Castleman's Disease : A Clinicopathologic Study of 12 Cases

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Abstract

Castleman's disease observed in 12 Thai patients was investigated. The male to female ratio was 1 : 3. Peak prevalence was in the third and fourth decades. It is suggested that the disease in Orientals tends to have extrathoracic mass more often than in Caucasians. Solitary non-tender slow growing mass was the most common symptom. Generalized lymphadenopathy in association with cutaneous plasmocytoma was noted in one example while asymptamatic pelvic lesion in a patient was discovered incidentally. Histologically, the hyaline-vascular type was found in 8 instances, the remainders were plasma-cell type. Surgery was effective for localized lesions while systemic form could benefit from chemotherapy.

In 1956, Castleman et al first described a series of 13 cases of localized mediastinal masses as benign lymphoid hyperplasia with excessive capillary proliferation[1]. Since then many cases and reviews describing similar lesions have been published under various terms such as Castleman's disease, follicular lymphoreticuloma, angiomatous lymphoid hamartoma, angiofollicular lymph node hyperplasia, and giant lymph node hyperplasia[2-5]. Such lymphoproliferative lesions are not only found in the mediastinum, they also occur in other regions of the body. The disease may manifest as a progressive slow growing solitary mass or generalized lymphadenopathy associated with systemic effects[5-11]. Histologically, the disease has been divided into two main types; the more common, 80 per cent to 90 per cent of the total is the hyaline-vascular (HV) type and the less common, plasma-cell (PC) type[5].

Our purpose here is to present 12 additional cases with some unusual clinicopathological aspects.

MATERIAL AND METHOD

Twelve cases of Castleman's disease were obtained from the Department of Pathology, Chu-

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Table 1. Clinical and pathological features in 12 cases of Castleman's disease.

Case No.	Age (yrs)	Sex	Size (cm)	Location	Duration	Symptoms and signs	Type of disease	Outcome
1.	15	F	3x3	R.cervical	6 yrs.	Slow growing neck mass	Hyaline-vascular	Doing well, 6 yrs.
2.	19	F	3x5	R.cervical	5 yrs.	Slow growing neck mass	Hyaline-vascular	Doing well, 5 yrs.
3.	22	F	3x5	L.cervical	2 yrs.	Slow growing neck mass	Hyaline-vascular	Doing well, 6 yrs.
4.	23	F	4x5	Retroperitoneum	4 mo.	Fever, abdominal dicomfort and pain	Hyaline-vascular	Doing well, 3 yrs.
5.	23	M	5x5	Mediastinum	1 mo.	Cough, dyspnea	Hyaline-vascular	Doing well, 4 yrs.
6.	31	F	5x6	L.cervical	2 yrs.	Slow growing neck mass	Hyaline-vascular	Doing well, 2 yrs.
7.	38	F	2x3	Bifurcation commom iliac artery	8 mo.	Abdominal pain	Hyaline-vascular	Doing well, 6 mo.
8.	42	F	1x2	L.cervical	8 yrs.	Slow growing neck mass, Weight loss	Hyaline-vascular	Recurrent 2 yrs. after surgery
9.	38	F	1.5x2	R.inguinal	6 mo.	Multiple skin plaques, anemia generalized nodes enlargement	Plasma-cell	Alive with sustain Clinical course, 6 yr.
10.	39	M	5x6	R.axillar	2 yrs.	Progressive growing mass	Plasma-cell	Doing well, 1 yr.
11.	50	M	2x4	Celiac	2 mo.	Abdominal discomfort, pain constipation, weight loss	Plasma-cell	Doing well, 10 mo.
12.	52	F	3x5	Pelvic	-	Incidental finding	Plasma-cell	Doing well, 2 yrs.

F = female ; M = male ; yr = year ; Mo = month ; L = left ; R = right

lalongkorn Hospital over a 15-year period (1980-1995). The clinical records were studied after review of the microscopic materials. All specimens were fixed in 10 per cent formalin and embedded in paraffin. Sections were stained with hematoxylin and eosin (H & E) and Gomori's silver impregnation.

RESULTS

The clinical features and pathological findings are given in Table 1. The twelve lesions were represented by 9 women and 3 men. Seven of the eight patients with HV type were women but there was an equal representation of 2 men and 2 women among the PC variant. The age of the patients ranged from 15 to 52 years with a mean age of 27 years for cases with HV type and 45 years for those of PC type. Five patients had neck mass, three complained of abdominal discomfort and pain, two had weight loss, one developed generalized lymphadenopathy with cutaneous plasmacytoma and anemia, one had chronic cough and dyspnea, and one had an axillary mass. Only one case was asymptomatic; the lesion was incidentally discovered during removal of the intrauterine device (case 12). The shortest duration of symptoms was 1 month, the longest was 8 years. The PC type was associated with a shorter time of illness. Sites of lesions favoured extrathoracic nodes. Among the HV type, five were located in the cervical nodes, one, each, in the mediastinum, retroperitoneum, and bifurcation of common iliac artery. As for the PC type, one affected the mesenteric node, one involved the pelvic region, one in the axillary node and one had multiple lesions.

Tumor sizes ranged from 1 to 6 cm in greatest diameter and the mean maximum dimension was 4.5 cm for HV type and 4.1 cm for the PC variant. Among the HV type, 6 masses were oval and regular in shape, two were nodular. A reddish brown cut surface was present in 5 lesions while 3 had a gray-white appearance. All PC lesions were well circumscribed with a gray-white cut surface. Microscopically, the HV lesions consisted of lymphoid follicles which were often small and showed atrophic germinal center as well as thick-walled vessels (Fig. 1). Many of these blood vessels were hyalinized with obliterated lumen. The endothelial cells were often plump. Excessive capillary proliferation was also noted between the lymphoid follicles. The silver impregnation clearly demonstrated network of blood vessels while the

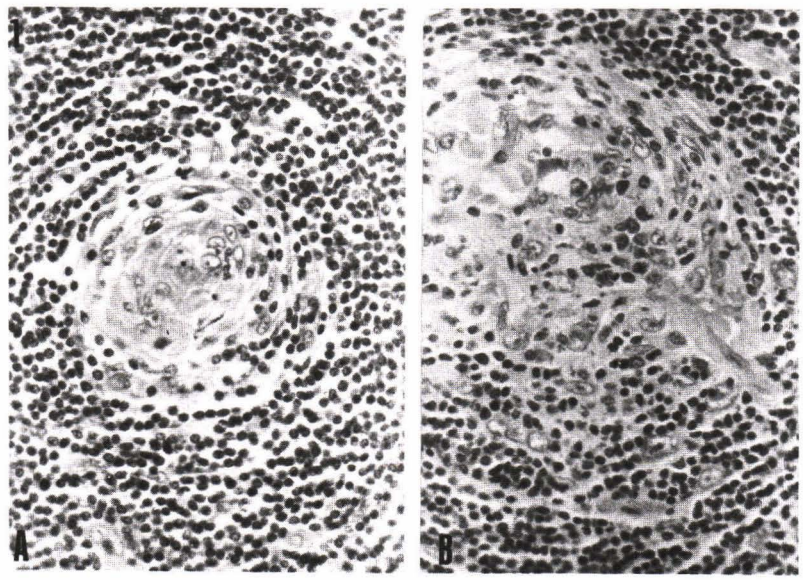

Fig. 1. Hyaline-vascular type
A. Small, atrophic germinal center with hyalinized vessel. Noted peripheral layering of small uniform lymphocytes. (H & E x 200)
B. Hyalinized germinal center with radially penetrating vessel. (H & E x 200)

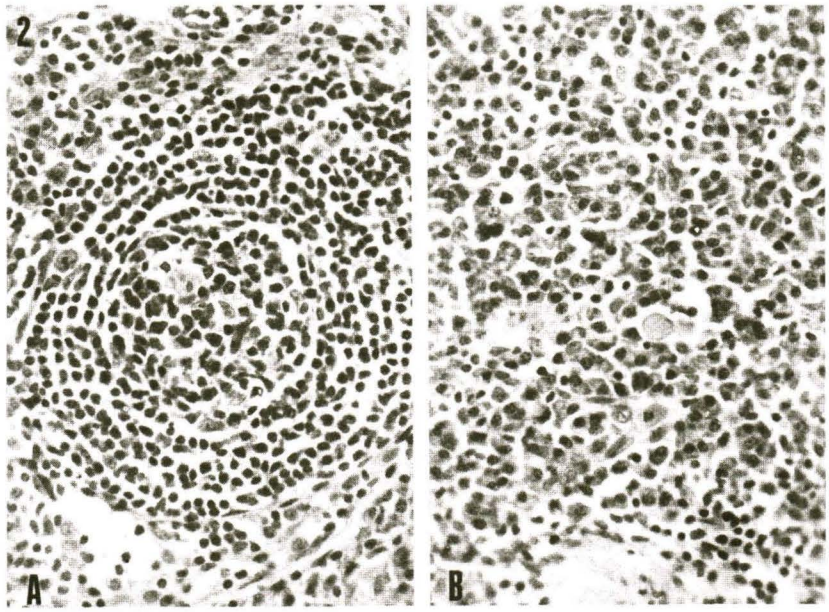

Fig. 2. Plasma-cell variant
A. Cellular follicle with adjacent plasma cell infiltration. (H & E x 200)
B. Interfollicular region showing a heavy infiltration by plasma cells. (H & E x 200)

follicles had scanty reticulin fibers. The PC variant showed normal or large follicles with heavy plasma cell infiltration in the intervening lymphoid follicles (Fig. 2). There was no particular vascularization or hyalinization in these follicle centers.

The primary mode of therapy in all but one case was surgery. Eleven patients had simple surgical extirpation of the mass. One instance with generalized lymphadenopathy received chemotherapy after the pathological diagnosis (case 9). There were no deaths in this series. Most patients were doing well when seen postoperatively at time from 6 months to 6 years. Only one example with HV type, the lesion had recurred 2 years after surgery (case 8). Although the skin lesions and lymphadenopathy still persisted in case 9, no new symptoms were seen during a 6 years follow-up.

DISCUSSION

The morphological findings described in our lymph node materials is characteristic of Castleman's disease which is classically recognized as the HV and PC types[3,5]. Most of the case reports are subclassified as HV variant as noted in our series[3-5]. Although the disease can occur at any age the median age for patients with HV type were younger than those with PC variant in our study but the number is small.

Regarding sex distribution, Keller et al stated that there was no particular sex preference although men predominated among AFIP cases[5]. On the other hand, Tung et al in a review of 62 cases disclosed that 34 patients were female, 27 were male and for one patient gender information was not available[3]. Their observation was confirmed in the present study. The lesions are more common in women. The disease has been frequently reported in Caucasians and rarely affects Orientals[3]. Additionally the great majority of the lesions are found in the mediastinum although they may be seen in other lymph-node bearing sites[1,3,5]. Unlike most reports, our study is the largest group of lesions occurring in Thais and all except one in our series were extrathoracic locations. The reasons for such differences are not known. Perhaps different factor (s) such as race, geographic distribution or different etiologic agents are involved. Based on these data, it is reasonable to suggest that extrathoracic lesions are more common in Orientals than those in the West.

The most common clinical manifestations in our patients are solitary, painless cervical mass followed by abdominal pain and discomfort. Such clinical features are of course related to the anatomic locations of the disease. It should be noted that our patients with abdominal lesions were associated with shorter duration of illness. The explanation for such variable duration of symptoms is probably related to the nature of signs necessary to bring the patient to medical attention. Symptoms of painless neck mass may be ignored while abdominal pain will impel the patients to be seen by a physician earlier.

An incidental finding of pelvic lesion as noted in one of our patients is uncommon[6,12]. According to Ylinen et al, only 11 cases with pelvic localization in women have been reported[6]. The disease is also a rare cause of an axillary mass and appears to have no other characteristic features. It was recorded in only one of 81 cases in a series reported by Keller et al, and one in a series of 62 cases reviewed by Tung et al[3,5]. Recognizing such unusual pelvic or axillary lesions is important because it can prevent an errorneous diagnosis of lymphoma or metastatic carcinoma particularly when a rapid diagnosis by frozen section is relied on. Such an error may result in palliative treatment of this benign disease. Therefore, the possibility of Castleman's disease should be considered when assessing a pelvic or an axillary mass.

Measuring growth rate by relating size of tumor to duration of symptoms is not a reliable method due to the different locations and cell types. The existence of asymptomatic masses is another problem to determine such a relationship. Some small tumors in our series were associated with either short or long duration of illness as were the large lesions. Although there is no real direct relationship between the size of the lesion and the duration of symptoms, it is reasonable to suggest that most tumors are slow growing and often are associated with a period of illness longer than 2 years. Our data also indicate that the PC type tended to be associated with a shorter duration.

Initially, the disease was described as a benign solitary mass. Recently multicentric form has been recognized as a distinct entity characterized primarily by generalized tumor-like condition affecting both lymph nodes and nonnodal tissues of various organs in the abdomen, chest, neck as well as central nervous system[7-11,13]. The systemic form is often associated with disorder immunity, an increased incidence of malignancy and an aggressive clinical course[7-11,13,14]. Evidence of developing cutaneous plasmacytoma in our example supports this view. With regard to the therapeutic management, surgery alone is effective for the localized form[1,3-5]. Radiation has been used with success in the treatment of the PC variant but only with some success in the generalized disease[13, 15-17]. We, however, suggest that generalized disease may have at least partially responded to chemotherapy as observed in our patient.

The mortality was nil in this series. All patients with localized disease did well postoperatively. A long term follow-up in our patients indicates the benign nature of the disease.

SUMMARY

Clinical data in 12 patients with Castleman's disease were correlated with pathological findings. The disease occurred predominantly in women. The age ranged from 15 to 52 years. Patients with the more common hyaline-vascular type were younger than patients with plasma-cell variant. Unlike most reports all except one were extrathoracic lesions. Our findings suggest that Orientals tend to have an extrathoracic mass more often than Caucasians. Solitary, painless enlarging neck mass was the most frequent symptom followed by abdominal discomfort and pain. The duration of illness and the tumor size varied without real direct relationship. Surgery is effective particularly for localized lesions while the generalized form may respond to chemotherapy. Mortality in this study was nil indicating the benign nature of the disease.

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โรคคาสเติลแมน : การศึกษาทางคลินิก – พยาธิวิทยา 12 ราย†

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ได้ศึกษาทางคลินิกพยาธิวิทยาในผู้ป่วยโรคคาสเติลแมน (Castleman's disease) จำนวน 12 ราย พบว่าผู้ป่วยส่วนใหญ่เป็นหญิง โดยมีอายุเฉลี่ย 27 ปี สำหรับผู้ป่วยด้วยชนิด hyaline–vascular และ 45 ปี สำหรับชนิด plasma–cell รอยโรคส่วนใหญ่ในรายงานนี้เกิดภายนอก mediastinum ซึ่งแตกต่างกับรายงานจากซีกโลกตะวันตก ผู้ป่วยมักมีก้อนเดียว ไม่เจ็บ ที่คอเป็นอาการนำ ตามด้วยอาการแน่นและปวดท้อง ไม่พบความสัมพันธ์ระหว่างระยะเวลาของอาการกับขนาดของรอยโรค การผ่าตัดได้ผลดี โดยเฉพาะผู้ป่วยที่มีก้อนเดียว เคมีบำบัดอาจได้ผลในผู้ป่วยที่มีรอยโรคหลายแห่ง ในรายงานนี้ผู้ป่วยทุกรายยังมีชีวิตอยู่ภายหลังการรักษา

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