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CASTLEMAN'S LYMPHOADENOPATHY: TWENTY YEARS OF OBSERVATION. II. GENERALIZED FORM

UN VENTENNIO DI OSSERVAZIONI SULLA LINFOPATIA DI CASTLEMAN. II. LA FORMA SISTEMICA

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The Authors continue the discussion on the etiopathogenesis of Castleman's lymphadenopathy and review the literature of recent years concerning the generalized form of this condition.
They describe five cases of the generalized form. The discussion points out the difficulties of a unique interpretation of heterogeneous clinical patterns linked only by histology.
Some pathogenetic hypotheses are proposed.

KEY WORDS: Generalized angiofollicular hyperplasia of lymph nodes, angiomatous lymphoid hamartoma, Castleman's lymphoadenopathy, venulo-capillary hyperplasia.

In a previous paper concerning Castleman's lymphadenopathy, we reported on our observations of five cases fitting the practically undisputed pattern of a single, benign neoformation which does not recur after surgical ablation.

In fact, throughout the written history of this singular entity, monoadenopathic localization and benign nature have always been the uncontested central theme of every treatise. Regarding the clinical picture, for a long time the absence of generalized symptoms was believed to characterize the disease.

Beginning in 1965, the possibility that in a minority of cases, the monoadenopathic localization of the process might be associated with

a systemic symptomatology resembling that of chronic aspecific inflammation was documented. In the literature, such systemic manifestations have been reported as occurring, for the most part, in the « plasma cell » histological variant and usually regress definitively after surgical removal of the mass [10 12 14].

The first move away from the dogma of a purely monoadenopathic localization of the disease came in 1973, in a case described by Leibetseder and Thurner [11]. Their observations covered a seven year period, during which, except for the appearance of mild splenomegaly, no particular tendency toward progression of disease was noted, thus prompting the authors to define the process as « benign ». As a matter of fact, the process was characterized by recurrent generalized lymph node enlargement (cervical, axillary, inguinal) which accompanied any infectious episode (furthermore, the patient seemed particularly prone to such episodes thus resembling an immunodepressed subject). Histologically, the disease evolves from an initial stage of aspecific lymphadenitis to a successive stage which is identical with that of the hyaline-vascular form of Castleman's lymphadenopathy. The ESR is slightly elevated and peripheral eosinophilia is sometimes present, even in the absence of infectious episodes. And thus, this report remained isolated and, for the most part, ignored for another five years, save being cited as an example of... monoadenopathy [8].

But in 1978, another case with analogous characteristics was published. Gaba et al.[8] described a patient presenting with lymph node enlargement in all superficial regions including the posterior mediastinum, a large pelvic mass and splenomegaly which was treated early by splenectomy. The histological picture was that of the hyaline-vascular variant of Castleman's lymphadenopathy with, however, areas of plasmacytosis. The patient had iron-deficiency anemia, markedly elevated ESR, polyclonal hypergammaglobulinemia (limited to IgM and IgA) and plasmacytosis in the bone marrow; cryoagglutinins in blood and papilledema were also present. The observations were made over a three year period in which no signs of evolution of the disease were evidenced. The case in question is the first in the literature with histologically documented splenic localization. Other cases of monoadenopathic Castleman's disease have been described in the last tenths of years [9], wherein clinical identification of splenomegaly should have authorized at least the hypothesis of a localization in more than one site.

In 1979, at the 27th Congress of the Italian Society of Hematology, Bellesi et al.[5] referred to a case of the hyaline-vascular type with left

cervical and bilateral axillary localization; one lymph node was biopsied, the other two lymph nodal enlargements regressed spontaneously and, with this, depression of cell-mediated immunity disappeared.

Presently, the study of a third case with multicentric characteristics is being prepared for publication by another Italian group [16]: over the span of fifteen years, almost all superficial lymph node regions have been involved and now the lumbo-aortic nodes have been shown by lymphography to be involved as well; there is no splenomegaly. Paradoxically, systemic manifestations are lacking; this fact, in addition to the long duration of the disease, is a factor in favor of the benign nature of the process. Histologically, in three biopsies performed over a period of many years, a very strong progressive increase in the interfollicular plasma cell component superimposed on a typically hyaline-vascular pattern has been observed.

Finally, Frizzera, at the end of 1979, announced [6] the imminent publication of 11 cases of Castleman's lymphadenopathy histologically intermediate between hyaline-vascular and plasma cell types with generalized lymph node as well as splenic localizations and general immunological disturbances [7]. Since the work has not yet been published, we do not know how many of Frizzera's cases are similar to the three cited above but, judging from the small amount of information we have concerning this work, it seems that a certain number of cases have many factors in common.

Thus, for seven years, more and more evidence has been accumulated that Castleman's lymphadenopathy may present not only with the clinical symptomatology and laboratory findings of an immunological disturbance but also with polyadenopathic involvement which has only recently come to light in the literature. Until now however, there have been no clear signs of malignancy even if Gaba's case and several of those announced by Frizzera would seem to indicate, more or less indirectly, that the compromised general conditions of the patient can entail the risk of fatal complications.

As far as we can ascertain, the next step forward was taken by Micoli and Spairani [13] in 1979. They reported a case of Castleman's lymphadenopathy with generalized lymph node enlargement and splenomegaly which followed a fulminant course with immunodeficiency leading to a severe terminal syndrome including hypogammaglobulinemia, confluent multifocal pneumonia and death within two months.

Along the same lines was the case published in 1980 by Bartoli et al.[4]: this was a hyaline-vascular variant of Castleman's lymphadenopathy but with interfollicular plasmacytosis. All superficial lymph

node regions were involved and splenomegaly, fever, cutaneous rash, anemia, polyclonal hypergammaglobulinemia (principally IgG) and a decline of the general condition notwithstanding cycles of COPP were all present. Death from sepsis occurred after nine months. Very similar to this case is the one soon to be published by Rizzo et al.[15]. It also presents a clinical picture and laboratory data having many features in common with those of an angioimmunoblastic lymphadenopathy with a particularly malignant course.

In the first of the three cases just cited, the immune disturbance is manifested in the terminal phase by hypogammaglobulinemia rather than the much more frequent polyclonal hypergammaglobulinemia (even though this increase is inefficacious for defense of the organism). This fact however, does not seem to contrast the strong resemblances among the three cases.

And thus, together with the picture of a general immunological disturbance and the multicentric nature of the lymphopathy, a malignancy with a particularly dramatic course emerges. And here we will introduce our observations. Five cases, multicentric in localization, were observed over a period of thirteen years, discussed repeatedly among hematologists and pathologists, and cited many times at various congresses[1,2] but never reported in print since we hesitated to prematurely present a problem which would not have received its just attention at that time. The current evolution of the concept of Castleman's lymphadenopathy seems a suitable environment for the introduction of a new clinical contribution. Even if our cases do not solve some fundamental problems, we hope that they at least serve to focus attention on them in all their complexity.

The five cases are presented not in chronological order but according to a certain progression of malignancy. Table I reports a synthesis of pertinent data.

Case descriptions

CASE 1. (V.A.) The patient, a 73-year-old male, was admitted to the department of medicine on May 6, 1978 for asthenia and an enlarged left axillary lymph node of one year's duration. Past history was devoid of relevant data. Except for slight elevation of ESR (KI=39) and polyclonal hypergammaglobulinemia (2.70 g/dl), no general signs or symptoms were present. The axillary lymph node was biopsied. Histological diagnosis: Castleman's lymphadenopathy, plasma cell variant. Since elevation of ESR and hypergammaglobulinemia persisted after surgical ablation and no other localization were documented

TABLE I.

Castleman's lymphadenopathy - generalized form.

Linfopatia di Castleman - forma sistemica.

Case (Sex)	Age and Yr. of onset	Localization (lymph node region)	Histological type	General symptoms	ESR (mm/h)	Gamma globuline (g/dl)	Lymphocytes/ eosinophils (µl)	Therapy	Evolution and Disease duration (mos.)
V.A. (M)	76 1977	left axillary lumbo-aortic	plasma cell	asthenia	39	2.70	1248/40	cortico-steroids	PR- 48
U.L. (M)	42 1965	bilateral cervical and axillary (splenomegaly hepatomegaly)	hyaline-vascular	asthenia dyspnea	52	2.73	368/370	radiation	death- 154
T.A. (M)	53 1949	bilateral inguinal and axillary skull (splenomegaly)	hyaline-vascular	fever pruritis (oscillatory recurrence and spontaneous remission)	38	2.86	1080/1260	monochemo-therapy and cortico-steroids	death- 228 mos. from clinical onset 11 mos. from histological diagnosis
D.N.S. (M)	46 1968	rt. cervical rt. axillary bilateral inguinal (hepatomegaly)	hyaline-vascular	fever asthenia (oscillatory recurrence and spontaneous remission)	14	1.98	1296/	monochemo-therapy	death- 72
M.C. (M)	57 1967	bilateral cervical axillary and inguinal (splenomegaly)	hyaline-vascular	fever vomiting cachexia auto-immune hemolytic anemia	104	4.24	812/66	monochemo-therapy and cortico-steroids	death- 18

by clinical examination or by radiological study of the thorax, lymphography was performed and revealed bilateral involvement of lumboaortic lymph nodes. The advanced age of the patient and the modest degree of decline of his general condition suggested a prudent course of therapy. The patient has been maintained in good condition on low doses of corticosteroids and has had no further hospital admissions.

CASE 2. (U.L.) The patient, a 42-year-old man, was admitted to the department of medicine on Feb. 6, 1965 for asthenia, dyspnea and lymph node enlargement (superficial lymph nodes of upper body and mediastinum) of one month's duration. On admission left cervical and bilateral axillary lymph node enlargement as well as accentuation of hilar shadows were noted. The lower border of the liver was 3 fingers and the lower edge of the spleen 10 cm below the costal margin. Laboratory data: ESR: KI=52; polyclonal hypergammaglobulinemia (2.73 g/mm^3); lymphopenia (minimum value reached was 368/mm^3); moderate eosinophilia (370/mm^3). A lymph node from the left cervical region was biopsied. As we can see now, the correct histological diagnosis should have been Castleman's lymphadenopathy — hyaline-vascular variant. At that time, the process was considered an atypical form of malignant granuloma and was treated by roentgenotherapy of the supradiaphragmatic sites of involvement. The patient returned to his home town and for the next two years he was frequently (on the average of once a month) admitted to the department of medicine because of the continued presence of lymph node enlargement. Roentgenotherapy was repeated often and the spleen was also irradiated. After 1967, the multicentric process became stabilized producing no further significant disturbances and the patient was not admitted again for this disease. In 1977, the patient died in a hunting accident, 12 years after the onset of the disease.

CASE 3. (T.A.) The patient, a 71-year-old man, was admitted to the department of medicine on Sept. 17, 1967. He had been followed in another town for a syndrome which had begun 18 years earlier and was characterized by remittent fever with itching and generalized lymphadenopathy. The condition had bimonthly peaks of activity and spontaneous remissions. For 15 years he was followed without therapy until the appearance of punched-out osteolytic lesions in the skull. Thereafter he was treated for two years with corticosteroids and chlorambucil without results. A lymph node biopsy performed during those years had revealed a histological picture interpreted then as « plasmacytoma ».

On admission to our hospital there was right cervical and bilateral axillary and inguinal lymph node enlargement. The lower edge of the spleen was felt 4 fingers below the costal margin. Laboratory data: ESR: 38 mm in the first hour; polyclonal hypergammaglobulinemia (2.86g/dl); circulating lymphocytes at the lower limits of normal (1080/mm^3); marked eosinophilia (1260/mm^3). The intradermal tuberculin reaction was negative. Areas of osteolysis in the skull were still present. No doubt was cast on the clinical diagnosis of Hodgkin's disease notwithstanding the unusual histological picture seen after a biopsy performed on an axillary lymph node. The histological diagnosis is today Castleman's lymphadenopathy — hyaline-vascular variant but with areas of plasmacytosis. Discharged on monochemotherapy (VELBE) and corticosteroids, the patient died the following year in his home town, 19 years after the onset of the disease.

CASE 4. (D.N.S.) The patient, a 47-year-old man, was admitted to the department of medicine on April 17, 1969 because of slight fever, asthenia and superficial lymph node enlargement of one year's duration with bimonthly periods of recurrence and spontaneous remission. The past medical history was insignificant. On admission there was a very strong positive intradermal tuberculin reactivity. Right cervical, right axillary, and bilateral inguinal lymph node enlargement was noted. Liver and spleen were within normal limits. No mediastinal involvement was noted. The ESR was 14 mm after the first hour. Moderate polyclonal hypergammaglobulinemia (1.92 g/dl) was noted. The peripheral leucocyte picture was unremarkable. A lymph node from the right side of the neck was biopsied. The histological picture to be discussed below did not significantly influence the clinical impression held by some physicians that the entity was an unusual variant of Hodgkin's disease. The patient was released with cyclophosphamide therapy to be carried out at home. Several admissions to the department of hematology of a hospital near his home did not alter the clinical situation. Further lymph node biopsies always disclosed the same pattern. In 1974, during one of the many hospital admissions, what would now, on a critical reappraisal of the case history, seem to have been hemolytic manifestations appeared. The patient's condition worsened and in June 1974, he died, 6 years (72 months) after the onset of the disease.

CASE 5. (M.C.) The patient, a 59-year-old man, was admitted to the department of medicine on Jan. 20, 1969 because of periods of fever and vomiting which had begun a year and a half earlier and always disappeared spontaneously. During the last month before

admission, a daily spiking fever preceded by chills appeared which did not subside spontaneously but was responsive to corticosteroids. The past medical history was insignificant. On admission the patient had a high fever and was anemic (Hb 8.80 g/dl; RBC $2.78 \times 10^6/mm^3$). Reticulocyte count was elevated ($139.000/mm^3$) and there were occasional erythroblasts in the peripheral circulation. Jaundice was present with elevated levels of indirect bilirubin. In other words, this was a patient with fever and hemolytic anemia. Bilateral cervical, axillary and inguinal lymph node enlargement was noted. The lower edge of the spleen was felt 3 fingers below the costal margin. The ESR was 104 mm after the first hour. There was a remarkable polyclonal hypergammaglobulinemia (4.24 g/dl). Sporadic plasma cells were found in the peripheral blood and lymphopenia ($812/mm^3$) was noted. Today we would say that such clinical findings and laboratory data would fit for an angio-immunoblastic lymphadenopathy; at that time the same phenomena could have been interpreted as related with an aggressive variety of Hodgkin's disease. After the biopsy of a cervical lymph node, the histological picture resembling Castleman's lymphadenopathy with peculiar aspects similar to the previous case was disclosed. Nevertheless, this finding did not influence the choice of therapy, suggested by the severe condition of the patient. Notwithstanding high dosages of corticosteroids and mechlorethamine, the patient died, little more than a month after therapy was started and less than 2 years from the onset of the disease. Table I reports the highlights of the data regarding the 5 cases.

The histological findings reported in the figures are the following: Case 1: a form of Castleman's lympadenopathy closely resembling the plasma cell variant but with sporadic interfollicular foci of venular hyperplasia and isolated follicles with hyaline-vascular morphology (Fig. 1 and 2); Case 2: typical hyaline-vascular variant of Castleman's lymphadenopathy (Fig. 3 and 4); Case 3: hyaline-vascular form of Castleman's lymphadenopathy but with several peculiarities (Fig. 5, 6, 7, 8). In fact, foci of plasmacytosis can be seen within the interfollicular venulo-capillary network; moreover, some of the follicles show remarkable plasmacytosis in the lymphocyte mantle and in some, plasmacytosis is even found in the germinal centers where, at times, the plasma cells may outnumber the other lymphoid cells. The follicular morphology in cases 4 and 5 is identical to that found in the hyaline-vascular variant of Castleman's lymphadenopathy (Fig. 9, 11, 12). However, in the interfollicular zones, there is still a clear-cut compartmentalization between paracortical and medullary areas, the former with an extensive venulo-capillary network, the latter with

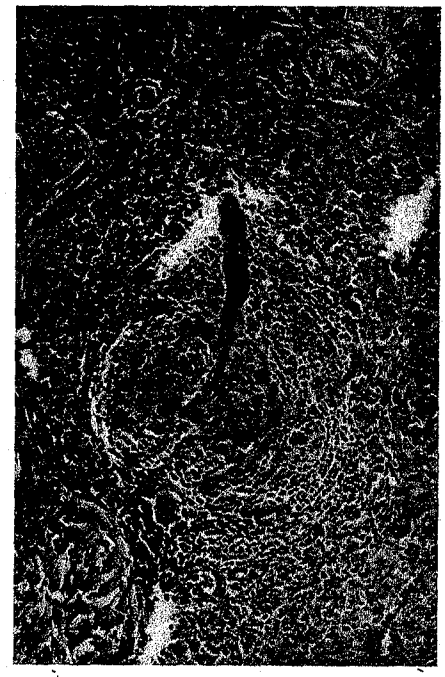

Fig. 1.

Case 1. Hyaline-vascular features of a follicle. HE 100×.

Caso 1. Aspetto jalino-vascolare di un follicolo. HE 100×.

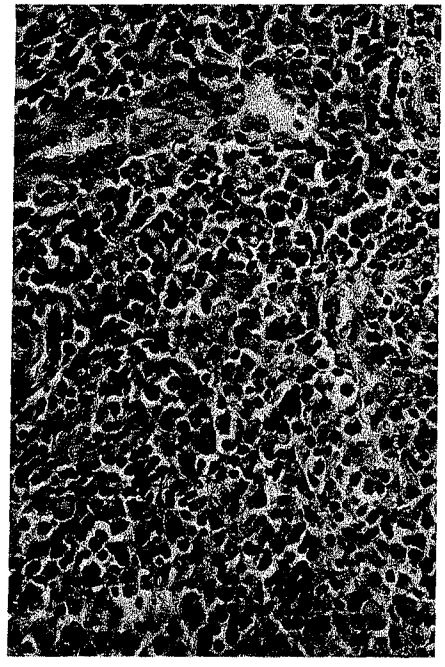

Fig. 2.

Case 1. A carpet of plasma cells in an interfollicular space. Presence of spheroids of a proteinaceous substance: a possible index of immunoglobulin secretion. HE 250×.

Caso 1. Tappeto di plasmacellule in uno spazio interfollicolare. Sferule di materiale proteico, possibile segno di attività immunosecretiva. HE 250×.

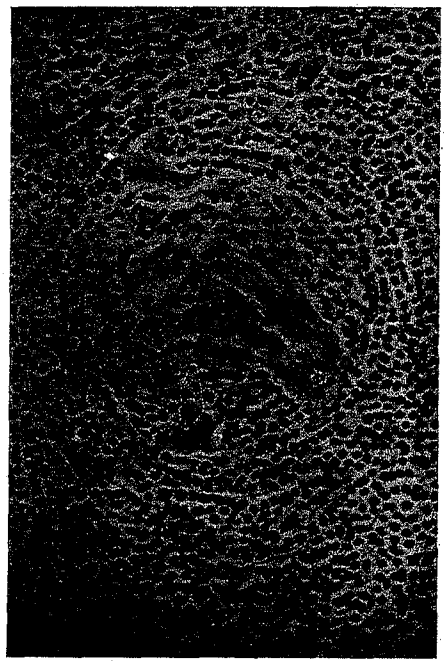

Fig. 3.

Case 2. Hyaline-vascular features of a follicle. HE 250×.

Caso 2. Aspetto jalino-vascolare di un follicolo. HE 250×.

Fig. 4.

Case 2. Vascular hyperplasia in the interfollicular spaces. HE 250×.

Caso 2. Iperplasia vascolare negli spazi interfollicolari. HE 250×.

Fig. 5.

Case 3. Characteristic features of a follicle. Van Gieson 250×.

Caso 3. Aspetto caratteristico di un follicolo. Van Gieson 250×.

Fig. 6.

Case 3. A marked plasmocytosis in a follicular corona. Giemsa 250×.

Caso 3. Forte plasmocitosi nella corona di un follicolo. Giemsa 250×.

Fig. 7.

Case 3. Venular hyperplasia in the interfollicular spaces. Giemsa 100×.

Caso 3. Iperplasia venulare negli spazi interfollicolari. Giemsa 100×.

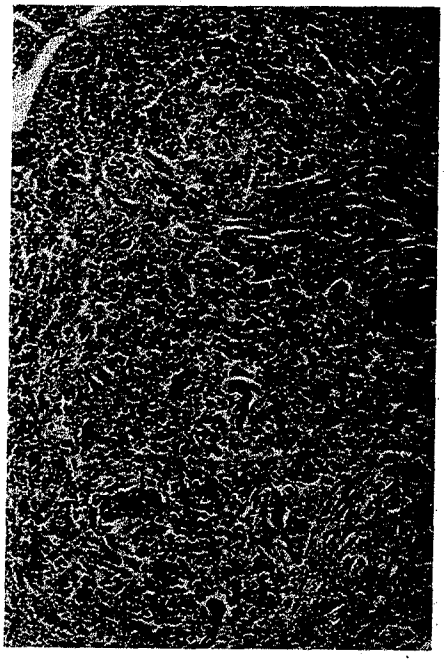

Fig. 8.

Case 3. Focal plasmocytosis inside the follicles and in the interfollicular spaces. Giemsa 100×.

Caso 3. Plasmocitosi focale nei follicoli e negli spazi interfollicolari. Giemsa 100×.

Fig. 9.

Case 4. Characteristic features of a follicle. Giemsa 100×.

Caso 4. Aspetto caratteristico di un follicolo. Giemsa 100×.

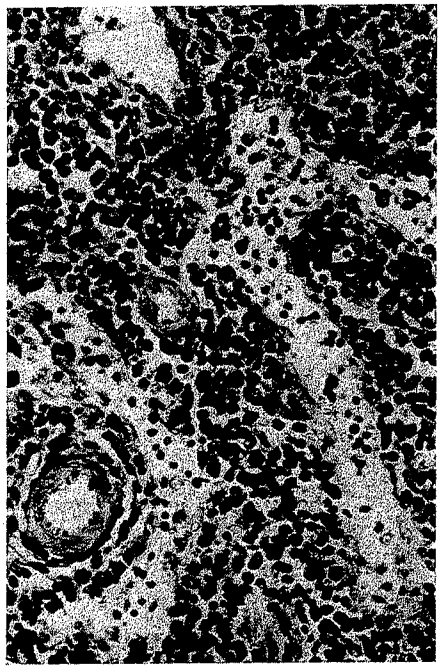

Fig. 10.

Case 4. Medullary sinuses and cords. The latter are filled with plasma cells. Giemsa 250×.

Caso 4. Sinusoidi e cordoni nella midollare. Questi ultimi infarciti di plasmacellule. Giemsa 250×.

Fig. 11.

Case 5. Hyaline-vascular features of a follicle. HE 250×.

Caso 5. Aspetto jalino-vascolare di un follicolo. HE 250×.

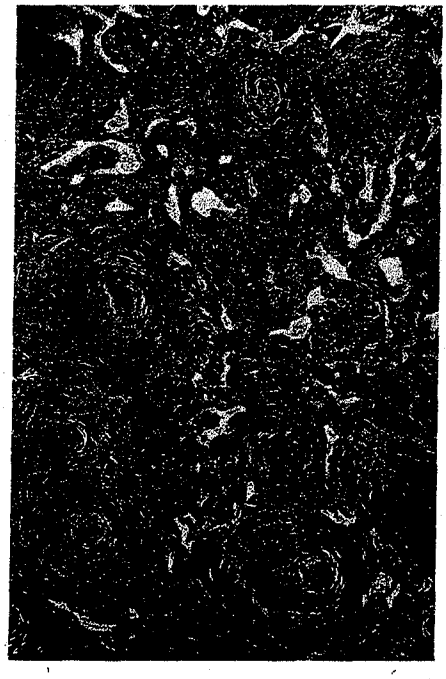

Fig. 12.

Case 5. General view. Hyaline-vascular features of follicles. Structure of the medullary region maintained. Plasmocytosis of the medullary cords. Giemsa 40×.

Caso 5. Veduta d'assieme. Aspetto jalino-vascolare dei follicoli. Conservazione della struttura della midollare con plasmocitosi dei cordoni. Giemsa 40×.

sinuses and cords. The cords are filled with plasma cells (Fig. 10, 12). This picture is therefore identical to the case of Gaba et al.[8].

Discussion and conclusions

Thus, we have 5 patients with topographically multicentric Castleman's lymphadenopathy; one of the plasma cell type, two of the hyaline-vascular type and two with the particular characteristics described above. All had systemic manifestations, the common denominator being polyclonal hypergammaglobulinemia. Patient number 1 (V.A.) presented with only polyclonal hypergammaglobulinemia associated with monocentric lymph node enlargement (axillary) and all clinical and laboratory findings fit the classical description. The only clue to the presence of other sites of involvement was the persistence of the dysproteinemia after surgical removal of the axillary lymph node. These other sites of involvement were then demonstrated by lymphography. As far as we know, the disease is still apparently benign notwithstanding its multicentric nature. It therefore resembles the case of Leibetseder and Thurner[11], that of Schieppati et al.[16] and perhaps that of Bellesi et al.[5]. The already advanced age of the patient and the increased probability that he will die of causes unrelated to the lymphadenopathy make it difficult to say what could be the future clinical course of the disease. In cases 2 (U.L.), 3 (T.A.), and 4 (D.N.S.), a marked systemic involvement of the organism characterized the lymphadenopathy from its very beginning. In two of them, T.A. and D.N.S., it was accompanied by slight fever and spontaneous remissions as in Hodgkin's disease. Another similarity with Hodgkin's disease was the presence, in cases 2 and 3 (U.L. and T.A.) of peripheral lymphopenia and eosinophilia. The patient with the longest period of survival, 19 years in patient 3 (T.A.) as well as the patient with the shortest, 6 years in patient 4 (D.N.S.), both succumbed as a result of a fatal systemic adenopathy. It is more difficult to say anything definitive about case 2 (U.L.) since he died accidentally 12 years after the onset of the disease, having lived his last 10 years in relatively good health. Regarding the multicentric cases reported as benign in the literature, one can therefore ask whether a longer period of observation is not needed to define the process as truly « benign »; that is, whether the generalized form of Castleman's lymphadenopathy is not, in reality, always a malignant process with a delayed final outcome. Finally, case 5 (M.C.), together with the cases reported by Micoli and Spairani[13], Bartoli et al.[4], and Rizzo et al.[15]

serve as a reminder of how the onset, clinical course, laboratory data and conclusion of Castleman's lymphadenopathy can resemble angioimmunoblastic lymphadenopathy. The only distinguishing feature is therefore the histological picture. Thus, the histological picture of Castleman's lymphadenopathy covers a variety of clinical situations. In fact, there is no clear-cut distinction between the monoadenopathic variant with slow, non-invasive growth pattern, lack of systemic manifestations, and complete remission after removal on the one hand and the generalized syndrome with splenomegaly, rapidly fatal course and impressive complement of clinical findings and laboratory data on the other but indeed, at least 2 intermediate conditions exist. These are: 1) the benign monoadenopathic form which does not recur after surgical removal but is characterized by systemic manifestations similar to those of chronic inflammation; 2) the generalized form which is characterized at times by splenomegaly, often, but not always, by systemic manifestations similar to those of chronic inflammation, and by a long clinical course which frequently (perhaps not always) is fatal.

Considering the wide variety of clinical patterns which are associated with a rather uniform histological picture, the problem of the nosographic classification of Castleman's lymphadenopathy can be looked at from 2 diametrically opposed points of view. 1) Either we are dealing with a heterogeneous entity whose deceptive unity is based on a histological picture which, in reality, explores only superficial epiphenomena or 2) we are dealing with a variety of clinical patterns converging into a single nosographic entity whose real homogeneity is revealed by the histological picture. We feel that the second point of view is more accurate. The histological presentation is not an aspecific phenomenon as would be, for example, a uniform carpet of lymphomatous cells. It is rather a complex and exceedingly characteristic picture which can not be the result of a chance convergence of epiphenomena. However, it still remains difficult to explain such a wide variety of clinical patterns. Therefore, we cannot overlook this matter in our discussion of what precisely is Castleman's lymphadenopathy. In a previous paper which dealt with the monoadenopathic form of the disease, after a discussion of its possible nosography, we concluded that the process is an autonomous rather than a reactive proliferation originating from the lymph nodes.

Following the same line of reasoning, we can state that, of the various entities grouped under the title of autonomous proliferations, the dysontogenetic processes can be immediately eliminated. The generalized form of Castleman's lymphadenopathy provides strong sup-

port for this statement. Thus not only are we not dealing with a « benign thymoma », nor with a hyperplasia of ectopic hemolymph nodes, or not even with an error in the formation of numerous lymph nodes in different regions which manifests itself in adult life. However, it is also difficult to accept a strictly neoplastic interpretation. In Castleman's lymphadenopathy, there is no one cell line, not even the plasma cell line, from which a lymphomatous-type clonal proliferation can be demonstrated. The only morphologically abnormal population was the centrofollicular mesenchymal one seen in one of our monoadenopathic cases [3]. Is Castleman's disease a primary disturbance of lymph node vascularization permitting an abnormal proliferation of endothelium in the follicular center?; or rather the formation of an abnormal line of pericytes?; or an abnormal line of dendritic cells? And furthermore, is the normal dendritic cell a transformed pericyte? In any case, how can one explain the intrafollicular plasmacytopoiesis?; the remarkable interfollicular plasmacytosis? These are, for the moment, questions without possible answers. In any case, it seems that the binomial reactive lymphadenopathy/neoplastic lymphadenopathy is becoming ever more inadequate in describing lymphatic pathology. For some years, a series of lymphopathies have been emerging, which are non-reactive i.e., they do not represent the response of normal lymphatic tissue to an abnormal stimulus. Nor are they lymphomatous in nature in that they do not exhibit aimless clonal expansion of a single lymphoid cell line. Most probably, these are primarily disturbances of the mechanisms of cooperation among different cell lines which increase the risk of subsequent lymphomatous transformation but are not lymphomas per se. It is probable that among these processes (perhaps those which Frizzera categorizes as « atypical immunoproliferative processes ») angiofollicular hyperplasia of lymph nodes can be placed near angioimmunoblastic lymphadenopathy.

It seems to us that further advances along this line of reasoning will one day permit us to clarify the pathogenesis of Castleman's lymphadenopathy.

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RIASSUNTO

Gli AA. riprendono la discussione sull'eziopatogenesi della linfopatia di Castleman iniziata in un precedente lavoro, ripercorrendo gli ultimi anni di segnalazioni bibliografiche relative alla forma polistazionale di detta linfopatia.

Effettuano poi la presentazione epicritica di cinque casi in cui la malattia si presentava in forma sistemica. Segue la discussione in cui viene fatta rilevare la difficoltà di interpretare unitariamente quadri clinici molto eterogenei unificati quasi solo dal quadro istologico. Il lavoro si conclude con un tentativo di inquadramento nosografico nei termini generici che le modeste conoscenze attuali per ora impongono.

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