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Radiological study of cervical spine and hand in patients with rheumatoid arthritis of 15 years' duration: an assessment of the effects of corticosteroid treatment

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SUMMARY Radiological abnormalities in the cervical spine were assessed in detail in a group of 62 patients with rheumatoid arthritis of approximately 15 years' duration, of whom 33 had been treated with corticosteroids and 29 had not. The 10 criteria of damage described by Bland (1974), which include subluxation, correlated as a whole with the severity of the disease in general but not with the duration of corticosteroid treatment. Subluxation alone, whether assessed in the cervical spine as a whole or in the atlanto-axial joint alone, was less closely related to disease activity, was on average greater in patients treated with corticosteroids, and tended to increase in relation to the duration of treatment. Corticosteroid treatment thus tends to produce, over the course of years, a degree of subluxation in addition to that caused by the disease itself.

Radiological signs of damage to the metacarpophalangeal (MCP) joints and carpal bones correlated with both the degree of damage and the degree of subluxation in the cervical spine as well as with corticosteroid treatment. Mutilans deformity at the MCP joints was associated with subluxation in the neck and with corticosteroid treatment.

Involvement of the cervical spine is common in rheumatoid arthritis (RA). Its incidence (Table 1) is variously reported as between 40 and 88% (Sharp and Purser, 1961; Bland *et al.*, 1963; Conlon *et al.*, 1966). Its pathology is well reviewed by Ball and Sharp (1971). It is generally accepted that deformities of the cervical spine in RA are more severe following treatment with corticosteroids, but a critical analysis is needed to determine to what extent this is so.

The main problem is to distinguish between the effect of the disease and the effect of the corticosteroids. Does corticosteroid treatment enhance the changes caused by the disease, or does it produce additional changes of a different nature? Or is it merely that those patients given corticosteroid treatment are automatically those with the worst and most destructive disease?

Also, an association has been noted between mutilans deformities in the hands and rheumatoid lesions in the neck, but this is a point on which specific information is lacking. Again, does corticosteroid treatment have a role in adding to, or in worsening these lesions?

We have attempted to answer these questions by radiological studies made during the course of a follow-up review of patients with RA of 15 years' duration, just over half of whom had been treated with corticosteroids. Our purpose here is (a) to identify radiologically the effect of the disease and the effect of corticosteroids on the cervical spine in a group of patients who had all suffered from RA for a similar period, (b) to relate these changes to the severity of the disease as a whole, and (c) to see what association exists between cervical spine lesions, corticosteroid treatment, and mutilans deformities in the hands and *x*-ray changes in hands and wrists.

Table 1 *Incidence of cervical spine involvement in RA*

Study	*No. of patients*	*Basis of evidence*	*Incidence (%)*
Bland *et al.* (1963)	100	*x*-ray	86
Conlon *et al.* (1966)	333	*x*-ray	50
Conlon *et al.* (1966)	333	Clinical	88
Sharp and Purser (1961)	44	Clinical	40

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The patients

The 62 patients studied (19 men, 43 women) were among the 65 survivors of an original group of 100 patients with definite or classical RA initially seen by J.A.C. within the first year of their disease. When first seen the mean duration of RA was 3·7 months. Features of the onset of the disease, and an 11-year follow-up have already been published (Jacoby *et al.*, 1973). At the time of this study the mean duration of the disease was 14·6 years (SD 1·75) and the mean age of the patients was 61·1 years (SD 12·8). In all, 65 of the original 100 were alive and were examined when the follow-up study was made in 1975, but our report is based on the 62 for whom satisfactory radiographs were available. Twenty-nine had never been treated with corticosteroids or ACTH, while 33 had been so treated for periods ranging from 1 to 17 years.

Methods

Lateral radiographs of the cervical spine were taken in full flexion and full extension, using a 5 ft tube-to-plate distance and centered on the second vertebra. *X*-rays were read according to an agreed plan and without knowledge of the clinical details. For the assessment of rheumatoid damage to the cervical spine we used the 10 radiological criteria for diagnosis of RA of the cervical spine, as given by Bland (1974), which we have called the 'Bland criteria' (Table 2). Bone demineralisation was assessed only subjectively as present or absent. Measurements of atlanto-axial space were made on the flexion film between the mid-point of the posterior surface of the anterior arch of the atlas and the nearest point of the odontoid process. McGregor's line (1948) between palate and occiput was used to assess vertical atlanto-axial subluxation.

In the lower cervical spine, loss of alignment of 1 mm or more between the posterior profiles of two adjacent vertebral bodies on the flexion film was also measured. We preferred the posterior profile to the more commonly used anterior measurement, as the anterior faces of the vertebrae in RA are often uneven making it difficult to measure subluxation accurately. The displacement (mm) at each disc level was recorded and summated to yield the 'luxation total'.

The clinical diagnosis of mutilans deformity was based on the presence of bony destruction and ligamentous laxity, permitting longitudinal 'telescoping' and volar subluxation at the metacarpophalangeal (MCP) joints. Radiological damage at the MCP joints and at the wrists was assessed separately, and abnormalities were graded as absent, mild, moderate, or severe (Table 3). If there was doubt about the presence of a radiological sign, it was regarded as normal.

The severity of RA in its effect upon the patient's health and activity cannot be expressed precisely, as can, for example, pulmonary function in patients with bronchial asthma. In assessing RA therefore we used indirect, clinical indicators of severity, namely ESR, haemoglobin, and Rose titre, and the widely accepted ARA grading into possible, probable, definite and classical RA, which is based on laboratory and clinical criteria (Table 4). Functional capacity was assessed by the 4 grades defined by Steinbrocker *et al.* (1949): 1=fit for all activities; 2=moderate restriction; 3=marked restriction; 4=confined to chair or bed. In addition, we recorded the presence or absence of rheumatoid nodules. There were thus 6 indicators of severity.

Results

EFFECTS OF RA ON CERVICAL SPINE

For each patient we compared the clinical indicators of severity with Bland's radiological criteria of damage. Table 5 sets out the statistical correlation between each of the 6 indicators and the Bland criteria. The latter are indicated as the total number

Table 2 *Radiological criteria for diagnosis of rheumatoid arthritis of the cervical spine (Bland, 1974)*

1	Atlanto-axial subluxation of 2·5 mm or more
2	Multiple subluxation of C2–3, C3–4, C4–5, C5–6
3	Narrow disc spaces with little or no osteophytosis
	(a) Pathognomonic of RA at C2–3 and C3–4
	(b) Probable RA at C4–5 and C5–6
4	Erosions of vertebrae, especially vertebral plates
5	Odontoid small, pointed, and eroded with loss of cortex
6	Basilar impression ('platybasia')
7	Apophyseal joint erosion; blurred facets
8	Generalised osteoporosis in cervical spine
9	Wide space (5 mm or more) between posterior arch of atlas and the spinous process of the axis (in flexion)
10	Osteosclerosis, secondary, of atlanto-axial occipital complex

Table 3 *Grading of radiological damage in MCP joints and carpal bones*

Absent	No abnormalities
Mild	Osteoporosis, 1 or 2 cysts
Moderate	Many cysts, some erosions
Severe	Destruction of joints and bone edges

Table 4 *Indicators of systemic severity of RA*

Laboratory	ESR (mm in first hour)
	Hb (g/dl)
	Rose titre (no. of tubes)
Clinical	Functional capacity
	Presence of nodules
Combined	ARA Grading

Table 5 *Correlation between clinical indicators of severity of RA, radiological evidence of damage in neck (Bland criteria), and 'luxation total'*

Indicator of severity	*Correlation with number of Bland criteria present*	*Correlation with individual Bland criteria 3–10**		*Luxation total (mm)*
		P<0·01	*P<0·05*	
ESR	NS	Criterion 3	Criterion 5	P<0·05 r=+0·280
Hb	P<0·05 r=−0·316	Criteria 3, 5	None	NS
Rose titre	P<0·01 r=+0·352	None	None	NS
Functional capacity	P<0·001 r=+0·462	None	Criteria 3, 5, 6	NS
Nodules	P<0·05 t=2·17	None	None	NS
ARA grade (see Table 6)	P<0·01	Criteria 5, 7	Criteria 3, 9	P<0·05

* See Table 2.

Table 6 *Correlation between ARA grading, radiological evidence of damage (Bland criteria), and luxation*

ARA grade	*No.*	*Number of Bland criteria*	*Luxation total (mm)*
Possible	6	2·8 (SD 1·2)	3·0 (SD 2·8)
Probable	0	—	—
Definite	27	5·9 (SD 2·3)	6·3 (SD 4·5)
Classical	29	7·3 (SD 1·8)	8·2 (SD 5·2)
Significance of difference		Possible and definite; P<0·01 Possible and classical; P<0·001	Possible and classical: P<0·05

Initially all patients were in the grades 'definite' and 'classical', but during the 15-year follow-up, 6 had improved and were placed in the 'possible' grade.

of criteria found for each patient, and also as individual criteria 3–10 (omitting 1 and 2, which concern luxation). Table 6 shows in more detail the ARA gradings related to the number of Bland criteria present.

Each of the 6 indicators of disease severity correlated in some degree with radiological criteria of damage. We interpreted this as meaning that damage to cervical spine other than luxation is closely related to the severity of the disease as a whole. The individual criteria of radiological damage which showed the closest association were 3 and 5, ie, narrowing of disc spaces without osteophytosis, and erosion of odontoid.

A similar comparison was made between the clinical indicators of disease severity and the 'luxation total' (Tables 5 and 6). Here correlation was less close, and was seen only with 2 of the 6 indicators of severity ie, the ESR and the ARA grading.

The observation that disease severity was more closely associated with radiological signs of damage in the cervical spine than with luxation was, we thought, consistent with the concept that luxation might be attributable in part to another factor, ie, corticosteroid treatment.

EFFECTS OF CORTICOSTEROID TREATMENT

We studied the 'luxation total' in relation to corticosteroid treatment and its duration. Fig. 1 shows that the 29 patients who had had no corticosteroids, had luxation totals ranging from 0–12 mm, while the 33 who had had corticosteroids showed a wider range, up to a maximum of 22 mm. Of the 62 patients there were 9 with luxation totals over 10 mm; 8 of these 9 had had corticosteroids for 7 years or more.

The mean 'luxation total' in the group without corticosteroids was 5 mm (SD 3·36) compared with 8·72 mm (SD 5·48) in the group given corticosteroids—a significant difference (P<0·01). Fig. 1 also shows a slight degree of correlation between the duration of corticosteroid treatment and the 'luxation total'.

We concluded that prolonged corticosteroid treatment has some effect in increasing luxation in the cervical spine, an effect which is separate from that of the rheumatoid arthritis.

MUTILANS DEFORMITIES

Ten of the 62 patients had mutilans deformities of the MCP joints. The presence or absence of such deformities was compared with the state of the

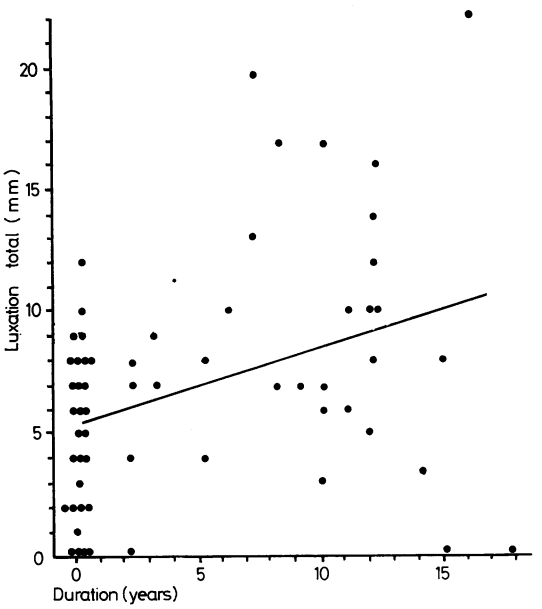

Fig. 1 *The 'luxation total' in the cervical spine shown in relation to the duration of corticosteroid treatment in 62 patients. Thirty-three had been treated for periods up to 17 years, and 29 had never had corticosteroids. The 'luxation total' is significantly greater ($P<0.01$, $r=0.3489$) in those given corticosteroids and tends to increase in relation to the duration of treatment.*

cervical spine, *viz*, the numbers of Bland criteria present, and the luxation total, and also with the duration of corticosteroid treatment (Table 7). Mutilans deformities were not associated with a higher number of Bland criteria, but were associated with a significantly greater luxation total, with corticosteroid treatment and with the duration of treatment. Moreover, in all 10 patients with mutilans deformities, corticosteroids had been given for over 3 years.

RADIOLOGICAL DAMAGE IN MCP JOINTS AND CARPAL BONES

Comparison with cervical spine

The severity of radiological damage in the MCP joints was compared with radiological signs of damage and of luxation in the neck. A significant association was found with the number of Bland criteria, with the luxation total and with corticosteroid treatment (Table 8). A similar comparison of radiological damage in the carpal bones showed the same association with changes in the neck and with corticosteroid treatment (Table 9).

Comparison with disease severity

Abnormalities in 5 of the 6 indicators of disease severity, ie, all but the ESR, were found to be significantly associated with the severity of damage in the MCP joints. A less close association, applying to only 3 of the 6 indicators, was found when comparing them with the severity of damage to the carpal bones (Table 10).

Close similarities were thus found, as might be expected, between radiological signs of damage in the hand and wrist, and the neck, with a relationship between hand and wrist damage and the severity of

Table 7 *Presence of mutilans changes in MCP joints compared with changes in cervical spine and duration of corticosteroid treatment*

Mutilans in MCPs	*No.*	*Number of Bland criteria*	*Luxation total (mm)*	*Corticosteroid treatment*	*Duration of corticosteroid treatment (years)*
Present	10	7·6 (SD 1·1)	12·1 (SD 6·2)	10	9·1 (SD 3·2)
Absent	52	6·0 (SD 2·4)	5·7 (SD 3·7)	23	3·9 (SD 5·6)
Significance		NS	P<0·001 t=3·73	P=0·0002 (Fisher's exact test)	P<0·01 t=2·84

Table 8 *Severity of radiological damage in MCP joints compared with changes in cervical spine and corticosteroid treatment*

Severity of damage in MCP	*No.*	*Number of Bland criteria*	*Luxation total (mm)*	*Corticosteroid treatment*	
				No	*Yes*
Absent or mild	24	4·6 (SD 2·2)*	4·1 (SD 3·0)*	16	8
Moderate	19	7·4 (SD 1·5)	8·1 (SD 3·9)	7	12
Severe	19	7·5 (SD 1·7)	9·4 (SD 6·1)	6	13
Significance		*P<0·001 compared with either moderate or severe classes		0·01<P<0·05 $\chi^2=6.34$	

Table 9 *Severity of radiological damage in carpal bones compared with changes in cervical spine and corticosteroid treatment*

Severity of damage in carpal bones	*No.*	*Number of Bland criteria*	*Luxation total (mm)*	*Corticosteroid*	
				No	*Yes*
Absent or mild	13	4·2 (SD 2·5)	3·8 (SD 2·7)	9	4
Moderate	12	5·3 (SD 2·4)	4·2 (SD 3·8)	8	4
Severe	37	7·3 (SD 1·6)	8·9 (SD 4·9)	12	25
Significance		P<0·01 absent or mild/severe P<0·01 moderate/severe		P<0·05 χ^2=7·61	

Table 10 *Correlation between clinical indicators of severity of RA and radiological damage to MCP joints and carpal bones*

Indicator of severity	*Correlation with severity of radiological damage*	
	MCP joint	*Carpal bones*
ESR	NS	NS
Hb	0·01<P<0·05	NS
Rose titre	0·01<P<0·02	P<0·01
Functional capacity	P<0·01	0·01<P<0·05
Nodules	P<0·01	NS
ARA grade	P<0·001	P<0·001

RA as a whole. However, mutilans deformities in the MCP joints differed somewhat in being related more to luxation in the neck and to corticosteroid treatment, than to structural damage in the neck.

ATLANTO-AXIAL SUBLUXATION

Twenty-six of our 62 patients (42%) had atlanto-axial subluxation (AAS) ie, an atlanto-axial space, as defined above, of 3 mm or more. We found associations between AAS and corticosteroid treatment, and the degree of severity of damage in the MCP joint and wrists, and the presence of nodules. Thus, the mean atlanto-axial distance was significantly greater in patients who had had over 5 years of corticosteroid treatment than in those who had never had corticosteroids (P<0·002, t=2·55). More severe radiological changes in the MCP joints were associated with the presence of AAS and a greater mean atlanto-axial distance (Table 11). The same relationship was found for carpal damage, the presence of AAS, and the mean atlanto-axial distance (Table 12). AAS was also significantly more frequent in patients having rheumatoid nodules (Table 13). In short, AAS was virtually only found in those patients with considerable damage to MCP joints and wrists.

VERTICAL ATLANTO-AXIAL SUBLUXATION

This was present in 20 of our 62 patients (32%) by McGregor's criterion of having the tip of the odontoid more than 4·5 mm above McGregor's line (McGregor, 1948). Of these 20, 8 had been treated with corticosteroids.

Table 11 *Severity of radiological damage in MCP joints compared with atlanto-axial subluxation (AAS)*

MCP damage	*No.*	*AAS present*	*Mean atlanto-axial distance (mm)*	*Significance*
None or mild	24	2	1·04 (SD 1·30)	$t^{mild/severe}$=3·82, P<0·001
Moderate	19	11	2·66 (SD 1·89)	$t^{mild/moderate}$=3·32, P<0·001
Severe	19	13	3·89 (SD 3·36)	NS

Table 12 *Severity of the radiological damage in carpal bones compared with atlanto-axial subluxation (AAS)*

Carpal damage	*No.*	*AAS present*	*Mean atlanto-axial distance (mm)*	*Significance*
None or mild	13	0	0·85 (SD 0·99)	$t^{mild/severe}$=3·55, P<0·001
Moderate	12	1	0·67 (SD 1·07)	$t^{moderate/severe}$=3·63, P<0·001
Severe	37	25	3·54 (SD 2·65)	

Table 13 *Atlanto-axial subluxation and the presence of rheumatoid nodules*

Nodules present	*No.*	*AAS present*	*Atlanto-axial distance (mm)*	*Significance*
Yes	15	13	3·80 (SD 1·86)	P<0·05
No	47	13	1·97 (SD 2·59)	t=2·53

Table 14 *Functional capacity related to treatment with corticosteroids*

Steroids given	*Functional capacity*			
	1	*2*	*3*	*4*
No	6	14	7	2
Yes	2	9	18	4
Significance	Combining classes 1 and 2, and 3 and 4 $\chi^2=6{\cdot}48$ and $0{\cdot}01<P<0{\cdot}05$ (ie, functional capacity is worse in patients given corticosteroids.			

CORTICOSTEROID TREATMENT AND SEVERITY OF THE DISEASE

Patients who had been treated with corticosteroids and those who had not, were compared to see whether corticosteroid treatment necessarily implied more severe RA. For the most part, indicators of severity of disease were not related to corticosteroid treatment. Thus ESR, haemoglobin, Rose titre, and the ARA grading did not significantly differ in the two classes. However, there was some evidence that functional capacity was worse in patients given corticosteroids (Table 14).

Discussion

In this study the duration of RA is not a significant factor in that all patients had had the disease for a similar period. Nor was selection of patients of importance, for entry into the original series of 100 patients 15 years previously was purely on the grounds of the patients then having newly developed RA, and attaining the ARA grades of 'definite' or 'classical' RA within 1 year of onset.

Fortuitously the numbers of patients treated and not treated with corticosteroids were roughly equal (33 and 29, respectively), making them groups suitable for comparison. In general, patients having corticosteroids had no evidence of more severe rheumatoid disease, with the exception of functional capacity, for which they rated rather worse than those not on corticosteroids. Matters may have been different at an earlier stage, before the introduction of corticosteroids, but we found it impracticable to take previous progress into account, and based our assessment purely upon the situation found at the 15-year survey. Similarly, the question of corticosteroid dosage was too complex to assess, for patients had been on variable regimes. We found it simplest merely to group together those who had had corticosteroids (including the few who had had ACTH), irrespective of dosage, and to confine our attention to duration of treatment.

In general, we found that the presence of Bland's radiological criteria of rheumatoid damage to the cervical spine correlated well with the indicators of severity of rheumatoid disease as a whole. The individual features of greatest significance in this sense were narrowing of disc spaces, and erosion and pointing of the odontoid process (criteria 3 and 5). Those of least significance were erosions of vertebral plates, generalised osteoporosis and osteosclerosis of atlanto-axial complex (criteria 4, 8, and 10).

Bland's criteria include subluxation between atlas and axis, and subluxation at lower levels (criteria 1 and 2), but we preferred to attempt a quantitative assessment of the process of subluxation throughout the neck in the form of the 'luxation total'. This was measured from a lateral radiograph taken with the neck in flexion. It is difficult to know how much this total figure may be influenced by the degree of flexion achieved, and in practice, such positioning for radiography cannot be precisely standardised. In the event, each patient was merely asked to bend his or her head forwards as far as possible, with chin on chest. The question arises of whether patients on corticosteroids can achieve a greater degree of flexion and thus subluxation, than those not on corticosteroids. However, from inspection of the *x*-ray films we have no reason to believe that there was any difference between these groups in their positioning for radiography.

Our analysis indicates that, while subluxation in the cervical spine occurs as a result of rheumatoid arthritis, the situation is worsened by corticosteroid treatment. There is some evidence that worsening subluxation is related to duration of corticosteroid treatment, both in the cervical spine as a whole and at the atlanto-axial articulation. Similarly mutilans deformity at the MCP joints, we found, was related to corticosteroid treatment rather than to the severity of the disease as a whole.

We suggest that subluxation is favoured in rheumatoid subjects in the absence of corticosteroid therapy, by reduction in bone mass and a weakening effect on ligaments and connective tissue. These changes can also occur in non-rheumatoid subjects on corticosteroid therapy and are naturally enhanced in rheumatoid patients given corticosteroids. It would be of interest to know whether cervical subluxation may also develop in non-rheumatoid patients on long-term corticosteroid treatment for other conditions.

Sharp *et al.* (1958) were among the first to draw attention to subluxation in the cervical spine due to rheumatoid arthritis. They also noted the association of rheumatoid damage in the cervical spine with damage to the hands and feet, pointing out the increased frequency of radiological changes in hands and feet in patients with more severe neck lesions.

We confirmed this, as regards the hands and

wrists, finding an association between the severity of damage in the MCP joints and carpal bones and the severity of damage in the cervical spine.

The forward subluxation of atlas on axis has been widely studied. Our incidence of 42% is rather higher than in surveys, ie, 9% quoted by Smith *et al.* (1972), 19% by Sharp and Purser (1961), 25% by Mathews (1969), 36% by Stevens *et al.* (1971), 37% by Meikle and Wilkinson (1971), and 37% by Serre *et al.* (1963). However, Martel (1961) quoted an even higher figure, 71%, based on a series of 34 severely affected rheumatoid patients. Some association between AAS and duration of disease, and corticosteroid therapy was found by Meikle and Wilkinson (1971), although details were not given of the degree of subluxation nor of the duration of corticosteroid therapy, and the series appeared to have been biased by the selection of patients with neck symptoms. Mathews (1969) also found a significant association between AAS and corticosteroid treatment and Smith *et al.* (1972) reported more rapid deterioration in neck lesions in corticosteroid treated patients. Serre *et al.* (1963) noted a higher proportion of AAS in those patients given prolonged high dose corticosteroids (62%) than in other rheumatoid patients (38%). Lourie and Stewart (1961) commented on the tendency for prolonged administration of corticosteroids in RA to produce 'disruptive changes' in the cervical spine.

As for other associations with AAS, Stevens *et al.* (1971) noted a relationship with 'hand deformities', and with nodules, as did Conlon *et al.* (1966) and as we did. Vertical atlanto-axial subluxation is recorded less commonly than AAS, being noted in only 1% by Smith *et al.* (1972) and 4% by Henderson (1975). Compared with this, our figure of 32% is surprisingly high. The role of corticosteroid treatment in inducing this form of subluxation appears to be of less importance than is the case with forward subluxation.

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