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Case Report

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Extra-nodal NK/T-cell lymphoma: colonic involvement and occult nasal primary.

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Abstract

This review aims to summarise the published literature on extranodal natural killer/T-cell lymphoma using a case report as a working example. Extranodal natural killer/T-cell lymphomas are rare, particularly in western countries and usually associated with Epstein-Barr infection. They most commonly affect the upper aerodigestive tract but can present at distant sites as primary lesions or as disseminated disease. The diagnosis of extranodal natural killer/T-cell lymphoma is often made at an advanced stage and prognosis is generally poor. A case of disseminated, upper aerodigestive tract extranodal natural killer/T-cell lymphoma affecting the colon initially treated by laparoscopic right hemicolectomy is presented. Follow up at one year following surgery demonstrated no residual disease. Surgery is rarely indicated in the management of extranodal natural killer/T-cell lymphoma but in selected cases it may offer potentially curative treatment in combination with chemotherapy and radiotherapy.

Key words: lymphoma, extra nodal, natural killer cells, colon, colectomy

Introduction

This review summarises the literature on extra-nodal NK/T-cell lymphoma and describes a case of upper aerodigestive tract NK/T-cell lymphoma with secondary involvement of the colon. A lethal, locally invasive nasal/palatal midline destructive disease process was originally described in the 19th century[1] and subsequently became known commonly as lethal midline granuloma. It is now recognized that this clinical entity comprises a number of pathological entities including extranodal NK/T cell lymphoma (ENKL). Aggressive natural killer (NK) cell neoplasms are classified along with mature T-cell neoplasms in the WHO classification and include ENKL and aggressive NK cell leukaemia,which may represent the leukemic phase of ENKL in some cases[2]. Extranodal NK/T cell lymphoma usually affects the upper aerodigestive tract and is associated with Epstein-Barr infection. It is known to disseminate to a variety of distant organs, although spread to the gastrointestinal tract is not common. Treatment of ENKL depends on the stage at presentation and usually involves chemotherapy with radiotherapy to involved fields if possible, since this is a radiosensitive tumour. Cure is more likely for localised disease and when chemotherapy is combined with radiation

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therapy[3].Surgery is not usually indicated due to the pattern of disease spread. Lymphomas of the gastrointestinal tract represent a form of extranodal non-Hodgkin's lymphoma (NHL) and account for 4-20% of all NHL[4, 5]. They can be primary, arising within the gastrointestinal tract, or secondary as a result of dissemination. The majority of primary gastrointestinal lymphomas arise in the stomach or small bowel with only 6-20% located in the colon[6-8]. Most are of B-cell origin with only 4-8% representing mature T cell types[9, 10]. Of all T-cell lymphomas found in the intestine, the majority are of unspecified peripheral T-cell lymphomas or enteropathy-type T cell lymphomas[9] according to the latest WHO classification[2].

Case Report

A 73-year-old gentleman presented to the surgical outpatient department with colicky abdominal pain and meteorism consistent with bowel obstructive symptoms. There was a history of weight loss without rectal bleeding. A recent magnetic resonance imaging scan of the head performed due to symptoms of nasal congestion demonstrated sinus infiltration thought to be infective.Examination revealed no lymphadenopathy or hepatosplenomegaly. Peripheral blood showed a normal full blood count, urea and electrolytes and liver function tests. The patient underwent a barium enema and a colonoscopy both identifying a mass in the caecum. Endoscopic biopsy of the mass was non-diagnostic. Staging CT scan of the chest, abdomen and pelvis confirmed a solitary primary lesion in the caecum and no local, regional or distant lymphadenopathy, see (figure 1) below: Due to the malignant appearance of the caecal mass on CT scanning and the presence of obstructive symptoms, the patient was scheduled for laparoscopic right hemicolectomy despite the biopsy histology being inconclusive. A bulky caecal mass adherent to the anterior abdominal wall and pelvic sidewall was found at laparoscopy. A laparoscopic right hemicolectomy was performed.

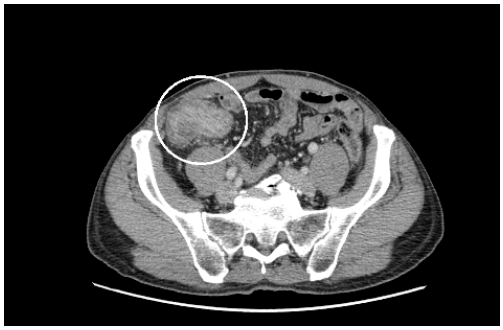

Fig. 1 Computed Tomography (CT) scan demonstrating the colonic tumour shown circled.

Macroscopic analysis of the specimen revealed a 38mm tumour in the caecum, 20mm from the nearest mesenteric resection limit and 20mm from the nearest longitudinal margin. Microscopy demonstrated large anaplastic tumour cells with brisk mitotic activity. Immunohistochemistry was performed to investigate the expression of a number of different antigens. The right colon tumour cells expressed mature T cell antigens CD3 and CD43 as well as CD45 and CD56 positivity. Cells had a negative immunophenotype for Alk-1, MNF-116, CD2, CD4, CD5, CD7, CD8 and CD10 markers. Tumour cells were granzyme B positive, perforin positive and EBER in situ positive. All of 22 lymph nodes showed reactive changes only. These results suggested a diagnosis of ENKL. The patient made a routine recovery and was discharged home on postoperative day eight. Following the bowel resection and the histological diagnosis of ENKL, the patient underwent nasal endoscopy and biopsy.Examination revealed a population of cells staining positively for CD56 and Epstein-Barr virus (EBV) representative of NK/T cell lymphoma. Bone marrow biopsy was normal. The patient received a course of methotrexate and asparginase chemotherapy along with nasal field radiotherapy. After treatment, CT scan and MRI scan of the head showed no residual or recurrent disease. At follow up at one year from the original diagnosis, the patient suffered some continuing nasal symptoms and a watering right eye with no signs of recurrent disease.

Discussion

Extranodal NK/T-cell lymphoma, nasal type (ENKL) is one of three NK cell lymphoma types described in the WHO classification of lymphomas[2]. ENKL is rare in Western countries with a higher incidence in Latin America and East Asia where it represents up to 9 % of all malignant lymphomas [11]. ENKL is almost twice as prevalent in men. The median age at diagnosis varies according to population and ranges between 46 years in Korea and 53 years in Japan [12, 13].

ENKL commonly involves the nasal cavity or surrounding upper aerodigestive tract, although primary 'extra-nasal' or 'nasal-like' tumours of nasal type can arise in a range of distant sites including skin, liver/spleen, gastrointestinal tract, lung, kidney, pancreas, testis and the central nervous system[12, 14-17]. Nasal tumours and those arising in other upper aerodigestive tract sites (paranasal) have common histological/immunological features and behave in a similar clinical manner[11, 13]. In contrast, tumours arising at distant sites are more likely to present with stage III/IV disease rather than stage I/II disease (59% vs. 15%)[13]. They also tend to have more aggressive biologic features, higher international prognostic index, poorer response to anthracycline-based therapy and shorter 5-year overall survival [13, 18]. Many authors therefore separate ENKL into either upper aerodigestive tract NK/T cell lymphoma or extra-upper aerodigestive tract NK/T cell lymphoma[11, 13, 18]. Tumours spread by local invasion, to regional lymph nodes and to distant organs by dissemination. Secondary involvement is often to a single organ site and can involve skin, liver/spleen, intestine, lung, kidney, testis, bone marrow, heart and penis[12, 19-22].Clinical presentation depends on the site of involvement. Typically, nasal/paranasal disease presents with nasal congestion, fever, purulent/bloody nasal discharge and headache[22].Systemic symptoms such as fever, weight loss and anaemia may be present. Colonic disease can present withabdominal pain, perforation and rectal bleeding, however, obstruction is rare[9, 23].

Treatment of ENKL of the colon depends on the site and stage of disease and involves chemotherapy, radiotherapy or a combination of both. Surgery is rarely indicated due to the distribution of disease and advanced stage at presentation. In one published case of primary NK/T cell lymphoma of the rectum associated with ulcerative colitis, proctocolectomy was performed as part of treatment[24]. The outcome in patients with disseminated NK cell neoplasms is generally poor and most data are based on case series from the East. Suzuki et al studied prognostic factors in 150 patients with ENKL [12]. Complete remission rate was 73% in stage I and 15% in stage IV. Median survival was 10 months overall and 4 months in stage IV disease. Multivariate analysis showed that stage, performance status, number of extranodal sites involved and extra-aerodigestive tract primary were significant prognostic factors. A recent analysis of 36 patients of French European descent has confirmed the importance of radiotherapy to the success of treatment[3]. Poor results with anthracycline based chemotherapy has led to the introduction of L-asparaginase based treatments [25, 26]which may lead to an improvement in survival prospects, although randomised comparisons are not available. There have been no previous reports of ENKL presenting with large bowel obstruction. This may be because although gastrointestinal involvement has been reported, it is uncommon and does not always involve the large intestine. In addition, the stage is often advanced with a short median survival determined by disease burden at other extranodal sites rather than local complications of colonic disease. Presentation with large bowel perforation has been recorded in a young patient with a 12cm tumour of the hepatic flexure[9]. This report describes the case of a patient who underwent laparoscopic right hemicolectomy for an obstructing caecal mass thought to be an adenocarcinoma which was subsequently found to be an extranodal NK/T-cell lymphoma, nasal type. Only when the histology suggested a nasal-type tumour

and when a previous history of nasal congestion was elicited, did the patient undergo internal examination of the nasal area. This allowed confirmation of a histologically similar nasal lesion which was thought to represent the primary tumour, the caecal tumour therefore representing secondary involvement.

Conclusion

Whilst ENKL affecting the colon is rare, it can occur, either as secondary involvement from nasal/paranasal disease or as a primary tumour. Presentation can be with symptoms relating to the local tumour or systemic features of lymphoma. In selected cases, surgery may be indicated, offering potentially curative treatment in combination with systemic chemotherapy and radiotherapy to involved sites. In cases of colonic lymphoma, a phenotype suggestive of NK lineage should prompt consideration of a nasal type tumour. If the diagnosis of ENKL is made, nasal endoscopy and biopsy is mandatory to complete staging and plan appropriate treatment.

Authors' Contribution

DB: concept design and manuscript preparation
LS: concept design and manuscript preparation
AK: concept design and manuscript preparation
PA concept design and manuscript preparation

Conflict of Interests

The authors declare that they have no conflict of interest.

Ethical Considerations

Written informed consent was obtained from the patient for publication of this case report.

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