



The first reported death of iNKLPD-GI: rethinking “watch and wait” strategy

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A 66-year-old man without underlying diseases was admitted due to 2-year diarrhea and 2-month progressive abdominal distension, with reduced exhaust and defecation. The male presented with marasmus, protuberant abdomen and attenuated bowel sounds. Laboratory tests showed decreased lymphocyte of 480 cells per μL , haemoglobin of 8.6 g/dL and prominent hypoalbuminemia of 20 g/L, with normal

blood smear, urinary protein and liver function. The whole-body enhanced CT with enterography revealed remarkable expansion of whole small intestine and gas-liquid level, without intestinal stenosis and extraintestinal involvement (*Figure 1*). ⁹⁹Tcm-labelled human serum albumin scintigraphy confirmed diffuse protein loss from small intestine (*Figure 2*). Gastroscopy and colonoscopy suggested

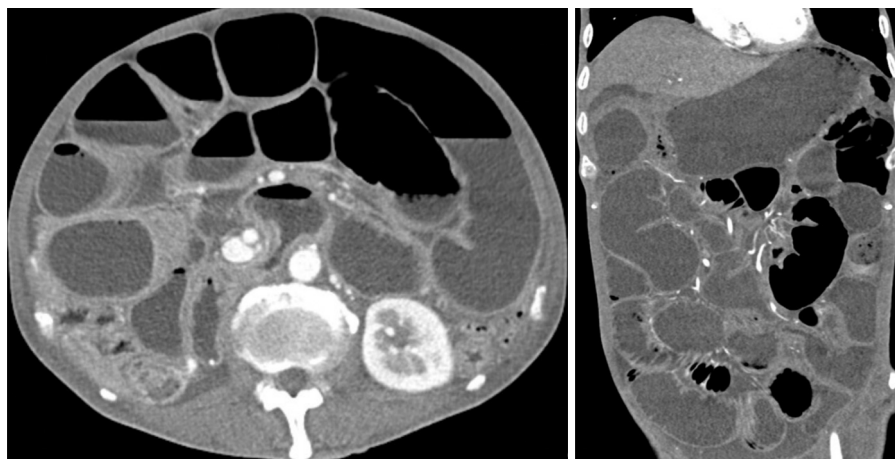


Figure 1 Computed tomography enterography showed remarkable expansion of whole small intestine with 5.4 cm in width and gas-liquid levels, with enhanced mucosa and no evidence of stenosis.



Figure 2 ^{99}Tcm -labelled human serum albumin scintigraphy revealed diffuse radioactive distribution in the abdominal cavity 5 hours after tracer injection.

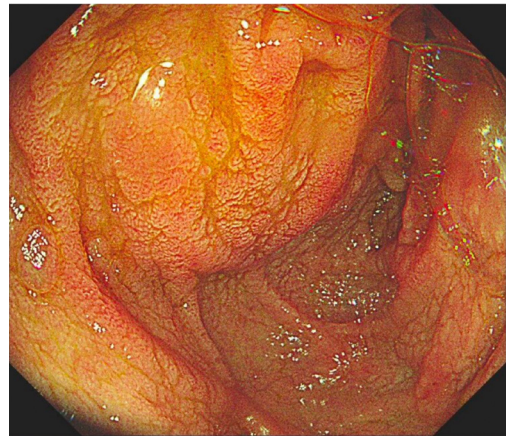


Figure 3 Gastroscopy indicated diffuse granular changes in the mucosa of duodenum.

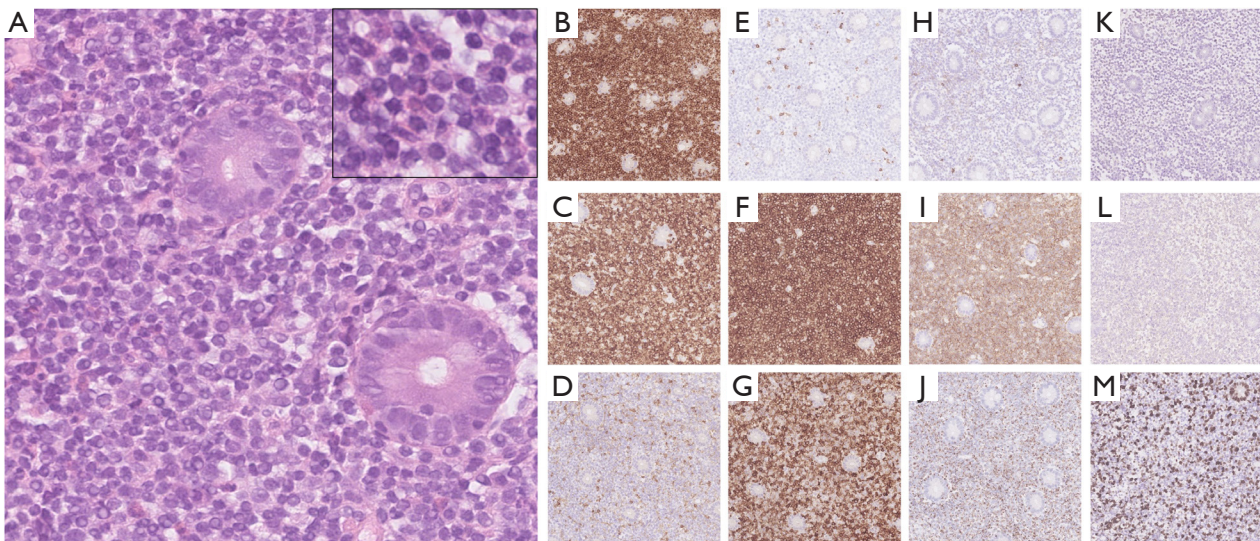


Figure 4 Atypical cells infiltrated the lamina propria and displaced the glands (A; HE, $\times 400$ magnification), paranuclear eosinophilic cytoplasmic granules could be seen in some cells (A inside; HE, $\times 800$ magnification). These tumor cells expressed CD2 (B), cytoplasmic CD3 (C), CD7 (F), CD8 (G), CD56 (I) and TIA1 (J), while negative for CD4 (D), CD5 (E), CD20 (H), TdT (K) and EBER (L), Ki-67 of about 40% (M) (B-M; $\times 200$ magnification). EBER, Epstein-Barr virus-encoded small RNA; HE, hematoxylin and eosin staining; TdT, terminal deoxynucleotidyl transferase.

diffuse granular changes in the mucosa of duodenum and terminal ileum (Figure 3). Multipoint biopsies showed medium to large size tumor cells in duodenum, terminal ileum and colon, with irregular nuclei, rare mitosis and apoptosis. Immunohistochemical stains confirmed indolent natural killer-cell lymphoproliferative disorder

of the gastrointestinal tract (iNKLPD-GI) (Figure 4). Analysis for T cell receptor (TCR) gene rearrangement was negative and next-generation sequencing (274 gene panel) revealed JAK3 K563_C565del mutation with 26.3% variant allele frequency. In spite of active conservative treatment, the male died of septicopyemia from gastrointestinal origin

due to persistence of severe dynamic bowel obstruction and protein loss enteropathy with diffuse involvement of small intestine and colon before the final biopsies came out. It is well recognized that iNKLPD-GI is a rare natural killer (NK) cell proliferative disorder with benign and self-limited course, and JAK3 mutations in partial patients (1,2). A “watch and wait” strategy is recommended (3,4). This case first reported “kindness” iNKLPD-GI with “evil” death behavior, calling for treatment strategy adjustment.

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Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article has undergone external peer review.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Written informed consent was obtained from the patient for publication of this manuscript and any accompanying image resources.

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