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RHEUMATOID LYMPHADENOPATHY*

BY

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Chauffard and Ramond (1896) are credited with the first description of lymphadenopathy occurring in patients with rheumatoid arthritis. The association has been confirmed by others (McCrae, 1904; Waterhouse, 1908; Coates and Delicati, 1931; Parkes Weber, 1944; Rotés-Querol and Ciscar Ruis, 1948; Motulsky, Weinberg, Saphir, and Rosenberg, 1952; Feldman, 1961; Makarenko, 1965), and has become generally accepted. Although lymphadenopathy is considered to be an intrinsic feature of Still's disease and Felty's syndrome, there is no general agreement as to its significance in rheumatoid arthritis as a whole. Short, Bauer, and Reynolds (1957), in their classic study of the clinical features of rheumatoid arthritis, found that the incidence of lymphadenopathy varied from 19 to 96 per cent. in reports published at that time. In their own series of 86 patients, 29·4 per cent. had significant lymph node enlargement compared with 8·9 per cent. of 26 control subjects. They noted a higher incidence in males, but could find no correlation with disease activity, type of onset, or subsequent course of the disease, and they made no attempt to define the sizes of lymph nodes which were significant, or to correlate lymphadenopathy with duration of disease and local joint activity.

Lymphangiography has been performed on patients with rheumatoid disease, but there is no general agreement on what constitutes the typical appearances or what their significance is (Málek, Belán, Kriegel, and Kolc, 1960; Lucherini, Bompiani, Porzio, and Spina, 1965; Michotte and van Bogaert, 1966; Wiljasalo, Julkunen, and Salvén, 1966).

It was therefore decided to make a more comprehensive clinical and radiological study of lymph node involvement in rheumatoid disease with a view to answering the following questions:

(1) What is the true incidence of lymphadenopathy in patients with rheumatoid disease, and how does it compare with a matched control series of patients?

(2) What is the relationship of factors such as age, sex, duration of disease, and disease activity to lymph node enlargement?

(3) Is there any correlation between such laboratory tests as the haemoglobin level, erythrocyte sedimentation rate, sheep cell agglutination test and lymphadenopathy?

(4) Is the lymphadenopathy related to local joint involvement or is it a manifestation of systemic rheumatoid disease?

(5) What are the lymphangiographic appearances and how do they correlate with the clinical features of the disease?

Material and Methods

Clinical Survey

This was conducted on 100 out-patients who were unselected except in having classical or definite rheumatoid arthritis (American Rheumatism Association, 1959). A group of 100 controls, drawn from both out-patient departments and wards, was suffering from a wide range of medical disorders, care being taken to exclude patients with known or suspected collagen or malignant disease and any other condition regularly associated with lymphadenopathy.

Details of duration of rheumatoid disease in years, previous therapy with gold or steroids, haemoglobin level as a percentage, Wintrobe sedimentation rate in mm./hr, SCAT, and latex titres were noted on a *pro forma* for all the patients with rheumatoid arthritis. Joint involvement was recorded for hand, wrist, elbow, shoulder, foot, ankle, knee, and hip joints on right and left sides, involvement of the cervical spine being recorded as a single joint. An arbitrary score of 3 points was given to each of these joints or joint groups if actively involved, and 1 point if involved but not actively at the time of examination. An overall assessment of disease activity as inactive, active, or very active, was also made (MRC and Nuffield Joint Committee, 1954); 1, 5, or 10 points were then added to the total joint score according to the overall assessment of disease activity.

*Based on a paper presented at the Conference of the European League against Rheumatism at Lisbon in October, 1967.

Lymph node enlargement in both the rheumatoid and control patients was recorded for right and left inguinal, axillary, and epitrochlear areas, the cervical region being counted as one area. Glandular enlargement was graded at each site as:

0 = no lymph node palpable,

1 = gland less than the size of a sixpenny piece (diameter < 2 cm.),

2 = gland less than the size of a halfpenny, but bigger than sixpence (diameter 2-2·5 cm.),

3 = gland between a halfpenny and a penny (diameter 2·5-3 cm.),

4 = gland greater than the size of a penny (diameter > 3 cm.).

A total gland score was then calculated without attempting to assess the number of palpable lymph nodes at any one site. A record was made of whether the glands were soft or firm, discrete or matted, and tender or non-tender. Enlargement of the liver and spleen was searched for and recorded, and finally a note was made of any other obvious factor predisposing to lymphadenopathy.

Lymphangiographic Method

Lymphangiography was performed on fifteen of the patients with rheumatoid arthritis (12 males and 3 females, mean age 56·5 years). The duration of the rheumatoid disease ranged from 4 months to 37 years (mean 9 years). The Waaler-Rose titre (SCAT) ranged from 1:64 to 1:2048.

The method used was based on that of Kinmonth and Taylor (1954). Patent blue violet was injected into the web space on the dorsum of a hand or foot. Following this, a small incision was made over a blue-staining of the skin, seen overlying lymphatic vessels proximal to the injected area. Cannulation of a vessel was then performed using a 30-gauge needle attached to a polythene tube. Lipiodol ultra fluid was used as the contrast medium, 7·5 ml. being injected into a lymphatic on the dorsum of each foot, mechanically at the rate of 1 ml. in 10 minutes. In the hand lymphatics, 2 ml. of Lipiodol ultra fluid were injected manually over 30 to 40 minutes, depending on the size of the vessel. *X* rays were taken on completion of the injection and were repeated after 24 hours. Follow-up *x* rays were repeated at later dates in some cases.

Although no attempt has been made to conduct a histological survey of rheumatoid lymphadenopathy, two case reports follow which show that confusion with malignant lymphoma can occasionally occur:

Case 1, a married woman, then aged 36, was seen by one of us (F.D.H.) in December, 1950. For 10 years she had suffered from rheumatoid arthritis which had progressed inexorably. A temporary remission had occurred when she became pregnant in 1943, but her condition relapsed rapidly in the puerperium, and this sequence of events was repeated in 1946. In 1949, her arthritis began to deteriorate more rapidly, and when seen in 1950 she had advanced changes of rheumatoid arthritis with nodules over the fingers and metacarpophalangeal joints and nodes in the left axilla. In July, 1952, glands appeared above the clavicles mostly in the left deep cervical chain. A biopsy report read:

"The gland architecture is replaced by a pleomorphic proliferation of cells including numerous reticulum cells of the Sternberg-Reed type. In view of the extreme cellularity, one would expect a poor prognosis."

A skin dose of 2,900r was given to the left cervical chain, and 1,200r to the right groin. Subsequently the glands rapidly disappeared, and gradually over the next few years her arthritis improved. Now, 15 years later, there has been no return of the glandular enlargement, and she is better than she was 10 years ago, both systemically and in her joints. The slides were reviewed in 1962. The diagnosis of Hodgkin's disease was not upheld, and the section was considered to show only simple inflammatory changes. Although the case is still under observation, the march of events strongly suggests that the second diagnosis is correct, and that the condition has throughout been a rheumatoid adenopathy.

Case 2, a married woman, aged 70 at her death in 1966, developed rheumatoid arthritis in 1958 when aged 61. The disease spread rapidly to involve most of her joints. She had had indigestion for many years and a gastric ulcer was discovered at this time. Waaler-Rose and latex tests were always strongly positive, the former in a titre around 1:1024. The spleen was not enlarged. Within a year of onset of the rheumatoid disease, glands were present in the inguinal areas, axillae, and epitrochlear areas, and later, as they extended up the arm as a chain of discrete painless lumps from elbow to axillae and also above the clavicles, a reticulosis was considered and even diagnosed by one observer. An axillary gland was removed: this showed a follicular pattern, the follicles being variable in size. The reticular pattern conformed to the follicles: the capsule was not invaded. Prof. Alan Morgan considered rheumatoid disease the most likely aetiology, but could not completely exclude a follicular lymphoma. As the indigestion worsened, a partial gastrectomy was performed; soft fleshy glands were also present inside the abdomen, of the same type as described above. The adenopathy did not worsen or abate, but her arthritis was actively progressive. She died last year of acute lobar pneumonia, with the rheumatoid and gland picture unchanged.

The case records of 35 patients with a former diagnosis of giant follicular lymphoma who attended the radiotherapy out-patient department at the Westminster Hospital between 1950 and 1966 were scrutinized for any evidence of rheumatoid arthritis. None was forthcoming.

Results

(A) Clinical Survey

Study Population

Table I (opposite) gives details of the age and sex of the patients studied and of the control group:

TABLE I

Group	Total No. of Subjects	Sex		Age (yrs)	
		Male	Female	Mean	Range
Rheumatoid Arthritis	100	37	63	56	22-80
Control	100	37	63	54	20-78

Incidence and Sex Difference

82 per cent. of patients with rheumatoid arthritis had lymphadenopathy compared with 52 per cent. of controls. In male patients the percentage with lymphadenopathy was 94 per cent. (controls 72 per cent.), and in females 77 per cent. (controls 36 per cent.). All glands were noted to be firm, discrete, and not tender.

Table II shows details of total and mean gland scores in patients with rheumatoid arthritis and in controls, with comparative figures for males and females. These differences are significant ($P < 0{\cdot}001$ for totals and males, and $P < 0{\cdot}05$ for females):

TABLE II

Group	Gland Score		
		Male	Female
Rheumatoid Arthritis	Total 441 Mean 4·41	235 6·35	206 3·27
Control	Total 213 Mean 2·13	103 2·78	110 1·75

Regional Incidence

Table III shows details of the percentage of rheumatoid and control patients with enlarged regional nodes and the mean gland score for each site. The differences are significant ($P < 0{\cdot}05$) for all except the cervical region:

TABLE III

Group	Cervical	Axillary	Epitrochlear	Inguinal
Percentage patients with glands	26	65	26	52
Mean gland score	0·27	2·4	0·54	1·2
Percentage controls with glands	23	41	10	29
Mean gland score	0·26	1·3	0·1	0·65

Duration of Disease

There was no relation between lymphadenopathy and duration of disease (correlation coefficient 0·0278 per cent.). The mean gland score for patients with rheumatoid arthritis of less than 3 years' duration was 4·3 compared with 4·8 for those of more than 10 years' duration. The mean duration of disease of patients with no glands was 8·2 years compared with 10·2 years for those with lymphadenopathy.

Age

Table IV shows the mean gland scores for patients with rheumatoid arthritis and controls in each decade:

TABLE IV

Patients' Age (yrs) ..		21-30	31-40	41-50	51-60	61-70	71-80
Mean gland scores	Rheumatoid Arthritis	0·5	5·3	4·6	3·7	4·9	5·0
	Control	1·6	2·2	2·2	1·8	2·2	3·0

Disease Activity

The mean gland score for patients with very active disease was 7·7 compared with 3·2 for those with inactive disease. This was highly significant ($P < 0{\cdot}001$), the mean joint score for those patients with lymphadenopathy being 41·8 compared with 28·4 for those without.

Local Gland-joint Relationships

The mean joint score of hands and wrists was 10·6 for patients with and without palpable epitrochlear glands. Table V shows the mean axillary and inguinal gland scores related to the total joint scores for the upper and lower limbs:

TABLE V

Joint Scores		0	1	2	3	4
Gland scores	Axillary	13·9	6	4·2	14·3	13
	Inguinal	8·4	11	10		

Sheep Cell Agglutination Test

Table VI shows the mean gland scores related to SCAT titres. The difference in mean gland scores for sero-positive and sero-negative patients is significant ($P < 0{\cdot}05$):

TABLE VI

Group ..	SCAT		SCAT Titre		
	Negative	Positive	<1/512	>1/512	>1/2048
Percentage patients	31	69	64	36	18
Mean gland score	3·8	4·5	3·5	4·9	5·7

Erythrocyte Sedimentation Rate

The mean gland score for patients with an erythrocyte sedimentation rate greater than 30 mm./hr was 5·1 compared with 3·5 for those whose rate

was less than this, an apparently significant difference; but there was no overall correlation between erythrocyte sedimentation rate and gland score (correlation coefficient 0·1176).

Haemoglobin

The mean gland score for patients with a haemoglobin level less than 80 per cent. was 4·8 compared with 4·1 for those whose haemoglobin was above this figure. There was no overall correlation between gland score and haemoglobin (correlation coefficient 0·1284).

Liver and Spleen

One patient had undergone splenectomy for Felty's syndrome, and one other patient had splenomegaly unassociated with Felty's syndrome. There was no significant hepatomegaly.

(B) Lymphangiographic Findings

The vessels in the calves, thighs, and arms of all the patients appeared normal, contrary to the findings of Kreigel, Málek, Belán, and Kolc (1961). Extravasation occurred, however, in patients in whom the Lipiodol was injected too quickly. The lymph nodes were found to be abnormal in most patients with rheumatoid arthritis, but not in all; there was considerable enlargement of the nodes which showed a normal outline, but with a coarse granular distribution of the Lipiodol within them as described by Wiljasalo and others (1966). In a normal lymph node, the granulation is usually fine-grained. In cases in which involvement of the lymph nodes was seen, it was always present in the nearest node draining the affected joints; in some cases only the nodes nearest the affected joints were enlarged, the more proximal nodes being normal in appearance. In none of the cases studied to date was any fibrosis seen within the node.

Three lymphangiograms from patients with rheumatoid arthritis are shown (Figs 1-3), together with one showing the changes of chronic inflammation (Fig. 4), and one showing Hodgkin's disease (Fig. 5).

The normal adult inguinal node diameter is 1-2 cm., and in the six patients on whom leg lymphangiograms were done, the mean diameter ranged from 2·25 cm. to 3·75 cm. In two of these cases, only the nodes nearest the affected limb were involved. In one case the nodes looked normal.

The normal adult axillary node diameter is 0·5-1 cm. and in the nine patients on whom arm lymphangiograms were done, the mean diameter ranged from 0·75-2·5 cm. In three cases only, the nodes nearest the limb were affected. In one case, the nodes looked normal. In two cases the supratrochlear nodes were outlined.

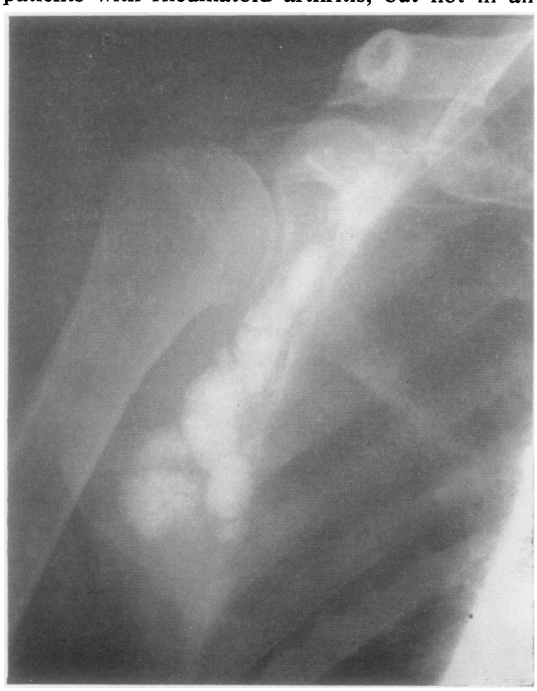

Fig. 1.—Arm. Lymphangiogram from a rheumatoid patient.

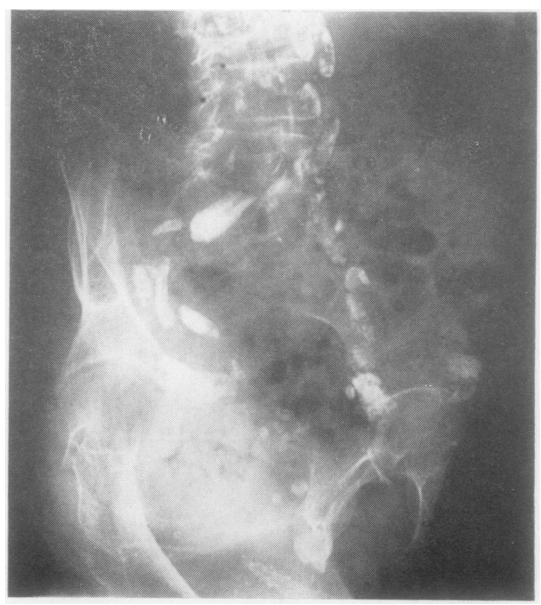

Fig. 2.—Pedal lymphangiogram from a rheumatoid patient.

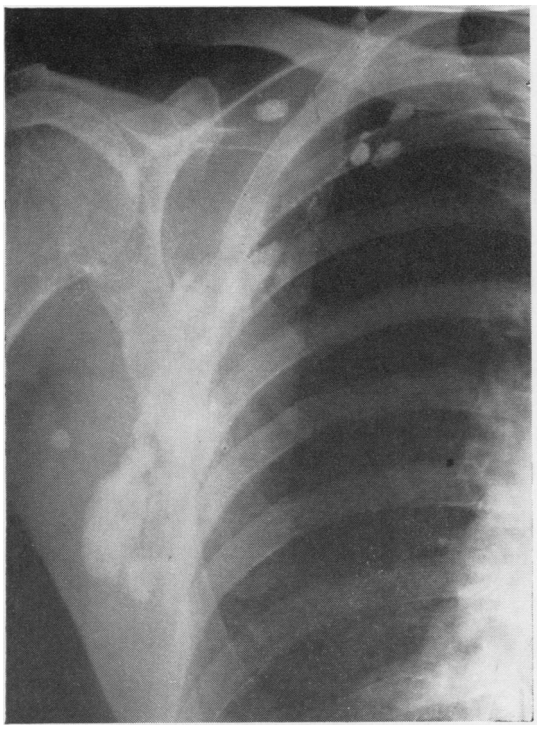

Fig. 3.—Arm. Lymphangiogram from a rheumatoid patient showing partial involvement of the chain only.

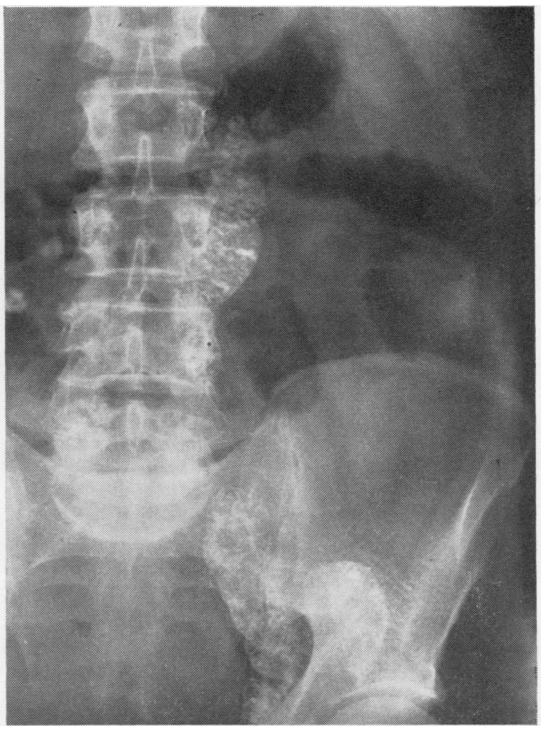

Fig. 5.—Pedal lymphangiogram from a case of Hodgkin's disease.

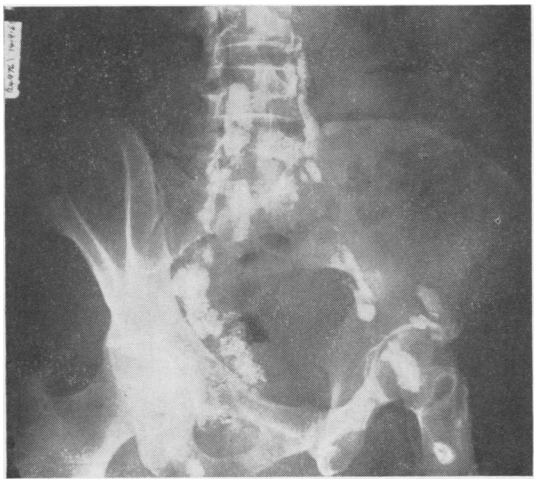

Fig. 4.—Leg. Lymphangiogram of chronic inflammation.

Discussion

The clinical survey reveals an incidence of lymphadenopathy of 82 per cent. in patients with rheumatoid arthritis compared with 52 per cent. of controls in a series carefully matched for age and sex. These figures are much higher than those of Short and others (1957), who reported an incidence of 29·40 per cent. in patients with rheumatoid arthritis compared with 8·9 per cent. in controls. Clearly their criteria for "significant" lymphadenopathy were different from those in this survey, where all palpable glands were noted and an attempt was made to grade glandular enlargement.

Without some such standardization, it is easy to see how the variation of incidence of lymphadenopathy in rheumatoid arthritis from 19 to 96 per cent. in published series collected by Short and his co-workers could arise.

It would appear that lymphadenopathy is an integral feature of rheumatoid disease. Indeed, in males it is almost universal, 94 per cent. of male patients having palpable nodes as compared with 77 per cent. of females. This sex difference was also noted by Short and others (1957). It is of interest that the figure for male control subjects was 72 per cent. and for female controls 36 per cent. A higher incidence of local trauma to the limbs in men may be a contributory factor. There appears to be no obvious correlation between age or duration of disease and lymphadenopathy, but a definite correlation with disease activity.

The fact that lymphadenopathy in the cervical region alone of all the regions showed no significant difference between patients with rheumatoid disease and controls, would seem to support the thesis that local joint activity is the determining factor (Baggenstoss and Rosenberg, 1943). Individual patients, such as a man who had had an arm amputated, and who had lymphadenopathy only in the opposite axilla, would appear to support this further. Again, the infrequency of epitrochlear involvement is not in favour of a generalized process. However, the figures for local joint and gland scores in both upper and lower limbs (Table V) show no statistical correlation.

The differential diagnosis of lymphography lies between:

(1) Malignant lymphoma (Brill-Symmers disease, Hodgkin's disease, lymphosarcoma, reticulum cell sarcoma, leukaemia);

(2) Simple chronic inflammatory changes;

(3) Sarcoidosis;

(4) Ankylosing spondylitis;

(5) Rheumatoid and other types of inflammatory arthritis.

The appearances of ankylosing spondylitis, rheumatoid arthritis, and chronic inflammation of a non-specific variety all look much the same, and differentiation between these three diseases on lymphangiographic grounds is not possible. The malignant reticuloses, however, have a different appearance, though an early case of lymphosarcoma or giant follicular lymphoma might be difficult to differentiate from the simple inflammatory or arthritic conditions. Hodgkin's disease has a characteristic appearance in which the nodes are more finely granular with wider spacing between the granules, there being a ghost-like appearance of the node. In addition to this, the lymph nodes in advanced malignant lymphoma tend to run together and appear like a continuous lymphoid mass with constrictions spaced along it; in none of the cases of rheumatoid arthritis investigated was this appearance observed. The size of the lymph nodes in rheumatoid arthritis, whilst considerably larger than normal, never showed the massive enlargement which is often seen in Hodgkin's disease and lymphosarcoma. Fibrosis is often seen in long-standing cases of malignant lymphoma, and this would appear to be another important differentiating feature. In some cases only the nodes closest to the affected joints have been involved, the more proximal nodes appearing normal. This suggests that initially there is involvement only of the regional lymph nodes, and that the involvement gradually spreads to include all the nodes along a chain, *i.e.* from the inguinal region to the para-aortic region. This agrees with the findings of Wiljasalo and others (1966).

The frequency of epitrochlear gland outlining at lymphangiography, 2/9, corresponds with our 26 per cent. frequency of finding palpable glands at clinical examination, suggesting that the failure to outline is not technical. It is known that only the superficial lymphatics from the skin on the medial aspect of the palm and forearm drain in part to the supratrochlear nodes, and that the deep lymphatics drain entirely to the lateral axillary chain (Gray's Anatomy: Davies, 1967). Superficial and deep chains do communicate along their course (Lockhart, Hamilton, and Fyfe, 1959). It would seem that this anatomical arrangement may very well explain the infrequency of supratrochlear node enlargement in rheumatoid disease, if gland enlargement truly reflects a drainage phenomenon.

Lymphography appears to be of little help in the diagnosis of rheumatoid arthritis.

However, it is important to be aware of the appearances of the nodes at lymphography, as two diseases may co-exist in the same patient. As Motulsky and others (1952) have pointed out, the histological features noted in some instances may lead to confusion in diagnosis because of the similarities of rheumatoid arthritis on histological grounds to the appearances of giant follicular lymphoma, lymphosarcoma, and Hodgkin's disease. There does appear to be a correlation between both local and general joint scores in relation to gland size as defined at lymphangiography, but it is difficult to draw any conclusions from these findings other than that both a local and general factor are contributing to gland enlargement.

The correlation between lymphadenopathy, erythrocyte sedimentation rate, and haemoglobin level was not statistically significant. There was, however, a significant difference between sedimentation rates above and below 30 mm. in 1 hour. The incidence of splenomegaly (2 per cent.) in this series is much lower than the usual incidences cited (Hutt, Richardson, and Staffurth (1951) 5 per cent.; McCrae (1904) 4/110; Makarenko (1965) 35/289; Dawson (1921) 5 per cent.; although Hench (1933) quoted only 1 per cent. No evidence of hepatomegaly was forthcoming in our patients.

Biopsies were not included as part of this study, as there are some excellent reviews of the histology of lymph nodes in rheumatoid arthritis (Motulsky and others, 1952; Cruickshank, 1958). However, diagnostic confusion can occur, on both histological and clinical grounds, as evidenced by our two cases.

Similar cases where diagnostic confusion with malignant lymphoma has occurred have been re-

ported previously (Poursines and Rochu, 1946; Motulsky and others, 1952; Cruickshank, 1958; Gardner, 1965). Whereas the usual histological appearance in rheumatoid arthritis is one of simple follicular hyperplasia or sinus catarrh, diffuse lymphocytic or histiocytic hyperplasia are sometimes seen, and occasionally the follicular hyperplasia is of such degree as to resemble giant follicular lymphoma (Brill-Symmers disease). Still more rarely the appearances resemble lymphosarcoma or Hodgkin's disease. Some workers have defined histological factors which allow differentiation of simple follicular hyperplasia from giant follicular lymphoma (Cruickshank, 1958; Baggenstoss and Heck, 1940). In none of the 35 patients who attended Westminster Hospital with giant follicular lymphoma was there any suggestion that they were suffering from rheumatoid arthritis. Although a true association between rheumatic disease and the reticuloses has been suggested (Lea, 1964; Cammarata, Rodnan, and Jensen, 1963; Cobb, Anderson, and Bauer, 1953) found no evidence of lymphoma in 191 autopsies on patients with rheumatoid arthritis.

Summary and Conclusions

(1) 100 patients with active rheumatoid arthritis were compared with 100 patients with a variety of other conditions. Lymph node enlargement was significantly more common and more marked in rheumatoid patients in axillary, epitrochlear, and inguinal regions, but not above the clavicles.

(2) Although in a few cases of rheumatoid disease there is a generalized lymph node enlargement, as in the second case reported here, in most cases the localization appears to be more in anatomical relation to actively inflamed joints.

(3) Lymph node enlargement was significantly greater in males than females in both rheumatoid and control groups of patients.

(4) More glandular enlargement occurred in SCAT-positive than SCAT-negative cases, with active disease rather than inactive, and with erythrocyte sedimentation rates over 30 mm. in one hour.

(5) Lymphangiographic studies in rheumatoid arthritis show a picture of non-specific inflammatory change which, though different from that seen in malignant lymphoma, is not sufficiently distinctive to be diagnostic in early cases. No evidence of lymphangiectasis or lymphatic blockage was seen. The appearance of localized involvement in a chain in some patients would be in keeping with the hypothesis that the main factor determining gland enlargement is local drainage.

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Adénopathie rhumatoïde

RÉSUMÉ

(1) On compara 100 malades atteints de polyarthrite rhumatoïde active avec 100 autres ayant des affections diverses. L'augmentation de volume des ganglions fut significativement plus commune et plus marquée chez les malades atteints de polyarthrite rhumatoïde dans les régions axillaire, épitrochléenne et inguinale mais non pas dans la région située au dessus de la clavicule.

(2) Bien que dans quelques cas de maladie rhumatoïde l'augmentation de volume des ganglions soit disséminée, comme dans le cas No 2 rapporté ici, en général la distribution paraît être plus liée à la région anatomique des articulations atteintes par des phénomènes inflammatoires actifs.

(3) L'hypertrophie ganglionnaire fut significativement plus importante chez les hommes que chez les femmes dans les deux groupes, polyarthritiques et témoins.

(4) L'hypertrophie ganglionnaire fut plus fréquente dans les cas où la réaction de Waaler-Rose était positive que dans ceux où elle était négative, lorsque l'affection était active plus que lorsqu'elle était inactive et lorsque la vitesse de sédimentation était supérieure à 30 mm. à la première heure.

(5) Des études lymphangiographiques faites dans la polyarthrite rhumatoïde montrent un tableau d'atteinte inflammatoire non spécifique qui, bien que différent de celui observé dans le lymphome malin, n'est toutefois pas assez caractéristique pour permettre de faire un diagnostic précoce. On ne vit pas de lymphangectasie ou de bloquage lymphatique. L'aspect de l'atteinte locale dans une chaine chez quelques malades s'accorderait avec l'hypothèse que le facteur principal déterminant l'hypertrophie ganglionnaire est lié au drainage local.

Adenopatía reumatoide

SUMARIO

(1) Se compararon 100 enfermos con poliartritis reumatoide con cien otros con otras varias enfermedades. El aumento de volumen de los ganglios fué significativamente más frecuente y más marcado en enfermos con poliartritis reumatoide en las regiones axilar, epitróclea e inguinal pero no encima de las claviculas.

(2) Aunque en algunos casos de enfermedad reumatoide el aumento de volumen de los ganglios fuese diseminado, como en el caso No 2 relatado aquí, en general la distribución parece relacionarse más con la región anatómica de las articulaciones afectas por el proceso inflamatorio activo.

(3) El aumento de los ganglios fué significativamente mayor en los hombres que en las mujeres tanto en los sujetos reumatoides como en los testigos.

(4) La adenopatía fué más frecuente en los casos con la reacción de Waaler-Rose positiva que en los con la reacción de Waaler-Rose negativa, más en la enfermedad activa que en la sin actividad, y cuando la velocidad de sedimentación eritrocitaria rebasaba 30 mm. en la primera hora.

(5) Estudios linfangiográficos en la poliartritis reumatoide ofrecen un cuadro de afección inflamatoria no específica que, aunque diferente de aquel observado en el linfoma maligno, no es bastante característico para permitir un diagnóstico temprano. No se observó linfangectasis o bloqueo linfático. El aspecto de la lesión local en una cadena en algunos enfermos se acuerda con la teoría de que el factor principal determinante de la hipertrofía linfática es el drenage local.