

CASE REPORT

Extranodal NK/T-cell lymphoma mimicking Crohn's colitis

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Abstract

Introduction: Extranodal NK/T cell lymphoma is a rare tumour, typically involving the upper aerodigestive tract. Even rarer is primary extranasal disease involving the skin, testis, soft tissue and gastrointestinal tract. **Case Report:** We report a case of a 46-year-old Chinese male who presented with six months history of abdominal pain, weight loss and rectal bleeding. Diagnostic colonoscopy revealed multiple aphthous ulcers within the ileo-caecal region and distal transverse colon, separated by normal mucosa, mimicking skip lesions of Crohn's colitis. Computer topography (CT) scan of the abdomen showed multiple circumferential thickenings involving predominantly the right colon. A clinical diagnosis of colonic Crohn's disease with possible perforation was made. An extended right hemicolectomy was performed due to uncontrolled rectal bleeding. Histopathology examination of the colon showed infiltration by malignant lymphoid cells associated with necrosis, angiocentricity and angiodestruction. Immunohistochemical studies confirmed T-cell monoclonality, presence of cytotoxic granules and Epstein-Barr virus (EBV) infection. A diagnosis of extranodal NK/T cell lymphoma of the colon was made. **Discussion:** These findings highlight that colonic NK/T cell lymphoma may clinically mimic other benign inflammatory lesions and should be one of the differential diagnoses in patients presenting with gastrointestinal lesions. The final diagnosis is only possible with appropriate histological and immunohistochemical studies.

Keywords: NK/T cell lymphoma, extranasal, gastrointestinal lymphoma, Crohn's colitis, EBV

INTRODUCTION

Extranodal NK/T cell lymphoma is an uncommon entity accounting for only 2% of non-Hodgkin lymphomas (NHL) in the West. The tumour is however more common among Asians and Latin-Americans making up to 8% of all NHL.¹ Primary gastrointestinal T-cell lymphomas are uncommon, accounting for less than 10% of gastrointestinal lymphomas and only about 0.2-0.4% of all malignant neoplasms at this site. Most colonic lymphomas are B-cell lymphomas, while T-cell lymphomas are typically seen in the small intestine.²

NK/T cell lymphoma is a predominantly extranodal lymphoma characterised by angiodestruction and coagulative necrosis, and is associated with EBV infection. Most commonly it occurs in the nasal cavity, nasopharynx, paranasal sinuses or palate, thus the synonym lethal midline granuloma. Less commonly,

NK/T cell lymphoma can manifest at extra-nasal locations such as the skin, soft tissue and testis.³

The colon is one such organ that is rarely involved by NK/T cell lymphoma.² The presenting complaints, clinical and colonoscopy examinations as well as radiology imaging of colonic NK/T cell lymphoma is non-specific and may mimic many other benign or malignant lesions. Due to the non-specific features of NK/T cell lymphoma, it is not uncommon that the diagnoses of mycobacterium infection, Crohn's disease, ulcerative colitis, carcinoma or other unusual infection are made. We describe a case of extranasal NK/T cell lymphoma presenting with colonic ulcerative lesions mimicking colonic Crohn's disease.

CASE REPORT

A 46-year-old Indonesian Chinese male with long standing Parkinson's disease presented with

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a 6-month history of passing mucous and blood per rectum, crampy abdominal discomfort and fever together with a weight loss of 10kg. He denied recent overseas travel or contact with tuberculosis. Physical examination revealed that the patient was thin and pale. There was no evidence of organomegaly and lymphadenopathy.

Routine blood tests revealed pancytopenia with a total white cell count of $4 \times 10^9/L$, haemoglobin of 10.2 g/dL and platelet count of $53 \times 10^9/L$. His renal profile showed hyponatraemia (129 mmol/L) and hypokalaemia (3.3 mmol/L) with normal urea level while liver function tests showed hypoalbuminaemia (26g/L), low total protein (55 g/L) and increased serum alkaline phosphatase (245 U/L). Serum bilirubin and transaminases were normal. C-reactive protein was increased to 5.70 mg/dL while serum erythrocyte sedimentation rate (ESR) was increased to 34mm/hr. A diagnostic colonoscopy was performed which showed multiple circumferential aphthous ulcerative lesions involving predominantly the ileo-caecal region. The aphthous ulcers were separated by

normal appearing mucosa, a finding that mimics skipped lesions in patient with Crohn's colitis (Fig. 1A). The lesions were biopsied and the patient was allowed home.

The following day, he presented to the emergency department with crampy abdominal pain along with profuse rectal bleeding. CT scan of the abdomen demonstrated eccentric and circumferential mural thickenings of the ileo-caecal region showing contrast blush, highly suspicious of tumoral bleed (Fig. 1B). Subsequently an emergency extended right hemicolectomy was performed. Gross examination of the hemicolectomy specimen showed multiple ulcers with heaped up edges measuring 15-30mm in diameter involving the ileum, caecum, ascending and transverse colon (Fig. 1C). The base of the ulcers was haemorrhagic, necrotic and covered by slough. The bowel wall was firm, thickened, and in areas showed luminal constriction. In between these ulcers, the uninvolved mucosa appeared unremarkable giving the appearance of 'skip lesions'.

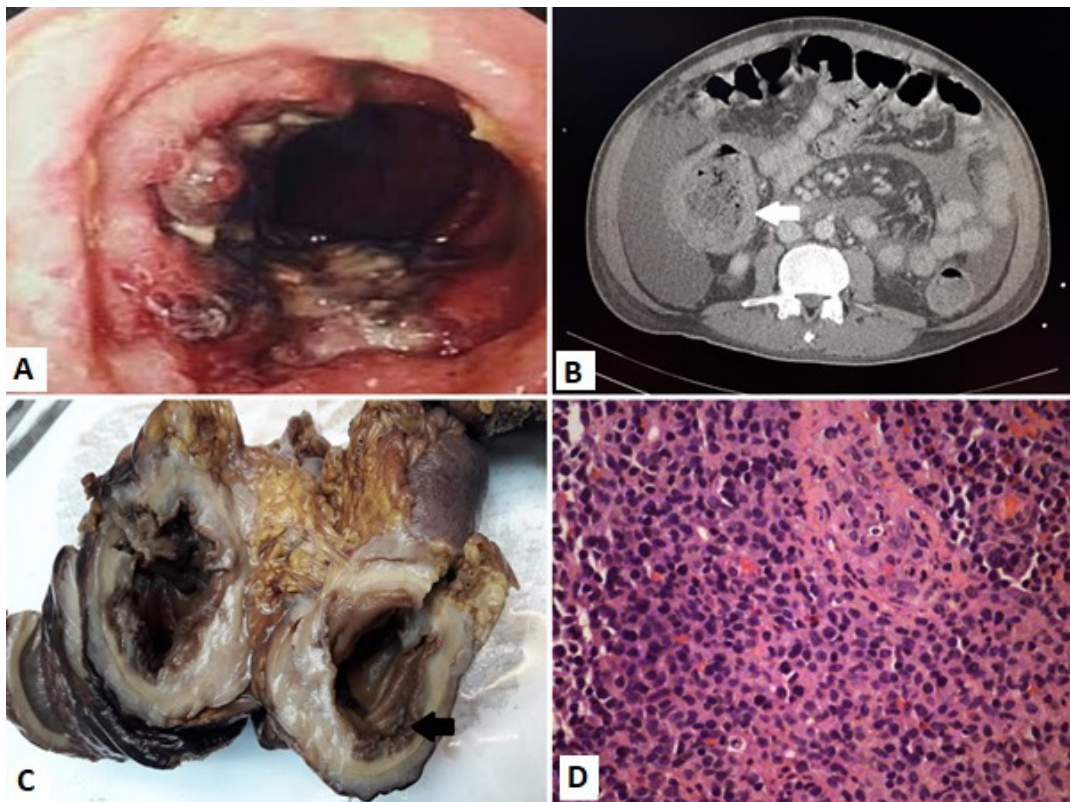


FIG. 1: (A) Colonic skip ulcers on colonoscopy. (B) CT abdomen showed circumferential mural thickenings of the colon (white arrow). (C) Macroscopic examination revealed thickened bowel wall and multiple ulcers (black arrow). (D) Microscopically there was diffuse dense lymphoid infiltrate with angiodestructive quality (H&E x600).

Microscopic examination revealed diffuse infiltration by malignant lymphoid cells involving the mucosa and submucosa, extending to the muscularis propria. The mucosa was ulcerated and abundant necrotic debris was present. The malignant cells were medium to large sized and exhibited hyperchromatic nuclei, inconspicuous nucleoli with scanty cytoplasm. Angiodestruction, angiocentricity and numerous mitotic figures were present (Fig. 1D).

On immunohistochemical examination, the malignant cells showed diffuse positivity for T-cell markers CD3 (Fig. 2A) and CD7 (Fig. 2B). There was aberrant loss of CD5 expression (Fig. 2C) and they were negative for CD56 (Fig. 2D). The malignant cells were mostly CD4 positive (Fig. 2E) and CD8 negative (Fig. 2F). They expressed TIA-1, a marker for cytotoxic granules (Fig. 2G). In situ hybridisation study was positive for Epstein-Barr virus (EBV)-encoded RNA (EBER) (Fig. 2H). Two out of 17 examined lymph nodes examined from the hemicolectomy specimen were also infiltrated by similar malignant cells. A diagnosis of extranodal NK/T cell lymphoma of the colon was made. Subsequently, the patient returned to Indonesia for continuation of treatment and received chemotherapy in his home country.

DISCUSSION

The World Health Organisation (WHO) defined NK/T cell lymphoma as a distinct lymphoma that expresses cytotoxic phenotypes and has association with Epstein-Barr virus (EBV).³ Typically NK/T cell lymphoma is a disease of the upper aerodigestive tract but rarely it can present at extranasal locations. The current case showed involvement of the gastrointestinal tract which is an unusual site of occurrence. It accounts for only 3% of all primary gastrointestinal Non-Hodgkin lymphomas⁴ and 7% of all NK/T cell lymphomas.⁵

One of the main differential diagnoses for this patient is an inflammatory bowel disease. However, the short duration of the presenting complaints make this diagnosis less likely. Moreover, the patient has severe constitutional symptoms typically observed in malignancy. It has been reported that for gastrointestinal NK/T cell lymphoma, the time interval between the onset of symptoms and the time of diagnosis ranged between 20 days to 3 years with a mean period of 6 months¹. Much like the present case, patients typically present with a wide range of non-specific complaints, the most common

being abdominal pain which can be associated with per-rectal bleeding, diarrhoea and fever. There may be complications such as perforation, bleeding, stricture and fistula.^{1,6}

In most instances, colonic lymphomas involve the caecum or ascending colon, followed by the rectum. However, in the present case the involvement is multifocal affecting the small intestine (ileum) and large intestine (caecum, ascending and transverse colon), which is rather uncommon.³ The ulcers were multiple and 'skipped', separated by uninvolved, normal intervening mucosa. Distinguishing it from Crohn's colitis was difficult. It has been reported that the ulcerative or ulcero-infiltrative lesions of NK/T cell lymphoma can indeed be unifocal, multifocal or diffuse, affecting the small bowel and right-sided colon more commonly than left colon.^{4,7} Less frequently, gut strictures and tumour masses may occur.⁷

Histologically the diagnosis of gastrointestinal NK/T cell lymphoma requires careful observation of the morphology and relevant use of ancillary studies. A diagnosis of lymphoma is suspected when there is diffuse effacement of the normal mucosa architecture associated with widely spaced or loss of mucosal glands³ due to malignant infiltrates which may extend into the submucosa and muscularis propria layer.⁷ There may be lympho-epithelial lesions¹ or the mucosal glands may be preserved and surrounded by the lymphoma cells.⁷ The atypical lymphoid cells are not necessarily large, as they can be medium-sized or small with irregular, folded nuclear membrane.³ The presence of coagulative necrosis, angiodestruction and angiocentricity are associated features typical of this tumour.

A panel of immunohistological markers and an evidence of Epstein-Barr virus infection are pertinent in the diagnosis of NK/T cell lymphoma. CD56 is an NK cell marker, and although it is not specific for NK/T cell lymphoma, it helps in the diagnosis as it is present in up to 60-100% of cases.⁴ However, CD56 can be negative in a proportion of cases as was shown in the present case. Virtually all cases of NK/T cell lymphoma demonstrate EBV infection, so much so that such a diagnosis should be accepted with scepticism if EBV is negative.³ T-cell lymphomas expressing cytotoxic molecules and positive EBV status even in the absence of CD56 expression are classified as NK/T cell lymphoma and they show similar outlook as those with CD56 positivity.³ On the other hand, absence of EBV even in the presence of all other features denies the diagnosis

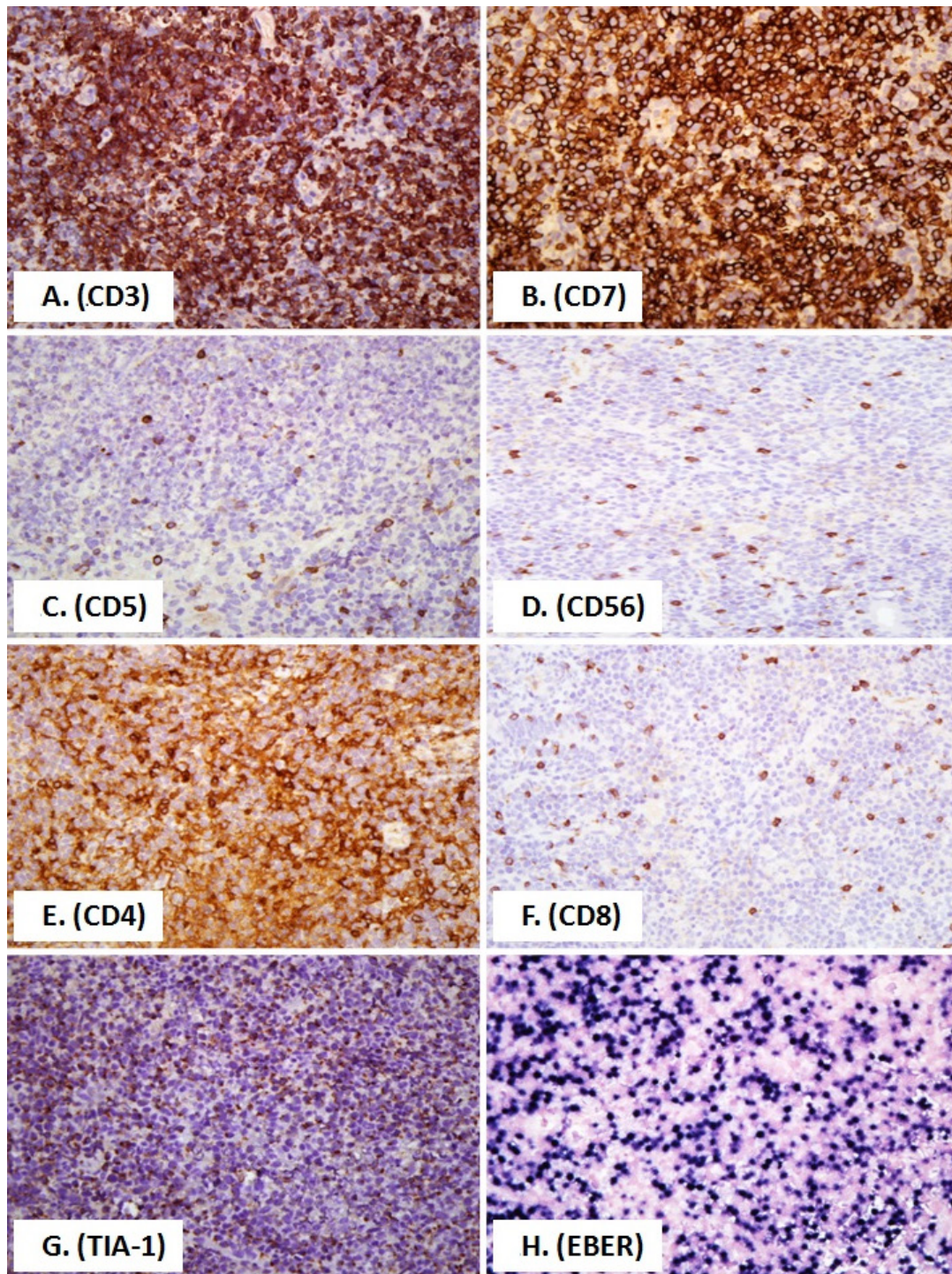


FIG. 2: (A) The malignant cells expressed T-cell associated antigen CD3+ (x400). (B) They were positive to CD7 (x400). (C) There was aberrant loss of CD5 (x400). (D) NK cell marker CD56 was negative (x400). (E-F) They were mostly CD4+/CD8- (x400). (G)The malignant cells expressed cytotoxic granules TIA-1 (x400). (H) Nuclear labelling for *in situ* hybridisation for EBV-encoded RNA (EBER) was positive (x400).

of NK/T cell lymphoma and the case should be classified as Peripheral T-cell lymphoma.³

CONCLUSION

Colonic NK/T cell lymphoma is rare and requires a high index of clinical, radiological, and endoscopic suspicion. Clinically it may mimic benign inflammatory or other malignant lesions. The final diagnosis is only possible with appropriate histological and immunohistochemical studies. When morphology and immunohistochemistry point towards a T-cell lymphoma, cytotoxic molecules and the EBV status help define the diagnosis.

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