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Clinical characteristics of primary intestinal NK/T cell lymphoma, nasal type: Case series and review of the literature

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ABSTRACT

Background: Primary intestinal NK/T cell lymphoma is rare but aggressive and exhibits a poor prognosis. Little is known about its clinical characteristics because few studies with small sample sizes have been reported.
Aims: To provide clinicopathological features and endoscopic findings and to summarize the treatment outcomes of primary intestinal NK/T cell lymphoma to improve our understanding of this disease.
Methods: Between January 2011 to December 2016, 13 patients with confirmed primary gastrointestinal NK/T cell lymphoma at our center were described, and an updated literature review was provided.
Results: In this series of 13 cases, 69.23% were men, the median age was 39 years, and the median survival was 6 months. The common clinical manifestations included abdominal pain (76.92%) and gastrointestinal bleeding (46.15%). Lymphomas were common in the large intestine (69.23%). In 76.92% of patients, the clinical staging was stage I, and all 13 patients manifested ulcerative lesions and no tumor mass on endoscopy. The clinical characteristics of primary intestinal NK/T cell lymphomas were similar to results in existing literature.
Conclusion: Intestinal NK/T cell lymphoma shows nonspecific clinical features and poor prognosis, which is mainly expressed as ulcers on endoscopy. Emergency surgery may be an adverse prognostic factor of lymphoma, since it is prone to progress toward gastrointestinal perforation.

1. Introduction

Extranodal NK/T-cell lymphoma, nasal type (ENKTL-NT) is a rare type (approximately 2% to 10%) of non-Hodgkin's lymphoma (NHL) [1–3]. It is rare in North American and European countries, but it is prevalent (it can account for upwards of 10% of NHL) in Asia and South America [4–7] and presents increasing incidence in the U.S. (less than 1% of all NHL) [8,9]. ENKTL-NT presents an aggressive clinical course and a poor prognosis, especially for advanced disease [10]. The estimated 5-year overall survival (OS) for ENKTL-NT is between 40 and 50%. Survival is heavily dependent on stage at diagnosis. Long-term follow up suggests a continued risk of relapse up to 10 years from diagnosis [11,12].

Most ENKTL cases (80%-90%) occur in the nasopharyngeal area, but other affected sites include the gastrointestinal tract, lung, skin, testis, and muscles [5,7,13].

Primary intestinal NK/T cell lymphoma (PIENKTL) is rare. Several studies have reported the epidemiology, disease presentation, and outcome data for patients with PIENKTL [14–16]. The results show that there are some distinctive ethnic and geographic differences. Little is known regarding the clinical characteristics of PIENKTL, which may be one of the main reasons for the delay in diagnosis and appropriate treatment.

To our knowledge, there has been no large sample epidemiological study on intestinal NK/T cell lymphoma. Therefore, we retrospectively analyzed the clinicopathological features and endoscopic findings of 13 primary intestinal NK/T cell lymphomas at our center and reviewed the current literature to improve our understanding of this disease.

2. Materials and methods

The Ethics Committee of the Third Military Medical University (Chongqing, China) approved this retrospective cohort study. Patients' information was anonymized for analysis.

2.1. Patients

Thirteen continuous patients with primary intestinal NK/T cell

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lymphomas, nasal type were selected in the files of the Department of Pathology, Xinqiao Hospital of the Third Military Medical University, Chongqing, China, from January 2011 to December 2016.

The pathological diagnosis of the tumor was based on the new World Health Organization classification of lymphomas (2016) [17]. All pathological results were reviewed by two pathologists. Specimens included endoscopic biopsy (n = 6) and surgical specimens (n = 7). The diagnosis and classification were based on immunohistochemistry, in situ hybridization for EBV-encoded small RNA (EBER), and genetic features.

2.2. Clinical data collection

Clinical data, including patients' demographic information, clinical symptoms, the presence of B symptoms (B symptoms refer to systemic symptoms of fever, night sweats, and weight loss), lactate dehydrogenase (LDH) level, lesion sites, endoscopic findings, complications, emergency surgery, treatment and last follow-up, were collected from the patients' records. The Ann Arbor staging system by Musshoff [18] was used for clinical staging.

The endoscopic findings of primary gastrointestinal NK/T cell lymphoma were divided into four types as described in Kim's study [15], including (1) superficial/erosive, (2) ulcerative, (3) ulceroinfiltrative and (4) infiltrative.

2.3. Statistical analysis

All analyses were performed using the SPSS Statistics 19.0 software (SPSS Inc., Chicago, IL, USA). Non-normal continuous variables were reported as medians (minimum – maximum). Overall survival (OS) was measured from the date of diagnosis to the date of death or the last follow-up visit. Survival curves were derived by the Kaplan and Meier method. Survival curves were plotted for gender, age, the location of lesion, whether they received emergency surgery and whether they received chemotherapy. P values < 0.05 were considered significant.

3. Results

3.1. General characteristics

From January 2011 to December 2016, of the 27 cases of confirmed intestinal T-cell and NK/T cell lymphomas, 13 cases (48%) with primary intestinal NK/T lymphomas, nasal type were included in the analysis. The general characteristics of these patients are listed in Table 1.

Of the 13 patients, the median age was 39 years (range: 15–72 years) at the time of diagnosis. Approximately 69.23% (9/13) of patients were men. Before the definitive diagnosis, the time between the onset of clinical symptoms and diagnosis was approximately 3.8 months (from 2 months to 9 months). The common clinical manifestations included abdominal pain (76.92%), gastrointestinal bleeding (46.15%), and diarrhea (23.08%). Six patients (46.15%) had B symptoms and 4 patients (30.77%) had elevated LDH levels at the time of diagnosis. Clinical staging was as follows: stage I, 10 patients (76.92%); stage II, 2 patients (15.38%); stage III, 1 patient (7.69%).

3.2. Endoscopic and pathological findings

All patients received endoscopic examination according to Kim's classification of endoscopic findings of gastrointestinal NK/T cell lymphoma [15], and specimen collection and pathological examination were performed. The endoscopic and pathological characteristics of each case are listed in Supplementary Table S1 and summarized in Table 2.

Of the 13 patients, the common locations of lymphoma were the large intestine (ileocecal junction, colon and rectum) (9 patients), small

Table 1
General characteristics of patients with primary intestinal NK/T cell lymphomas.

Case	Sex	Age (years)	Diagnosis of time	Clinical staging	Max-diameter(cm)	Clinical symptoms	B symptom	LDH	complication	Emergency surgery	chemotherapy	Overall survival
1	M	30	3 months	I	3	abdominal pain, hematochezia	No	Normal	Massive hemorrhage	Yes	none	1 day
2	M	39	2 months	I	4	abdominal pain, hematochezia	Yes	Normal	Bowel perforation	Yes	none	6 months
3	M	51	2 months	I	1.5	Abdominal pain	Yes	Normal	No	No	none	3months
4	M	54	2 months	II	2	abdominal pain, hematochezia	No	Normal	Bowel perforation	Yes	CHOP	8months
5	M	71	6 months	III	4	abdominal pain, hematochezia	No	Normal	Bowel perforation	Yes	none	7days
6	F	34	1 month	I	3	Hematochezia,	Yes	elevate	No	No	CTOD	3days
7	M	15	3 months	I	5	abdominal pain, diarrhea	No	elevate	No	No	COTP	13months
8	M	50	5 months	I	5	diarrhea	No	Normal	No	No	CHOP	8months
9	F	49	5 months	I	4	abdominal pain, diarrhea	No	Normal	Bowel perforation	Yes	none	4days
10	M	20	5 months	I	5	abdominal pain, hematochezia	No	elevate	Bowel perforation	Yes	none	9months(alive)
11	F	47	5 months	I	6	abdominal pain	Yes	elevate	Bowel perforation	Yes	none	7days
12	F	32	2 months	II	4	abdominal pain	Yes	normal	No	No	TAOD + L-ASP	4month(alive)
13	M	32	9 months	I	5	abdominal pain	Yes	Normal	No	No	CVTLD	3month(alive)

1. Diagnosis of time means the time between symptom onset and diagnosis.
2. CHOP (cyclophosphamide, vincristine, doxorubicin, and prednisone), CTOD, (cyclophosphamide, pirarubicin, vincristine and dexamethasone) COTP (cyclophosphamide, vincristine, pirarubicin, prednisone), TAOD + L-ASP (cytarabine, pirarubicin, vindesine, dexamethasone and pegaspargase), and CVTLD (cyclophosphamide,vincristine, pirarubicin, dexamethasone and pegaspargase).