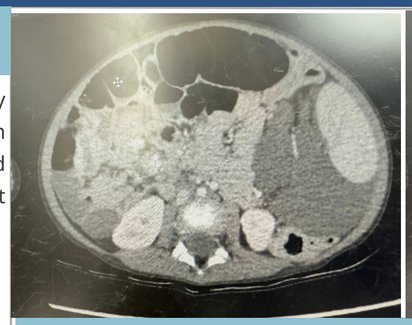
BACKGROUND

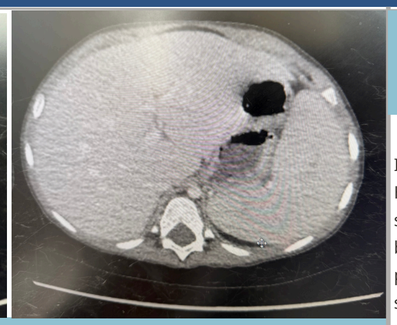
Activated PI3K Delta Syndrome (APDS) is a rare inborn error of immunity caused by pathogenic variants in the PIK3CD or PIK3R1 genes. It presents with recurrent infections, lymphoproliferation, autoimmunity, and an increased risk of malignancy. Without prompt diagnosis and treatment, APDS can result in severe complications and high mortality.



CASE REPORT

- The patient exhibited chronic diarrhea, significant growth retardation, and generalized weakness.
- On physical examination, hepatosplenomegaly were noted.
- Laboratory analysis revealed anemia and thrombocytopenia, as well as T CD4 lymphopenia with normal serum immunoglobulin G, A, and M levels.
- Imaging studies, including ultrasound and CT, revealed hepatomegaly, splenomegaly, and an abdominal tumor of unknown etiology. MRI findings were pending at the time of this report.
- Biopsy of the ileum and colon demonstrated malakoplakia, an unusual histopathological finding that may suggest underlying immune dysregulation.
- Veritas Primary Immunodeficiency Gene Panel revealed...* revealed a heterozygous pathogenic variant, c.3061G>A (p.Glu1021Lys), in the PIK3CD gene, confirming the diagnosis of APDS.
- Based on the clinical and genetic findings, treatment included monthly intravenous immunoglobulin (IVIG), everolimus to control lymphoproliferation, and antibiotic prophylaxis. The patient is under evaluation for hematopoietic stem cell transplantation (HSCT), a potentially curative option.





IMMUNE EVALUATION

IgG	1384 mg/dl
IgA	110 mg/dl
IgM	304 mg/dl
IgE	54 IU/ml

CD3	62.37% (912 cells/uL)
CD4	21.03% (307 cells/uL)
CD8	35.99% (526 cells/uL)
CD19	20.66% (302 cells/uL)
CD56	16.97% (248 cells/uL)
CD4/CD8	0.58

BIOPSY

Ileal biopsy:
Histochemical findings show Michaelis Gutmann's bodies which are also positive for Van Kossa's staining, compatible with malakoplakia.

ENDOSCOPY COLONOSCOPY

ENDOSCOPY
- ANTRAL NODULAR GASTROPATHY
- NODULAR DUODENITIS
- GASTRIC VASCULAR MALFORMATION: LIKELY ANGIODYSPLASIA

COLONOSCOPY:
- SEVERE PANCOLITIS: D/C TB VS IBD
- NODULAR ILEITIS

GENETIC EVALUATION

Primary Immunodeficiency gene panel (Veritas, Spain): Heterozygous pathogenic variant c.3061G>A (p.Glu1021Lys) in PIK3CD, VUS in ARHGEF1, ARPC1B, BRCA2, CSF2RB, DNAH11, DSG1, KLHDC8B, KMT2A, LCK, PRKDC, PUS1, RANBP2, RNF31, TCF3, TTC37, ZNF341

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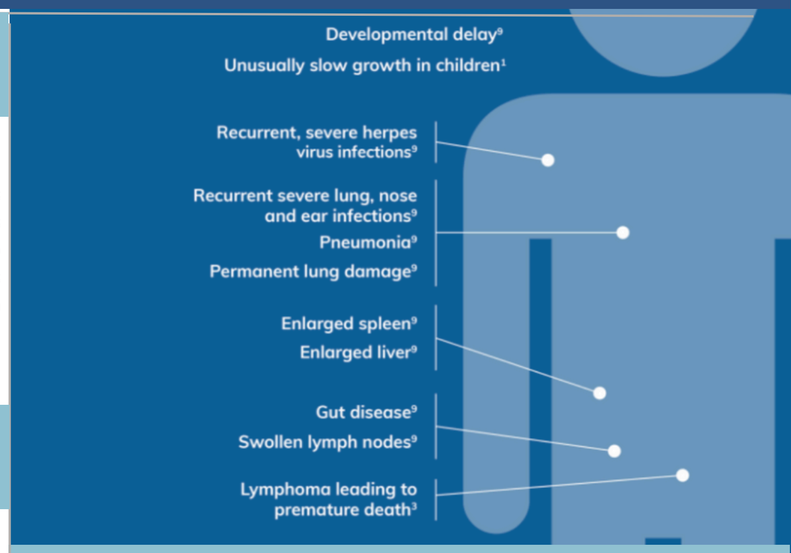

DISCUSSION AND CONCLUSION

- APDS is a challenging condition to diagnose due to its variable presentation.
- This case highlights the importance of genetic testing in patients with unexplained immune dysfunction and lymphoproliferative features. The finding of malakoplakia in this patient is notable and underscores the spectrum of immune dysregulation associated with APDS.
- The use of everolimus reflects an evidence-based approach to managing lymphoproliferation, as supported by emerging literature. HSCT remains the only curative therapy for APDS, but it is associated with significant risks.
- Early initiation of supportive treatments, such as IVIG and prophylactic antibiotics, is crucial while evaluating candidates for transplantation.
- Our team at Hospital Nacional Edgardo Rebagliati Martins remains committed to improving the diagnosis and management of inborn errors of immunity.

REFERENCES

- Berglund, L.J. Modulating the PI3K Signalling Pathway in Activated PI3K Delta Syndrome: a Clinical Perspective. J Clin Immunol 44, 34 (2024). https://doi.org/10.1007/s10875-023-01626-0
- Activated PI3K Delta Syndrome: http://www.immunodeficiencyuk.org/static/media/up/IPOPIADPS.pdf (accessed June 2022).