

The clinicopathological behaviour and surgical treatment of abdominal Castleman's disease

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ABSTRACT

Introduction: Castleman's disease, a rare atypical lymphoproliferative disorder of the lymphoid tissue with unknown cause, remains a diagnostic challenge. This study was conducted to analyse the clinicopathological behaviour and reasonable surgical treatment for patients with abdominal Castleman's disease.

Methods: The medical records of seven patients with abdominal Castleman's disease were reviewed.

Results: The patients comprised two men and five women, and their median age was 42.3 (range 29–53) years. The main clinical manifestation was an abdominal mass or an enlargement of the retroperitoneal lymph node. Other clinical manifestations included anaemia, loss of body weight and hypoalbuminaemia. The mean size of the tumour was 5.5 (range 4.0–8.0) cm. Postoperatively, all the patients were diagnosed with a hyaline vascular type of the disease, and had localised manifestations of the disease. All seven patients underwent complete surgical resection, two of whom also received adjuvant irregular chemotherapy (CHOP) and steroids postoperatively. All the patients survived, with no evidence of recurrence. One patient had survived for more than two years, four patients for more than three years, and two patients for more than five years.

Conclusion: Abdominal Castleman's disease is difficult to diagnose preoperatively, and surgical excision remains the treatment of choice, especially for localised disease.

Keywords: angiofollicular lymphoid hyperplasia, Castleman's disease, clinicopathological behaviour, surgical procedures

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INTRODUCTION

Castleman's disease, or giant lymph node hyperplasia, is an unusual lymphoproliferative disorder. It was first described by Castleman and Towne in 1954.⁽¹⁾ Little is known about the cause of this disease, which may occur anywhere along the lymphatic chain, but it is most commonly located in the mediastinum.^(2,3) It usually presents as a localised soft tissue mass in the neck or the mediastinum; however, it has also been reported that the mesentery, pelvis, pancreas, adrenal and retroperitoneum may also be included in other extrathoracic involvement.⁽²⁻⁷⁾ As this disease is rare and poorly understood, the optimal therapy is unknown. This study was conducted to analyse the clinicopathological behaviour and reasonable surgical treatment for patients with abdominal Castleman's disease.

METHODS

The medical records of seven patients who had received a histological diagnosis of abdominal Castleman's disease between March 2003 and November 2007 at the First Affiliated Hospital of Wenzhou Medical College, Zhejiang Province, China, were reviewed retrospectively. Two independent pathologists examined the histological features of the lymph nodes collected from the patients and confirmed the histological diagnosis. None of the patients had autoimmune diseases such as rheumatoid arthritis or Sjögren syndrome. The diagnosis of Castleman's disease was made based on the postoperative histopathological examination. The extent of the disease was assessed with the help of computed tomography (CT) of the chest, abdomen and pelvis, and routine blood chemistry analyses, including electrolytes, liver function studies, haemogram, bone marrow biopsy and aspiration. In addition to lymphadenopathy, some patients had constitutional symptoms that included unexplained fever higher than 38°C, drenching night sweats, and unexplained weight loss of more than 10% of the total body weight in the six months prior to diagnosis.⁽⁸⁾

Castleman's disease was categorised as either localised or disseminated, and was further subdivided

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into three histological types: (1) the hyaline-vascular type, which is more frequent and characterised by small hyaline-vascular follicles and interfollicular capillary proliferation; (2) the plasma cell type, which is characterised by large follicles with intervening sheets of plasma cells; and (3) mixed histopathological patterns.^(2,6,9) Before making a diagnosis of plasma-cell Castleman's disease, diseases such as rheumatoid arthritis, syphilis, skin diseases and Wiskott-Aldrich syndrome should be excluded. In addition, the definition of extranodal involvement required a biopsy result that showed the features of Castleman's disease in the involved organ.

Patients were categorised as having localised disease if the histological evidence of Castleman's disease was found in one region of the lymph node mass without clinical or radiographic evidence of lymphadenopathy elsewhere. Disseminated disease was defined based on histological evidence of Castleman's disease in two or more lymph node regions with radiographic or clinical evidence of lymphadenopathy. Clinically, the hyaline-vascular type is usually asymptomatic, whereas the less common plasma cell type is sometimes associated with systemic manifestations such as fever, anaemia, weight loss, night sweats and hypoalbuminaemia.

Follow-up information was obtained through office visits and telephone contact with the patients until the time of the patients' death or till the end of this study. Local recurrence was defined as tumour relapse within the region of operative files. Actuarial progression-free survival was calculated from the time of diagnosis to the time of documented disease progression or recurrence. Upon discharge from the hospital, the patients were followed up at least four times a year, i.e. every three months in the first five years, and half-yearly thereafter. Physical examinations, basic routine radiographic examinations, abdominal ultrasonography (US) and CT of the abdomen (twice a year) were performed. If necessary, chest or head examinations were included in these tests.

RESULTS

This study comprised seven patients, of which two were male and five were female. The patients' median age was 42.3 (range 29–53) years. The main clinical manifestation was an abdominal mass or an enlargement of the retroperitoneal lymph node, with rare abdominal pain. The median duration of disease was 2.3 years (range two months to six years). Other clinical manifestations included anaemia ($n = 1$, 14.3%), loss of body weight ($n = 1$, 14.3%) and hypoalbuminaemia

($n = 1$, 14.3%). The erythrocyte sedimentation rate was elevated in four patients. None was seropositive for the human immunodeficiency virus. The mean size of the tumour in the enlarged lymph node was 5.5 (range 4.0–8.0) cm. The detection rates of the lymph node mass by CT and US were both 100%. All the patients were pathohistologically diagnosed with the hyaline vascular type of Castleman's disease postoperatively; there was no instance of plasma cell type or mixed type disease. Clinically, all the patients had localised manifestations, and disseminated disease was present.

All seven patients underwent complete surgical resection. For five patients, this involved the en bloc removal of a lymph node mass, and for two patients, it involved the en bloc removal of a lymph node mass and combined small bowel. Two patients received postoperative adjuvant irregular chemotherapy. One patient received three cycles of CHOP regimen chemotherapy, which consisted of cyclophosphamide (750 mg/m²), doxorubicin (50 mg/m²), vincristine (1.4 mg/m², maximum 2 mg/body) administered intravenously on Day 1, as well as prednisolone (100 mg/day) administered orally on Days 1–5. The course of treatment was repeated every three weeks, unless the peripheral leukocyte or platelet counts became too low to administer the next cycle. The other patient received adjuvant irregular chemotherapy with chlorambucil (0.2 mg/kg/day) administered orally for six weeks continuously and prednisone (100 mg/day) administered orally on Days 1–5. All the patients survived, with no evidence of recurrence. One patient had survived for more than two years, while four had survived for more than three years and two had survived for more than five years.

DISCUSSION

Castleman's disease is classified as being either localised or disseminated, and is further subdivided into three histological types: the hyaline-vascular type, plasma cell type and mixed type.^(2,9,10) Clinically, localised Castleman's disease typically has mild biological behaviour, whereas the disseminated form is usually malignant, has a poor prognosis and has severe systemic manifestations (such as fever, anaemia, weight loss, night sweats, polyneuropathy, organomegaly, Kaposi sarcoma and acquired immune deficiency syndrome).^(8,10-15) Although all the patients in this study had the localised plasma cell type Castleman's disease, a previous review found 35 cases of abdominal Castleman's disease reported in the Chinese literature over the last 15 years, with 20 cases of hyaline vascular type, 14 cases of plasma cell type and one case of mixed type.⁽¹⁰⁾

Keller et al reported that the localised form of Castleman's disease was limited to the mediastinum, the abdomen and the periphery in 86%, 3% and 11% of their 81 patients, respectively.⁽²⁾ In a combined analysis of 78 patients with localised disease, Frizzera et al reported that the mediastinum (46%) was the most common location, followed by the abdomen (39%) and periphery (15%).⁽⁵⁾ In addition, among the seven cases of localised disease, only one (14%) was localised to the mediastinum, two (28%) were localised to the abdomen and four (58%) were localised to the peripheral lymph node areas.⁽⁵⁾

In the seven patients with abdominal Castleman's disease in our study, the median age at diagnosis was 42.3 (range 29–53) years. This is not significantly different from the data reported in previous studies.^(6,9,10) Constitutional symptoms and laboratory abnormalities were found almost exclusively in patients with plasma-cell disease, which is in keeping with previous reports.^(2,5,9) The systemic manifestations of localised disease seem to be less common than those of disseminated disease, which suggests that the number of areas of involved lymph nodes may be related to the intensity of the symptoms. In this study, all patients with abdominal Castleman's disease presented with the localised type of plasma-cell disease.

Although the optimal treatment of abdominal Castleman's disease is yet unknown, surgical excision is generally the option for treatment of both the hyaline-vascular and plasma cell types of localised disease.^(3,4,6,9,16) When complete resection is impossible, palliative resection or radiotherapy may be used to control possible systemic manifestations.^(3,4,7,17,18) Keller et al reported that all their cases of localised Castleman's disease had an indolent clinical course and mild biological behaviours, with the elimination of all systemic symptoms after complete resection.⁽²⁾ Disseminated Castleman's disease, regardless of the histological subtype, is a more aggressive clinical illness that usually has a malignant or rapidly fatal course, but the optimal treatment has not been definitively established.^(3-5,14,15) In this study, complete surgical excision was performed in the patients, and no evidence of tumour recurrence has been detected since surgery.

Combination chemotherapy and steroids have been considered the mainstay of treatment for disseminated Castleman's disease. For instance, chemotherapy (in the form of a single agent, an agent together with steroids, or a combination regimen) has been shown to produce clinical responses in 93% (14 out of 15) of reported cases.^(5,9,15,19-21) In a study conducted by

Herrada et al,⁽⁹⁾ 46.7% (7 out of 15) of the patients were reportedly alive and 26.7% (4 out of 15) had sustained complete remission. Of the four patients who had sustained remission, two had received chlorambucil alone or with prednisone at the time of diagnosis, one had received cyclophosphamide plus prednisolone after an initial therapy with azathioprine plus prednisolone, and one had received high-dose melphalan with bone marrow transplantation after the failure of CHOP.^(5,9,15,19-21) Among those with disseminated disease reported by Herrada et al,⁽⁹⁾ three patients treated with combination chemotherapy were alive and free of the disease, two who had been treated with prednisolone were alive but still required intermittent maintenance therapy for disease reactivations, and two who were treated solely with surgery had died. In the current study, two patients accepted irregular chemotherapy (CHOP) and steroids postoperatively.

The review by Keller et al found that all 81 patients with localised Castleman's disease had a benign clinical course, and that complete surgical excision completely removed the systemic symptoms present at diagnosis, with only occasional local recurrences.⁽²⁾ In the above reported cases of Castleman's disease, about 80% of the localised disease cases were of the hyaline vascular type, while 20% were of the plasma-cell type, and only the occasional case was of the mixed type. Most of these patients with localised plasma-cell disease were children or young adults who presented with abdominal, mediastinal or peripheral masses.⁽²⁾ In a review of the Chinese literature on abdominal Castleman's disease conducted by Han et al, among 26 cases with recorded survival, 13 patients survived after three years, eight patients after five years and five patients after ten years, while one patient improved and one deteriorated.⁽¹⁰⁾ Bowne et al studied 16 cases of Castleman's disease and reported that no clinical or radiographic recurrence of symptoms was found among the localised hyaline-vascular disease patients (n = 8) who underwent complete surgical excision, whereas two patients were reported to remain asymptomatic following partial resection or radiation therapy for an unresectable unicentric hyaline-vascular Castleman's disease mass.⁽⁶⁾ In the current study, all patients with abdominal Castleman's disease are still alive, with no evidence of recurrence postoperatively. To conclude, abdominal Castleman's disease is difficult to diagnose preoperatively, and surgical excision is the treatment of choice for the disease, especially for the localised form.

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