Case report

Report of two cases of Castleman's Disease: a case of benign localized disease and a case of fast progressive multicentric disease

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Abstract. Castleman's Disease is a rare tumour involving lymph node tissues; a case of benign localized disease and a case of rapid progressive multicentric disease are reported. *Case report 1:* A 19-year-old man presented with four months of hypogastric and left iliac pain. Castleman's Disease was suspected after CT-scan. A CT-guided fine-needle biopsy of the lesion was performed revealing hyaline vascular type Castleman's Disease. The patient underwent open surgery with radical excision of the lesion. No adjuvant therapy was performed after surgery. The patient is alive and disease-free after 24 months. *Case report 2:* A 58-year-old woman presented with a right axillary palpable lymph node and vague abdominal discomfort. Abdomen CT demonstrated hepatosplenomegaly associated with adenopathy at the hepatic hilus and splenic hilus; dilatation of intra-hepatic biliary ducts was present. The axillary node was excised, the mass at hepatic hilus was biopsied. The diagnosis was Castleman's Disease in both sites. In course of steroid therapy retroperitoneal multiple nodes appeared associated with fast-progressive mechanic jaundice and liver failure. Progressive multi-organ failure arose within 1 week, with irreversible clinical worsening to death. (www.actabiomedica.it)

Key words: Castleman's disease, angiofollicular lymph node hyperplasia, giant lymph node hyperplasia, lymphoproliferative disorders

Introduction

Benjamin Castleman firstly described Castleman's Disease (CD) in 1954 (1). Synonyms are: Angiofollicular Lymph Node Hyperplasia, Angiomatous Lymphoid Giant Benign, Lymphoma Hamartoma of the Lymphatics, Giant Lymph Node Hyperplasia. It is a rare disorder characterized by non-cancerous growth that may develop in the lymph node tissue throughout the body. Localized or multicentric forms are described (2, 3). Two cases are here reported: a case of localized Castleman's Disease (LCD) with benign behaviour and a case of progressive multicentric CD (MCD) with unfavourable prognosis.

Case report 1

A 19-year-old man presented to our observation for a four-month history of hypogastric and left iliac pain. Clinical examination was negative for palpable lymph-nodes or organ megalia. Ultra-sound sonography detected a mass near the left iliac vessels and iliopsoas muscle. Positron emission tomography with the glucose analogue fluorine-18 fluorodeoxyglucose (FDG-PET) demonstrated an area in left iliac region, with Standard Uptake Value (SUV) max = 6.46. The CT-scan showed an oval 47x26 mm mass with high homogeneous enhancement after infusion of contrast (Figure 1). For this reason the hypothesis of Castle-

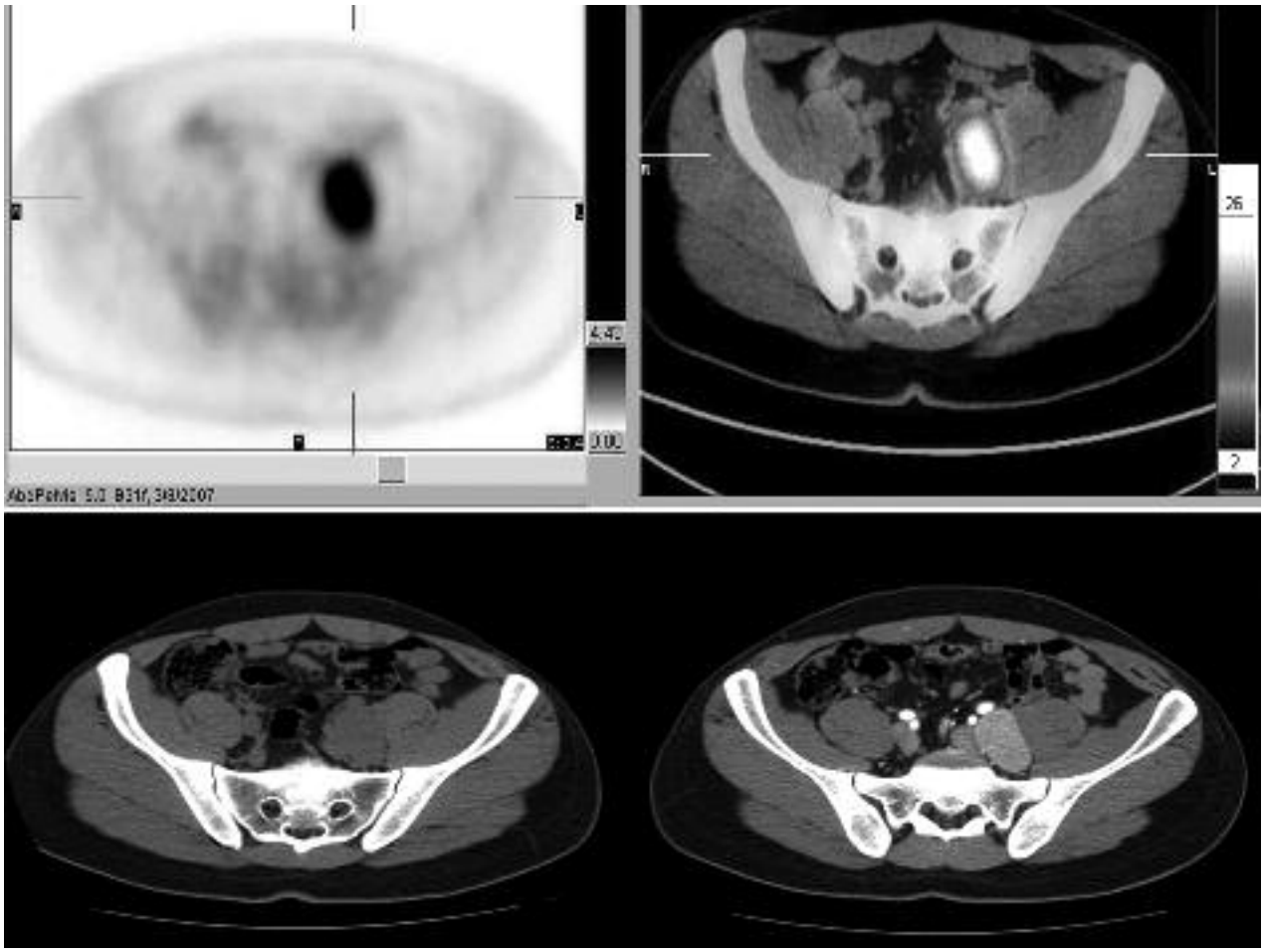

Figure 1. Case 1. FDG-PET demonstrated a positive area (SUV max = 6.46) in left iliac region. CT-scan confirmed an oval mass with high homogeneous enhancement after infusion of contrast

man Disease was formulated (4,5). Serum tests for HIV, Epstein–Barr virus, human T-cell lymphotrophic virus types 1 and 2 (HTLV-1 and HTLV-2), cytomegalovirus (CMV), toxoplasma, mycobacterium tuberculosis and Kaposi's sarcoma herpesvirus (HHV-8) were negative. Serum protein electrophoresis demonstrated the absence of monoclonal or polyclonal hypergammaglobulinemia.

CT-guided fine-needle sampling of the lesion was performed, revealing CD. The patient underwent open surgery with radical excision of the lesion. The sized 7x5x2 cm mass, was lying on the iliopsoas muscle, in the left iliac fork, between the iliac artery and vein. Because the site was close to vessels, open surgery was preferred to laparoscopy (Figure 2). The pathologic response was CD, lymph node hyperplasia (B-lymphocytes CD20+) with hyaline-vascular degeneration (Figure 3). No adjuvant therapy was performed after surgery. Six-monthly, CT-based follow-up was decided. The patient is alive and disease-free after 24 months.

Case report 2

A 58-year-old woman was admitted to our hospital with a right axillary palpable lymph node; no other superficial lymphadenopathy was present. Vague abdominal discomfort without clinic objectivity was referred. Laboratory findings were abnormal but not specific: slightly elevated erythrocyte sedimentation

Figure 2. Case 1. The mass was lying on left iliopsoas muscle, close to the iliac vessels

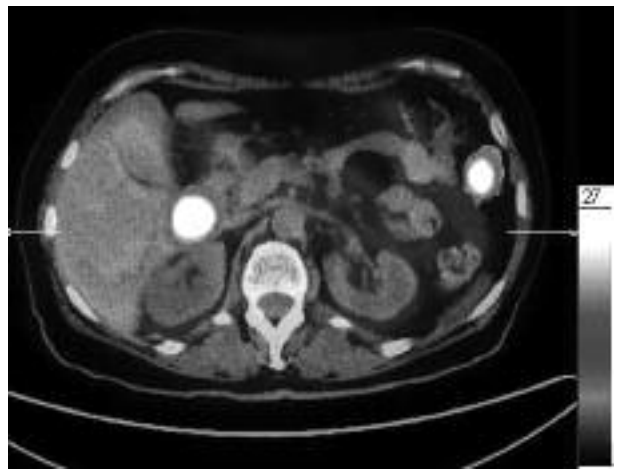

Figure 4. Case 2. Hepatic and splenic adenopathies appeared as hypermetabolic lesions at FDG-PET scan

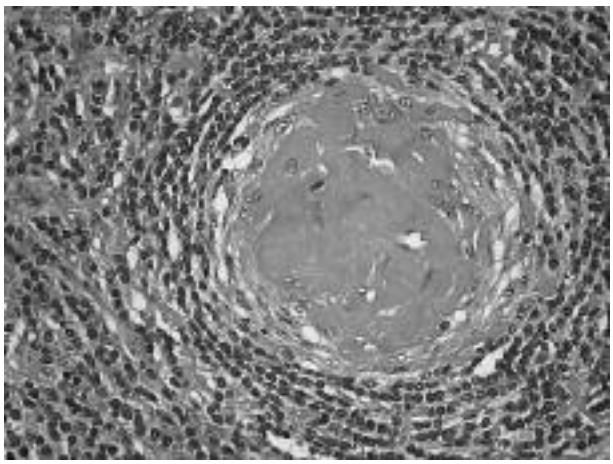

Figure 3. Case 1. Histology of the mass: lymph node hyperplasia with hyaline-vascular degeneration

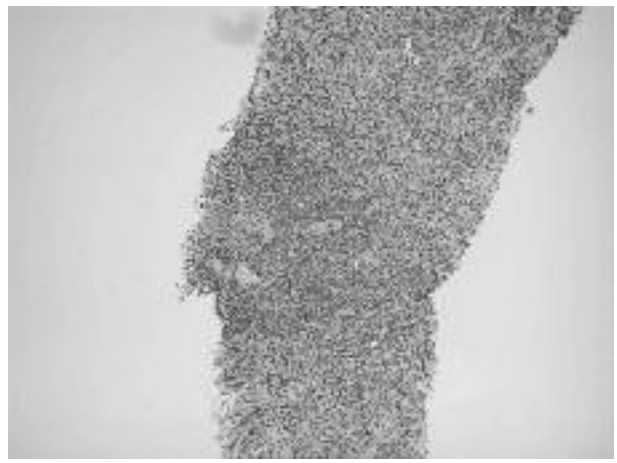

Figure 5. Case 2. CT-guided fine-needle sampling of the perihepatic lesion: diagnosis was again Castleman's Disease

rate and C-reactive protein (C-RP); tumour serum markers were within normality. Abdomen CT demonstrated hepatosplenomegaly associated with adenopathy at the hepatic hilus (4x4 cm) and splenic hilus (5x4 cm); dilatation of intra-hepatic biliary ducts was present. Such enlarged hypervascular lymph nodes enhanced homogeneously with contrast: except for the nodes at hepatic hilus, wich appeared less homogeneous. FDG-PET detected the lesions: SUV of axillary, hepatic and splenic adenopathies was 4.8, 6.4 and 5.7, respectively (Figure 4). The axillary node was excised. Histologic response was CD with hyaline-vascular degeneration. Serum tests against HIV, CMV, HTLV-1 and 2, Epstein–Barr virus, Toxoplasma, Mycobacterium tuberculosis, Kaposi's sarcoma herpesvirus (HHV-8) were negative even in this case. Due to doubts about the origin of abdominal lesions (and for we live in a high-risk area for gastric cancer) endoscopy of upper digestive tract was performed without finding any primary neoplasm. It was followed by CT-guided fine-needle sampling of the perihepatic lesion: once again the diagnosis was CD (Figure 5). It appeared to be a rare case of multicentric CD with hyaline vascular features, B-lymphocytes

CD20+. High-dose steroid therapy was started. Relapse of abdominal symptoms was achieved for a period of two months; US-scan confirmed partial regression of lesions and absence of biliary tree dilatation. A rapid-progressive mechanic jaundice associated with liver failure arose three months after the initial diagnosis. A CT-scan showed a 5x6.5 cm lymph-nodal lesion at the hepatic hilus, obstructing the common bile duct; spleen nodules were increasing in size; retroperitoneal pathologic (lower diameter >1 cm) nodes were also observed in the aorto-caval space, as well as along the right renal and iliac vessels. External biliary drainage was performed for palliation of jaundice. Progressive multi-organ failure arose within 1 week, with irreversible clinical worsening leading to death.

Discussion

Castleman's Disease is an uncommon tumour involving lymph node tissues. This nosologic entity is divided into the - more frequent - localized CD (LCD) and multicentric CD (MCD), involving 10% of cases. Systemic symptoms are rare with LCD. In contrast, MCD has frequent multi-organ involvement with systemic features (1, 6, 7).

CD presents two main histological variants: hyaline vascular type (80-90% of cases) and plasma cell type (10-20%). Hyaline vascular CD is found in 90% of localized forms, but it is rare in MCD, as in our second reported case (2, 3, 8).

Many theories have been proposed to explain the pathogenesis of CD. It has been attributed to a harmatomatous process, autoimmune disease, immunodeficiency and infection. It is often associated with infection due to Kaposi's sarcoma herpesvirus (HHV-8), Epstein–Barr virus, Toxoplasma, Mycobacterium tuberculosis. It shows an increased incidence in HIV-positive patients due to the increased incidence of Kaposi's sarcoma herpesvirus infection in this population (9-11). In our two cases no evidence of such conditions was found.

The definitive diagnosis of CD is histologically established through lymph node biopsy. The role of radiologic imaging (mainly CT with contrast) is important to suspect this pathology before bioptic confirmation. In hyaline vascular type CD, the more frequent CT findings are enlarged hypervascular lymph nodes that homogeneously enhance with contrast. The plasma cell type shows a low level of CT contrast enhancement (4, 5, 8). In the second case here reported, our radiologist was not absolutely certain of a CD diagnosis for abdominal lesions in spite of histology of excised axillary node. For this reason fine-needle biopsy even of deep lesion was performed, so postponing the therapy for about three weeks.

A standard treatment for CD is not available; surgery, when feasible, is the mainstay for the localized form (7, 11). Among 112 patients in six series of patients with hyaline vascular CD, only 3 deaths were reported, none of which was attributed to the CD. Other three patients showed residual disease, but were otherwise well. Local recurrence after complete resection has rarely been reported (12).

On the contrary, surgery shows a limited role in MCD because complete surgical debulking is rarely possible. A variety of treatments have been tried. Steroids have yielded variable results, but patients who respond to steroids must be indefinitely maintained on treatment in order to avoid recurrence. Chemotherapy, including single-agent and combination regimens, has produced an estimated response rate more than 90%, but complete remission rates of less than 30%. In case of splenomegalia, splenectomy may have a therapeutic benefit. Specific immunotherapy has also been used for treatment of MCD. Interferon alfa has been administered either alone or in combination with highly active anti-retroviral therapy (HAART) or chemotherapy both to induce remission and as maintenance therapy (13, 14). In the case of MCD we are reporting, a partial response to steroid therapy was obtained, followed by fast-progressive unexpected relapse; due to clinical worsening, any further treatment of primary disease was not possible.

Conclusions

Localized CD may be considered a disease with a benign prognosis after radical surgery, and a low rate of recurrence. Clinical and radiologic follow-up is necessary. In multicentric CD prognosis may be poor de-

pending on number and location of the lesions. Clinical behaviour is often unpredictable with high rate of recurrence and bad prognosis (15). Standard treatment is not yet available. Such patients are probably in a state of immunodeficiency, even when this is not detected through serum tests. For this reason HAART and specific immunotherapy have been used in selected patients in case of failure of steroids or chemotherapy.

References

1. Castleman B, Iverson L, Menendez VP. Localized mediastinal lymph node hyperplasia resembling thymoma. *Cancer* 1956; 9: 822-30.
2. Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. *Cancer* 1972; 29: 670-83.
3. Menke DM, Camoriano JK, Banks PM. Angiofollicular lymph node hyperplasia: a comparison of unicentric, multicentric, hyaline vascular, and plasma cell types of disease by morphometric and clinical analysis. *Mod Pathol* 1992; 5: 525-30.
4. Wen L, Zhang D, Zhang ZG. CT characteristics of cervical Castleman's disease. *Clin Imaging* 2005; 29: 141-3.
5. Zhou LP, Zhang B, Peng WJ, Yang WT, Guan YB, Zhou KR. Imaging findings of Castleman disease of the abdomen and pelvis. *Abdom Imaging* 2008; 33:482-8.
6. *Kardziev B, Hotzel B, Jachmann M.* The angiofollicular lymph node hyperplasia Castleman - casistic and review of the literature. Pneumologie 2006; 60: 229-34.
7. Herrada J, Cabanillas F, Rice L, Manning J, Pugh W. The clinical behaviour of localized and multicentric Castleman disease. *Ann Intern Med* 1998; 128: 657-62.
8. Martin JM, Bell B, Ruether BA. Giant lymph node hyperplasia (Castleman's disease) of hyaline vascular type. Clinical heterogeneity with immunohistologic uniformity. *Am J Clin Pathol* 1985; 84: 439-46.
9. Cathomas G. Kaposi's sarcoma-associated herpesvirus (KSHV)/human herpesvirus 8 (HHV-8) as a tumour virus. *Herpes* 2003; 10: 72-7.
10. Suda T, Katano H, Delsol G, et al. HHV-8 infection status of AIDS-unrelated and AIDS-associated multicentric Castleman's disease. *Pathol Int* 2001; 51: 671-9.
11. Waterston A, Bower M. Fifty years of multicentric Castleman's disease. *Acta Oncologica* 2004; 43: 698-704.
12. Chen CH, Liu HC, Tung KY, Lee JJ, Liu CL, Liu TP. Surgical outcome of superficial and deep Castleman disease. ANZ J Surg 2007; 77: 339-43.
13. Strohal R, Tschachler E, Breyer S, et al. Reactivation of Behcet's disease in the course of multicentric HHV8-positive Castleman's disease: long-term complete remission by a combined chemo/radiation and interferon-alpha therapy regimen. *Br J Haematol* 1998; 103: 788-90.
14. Nord JA, Karter D. Low dose interferon-alpha therapy for HIV-associated multicentric Castleman's disease. *Int J STD AIDS* 2003; 14: 61-2.
15. Bartoli E, Massarelli G, Soggia G, Tanda F. Multicentric giant lymph node hyperplasia. A hyperimmune syndrome with a rapidly progressive course. *Am J Clin Pathol* 1980; 73: 423-6.

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Stop TB

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8.15 Registrazione partecipanti
8.45 Saluto autorità, presentazione del Convegno
G. Besozzi
9.00 **Lettura**
La grande guerra contro la tubercolosi
C. Grassi

I SESSIONE
Moderatori: *C. Grassi - M. Battaglione*

9.30 **La sfida della complessità**
M. Casali
10.15 **TB: una malattia nella storia dell'uomo**
F. Perozziello
10.45 Coffee break

II SESSIONE
Moderatori: *L. Richeldi - A. Mangiaracina*

11.15 **Sistema Europa e tubercolosi**
M. Battaglione
12.00 **Impatto della malattia sui sistemi socio economico** - *A. Messa*
sanitario - *M. Bugiani*
12.40 **Modello teorico di intervento di cooperazione**
S. Grandi
13.00 Colazione di lavoro

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Sala 6

SESSIONE per INFERMIERE e ASSISTENTE SANITARIO

II SESSIONE
Moderatori: *M. Ferrarese - P. Bandozzi*

16.00 **Rischio biologico negli operatori sanitari**
M. Bandini
14.30 **La diagnosi dell'infezione: procedure diagnostiche**
S. Rossetti
15.00 **La terapia dell'infezione**
L. A. Codecasa
15.30 **Il sistema di controllo e i flussi informativi**
P. Bandozzi
16.00 Coffee break
16.30 **La diagnosi di malattia: laboratorio e clinica**
M. Ferrarese
17.00 **Trattamenti ospedalieri ed ambulatoriali**
A. Allieri
17.30 **La gestione del paziente con TB**
E. Arighi
18.00 **Verifica questionario di apprendimento e chiusura lavori**

Venerdì, 14 ottobre 2011

Salone Centrale

SESSIONE per MEDICO CHIRURGO

II SESSIONE
Moderatori: *A. Allieri - A. Gori*

14.00 **Storia naturale della malattia**
S. Rossetti
14.30 **Il tisiologo e la diagnosi di tubercolosi**
L. M. Codecasa
14.45 **L'infettivologo e la diagnosi di tubercolosi**
A. Matteelli
15.00 **La diagnosi di tb extrapolmonare**
S. De Lorenzo
15.30 Coffee break

IV SESSIONE
Moderatori: *M. Bugiani - C. Grandi*

16.00 **IGRA test e diagnosi di TB**
L. Richeldi
16.30 **Novità diagnostiche di laboratorio**
D. Goletti
17.00 **I protocolli terapeutici**
A. Gori
17.30 **I protocolli terapeutici personalizzati**
G. Besozzi

SIMPOSIO

18.00 **"TB: the unfinished Agenda" Bill & Melinda Gates Foundation action plan**
Giorgio Mosconi

18.15 **"L'impegno sociale della Lyli per la TB" Lyli MDR-TB Partnership**
Luciano Di Gaudio

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SESSIONE per MEDICO CHIRURGO

V SESSIONE
Moderatori: *A. Iannaccone, F. Blasi*

9.00 **Tb e patologie respiratorie concomitanti**
L. Casali
9.30 **Tubercolosi e trapianti**
F. Sinardi
10.00 **Le interazioni farmacologiche età correlate**
A. Allieri
Coffee break

VI SESSIONE
Moderatori: *R. Grossi, L. Casali*

11.00 **La Tb farmacoresistente**
S. De Lorenzo
11.30 **La TB nei sieropositivi**
P. Scarpellini
12.00 **TB: una malattia di sistema**
G. Besozzi
12.30 **Verifica questionario di apprendimento e chiusura lavori**

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