

CORTICOSTEROIDS CAUSING SEVERE GROWTH SUPPRESSION IN JUVENILE RHEUMATOID ARTHRITIS

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SUMMARY

Two children with Juvenile Rheumatoid Arthritis (JRA) and severe growth suppression from corticosteroid therapy are described. Prolonged 'tailing-off' of steroids occurred during outpatients follow-up and this may be related to the high turnover of doctors involved. Suggestions for improving such follow-ups and caution against the continuous use of steroids are made.

INTRODUCTION

Since its classical description by Still in 1897,¹ the features of Juvenile Rheumatoid Arthritis (JRA) have been well described by several authors.^{2,3} Systemic corticosteroids are rarely used in treatments because they may cause a multiplicity of side-effects when administered over a long period. In children, lack of vigilance during treatment with corticosteroids may lead to severe growth suppression. Two such cases in children with JRA treated with steroids are reported.

CASE REPORT 1

S.H. is an eleven-and-a-half year-old Malay boy. At the age of six, he presented with generalised joint pains and swellings. On clinical examination, he was febrile with warm and tender wrist, elbow, knee and ankle joints. He had generalised lymphadenopathy. He weighed 14.5 kg but the height was not measured.

Investigations included the following: ESR 60, Anti-Streptolysin O Titre (ASOT) — not raised; RA factor — positive on the latex agglutination test. The anti-nuclear antibody test was negative. HLA typing was not done. Haemoglobin and serum albumin were normal. The chest X-ray was normal, as were X-rays of his hands and feet. He was started on Aspirin 1.2 g daily without symptomatic benefit and Prednisolone (12 mg daily) was added a fortnight later with rapid improvement in symptoms.

His disease followed a (Type 1) pauciarticular, relapsing and remitting pattern,⁴ mainly affecting the knee and ankle joints. The eyes were not affected. All relapses were mild in that although the joints were warm and tender, the patient remained fully mobile.

During follow-up of the next five-and-a-half years he was seen by no less than ten doctors and was maintained on a dose of Prednisolone, varying between 2.5 — 20 mg daily. He was taken off prednisolone for two, relatively short periods (nine weeks and three weeks) during that time. The

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dose of Aspirin remained unchanged at 1.2 g daily throughout. Follow-up X-rays of the hands at age eleven-and-a-half years showed minimal soft tissue swelling with juxta-articular osteoporosis. Thoracolumbar spine X-rays were normal.

The five-and-a-half-year relevant follow-up data in relation to steroid dosage are represented diagrammatically in Fig. 1.

Weight at ages 6, 7½ years were 14.5 kg, 15 kg, and 18.5 kg respectively (Fig. 2). Heights at ages 7½ and 11½ years were 105 cm and 118.5 cm respectively (Fig. 3).

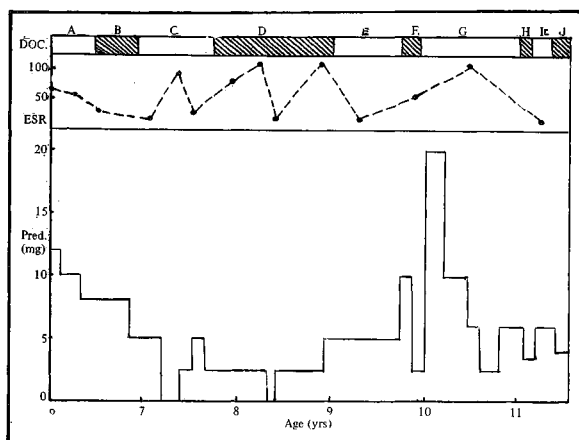


Fig. 1 History of Case 1 showing dose of steroids at various times of follow-up. Disease activity is indicated by ESR values. Doctors involved are indicated by alphabets.

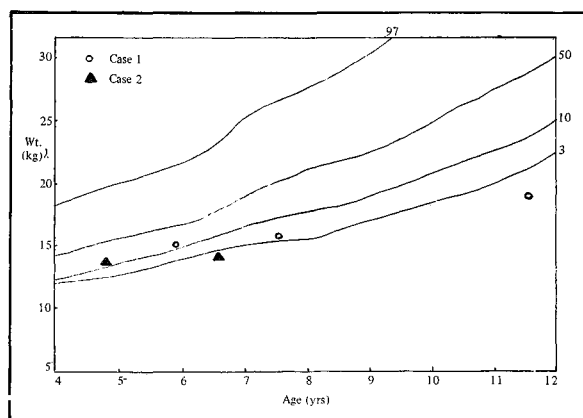


Fig. 2 Weights of patients in relation to percentile charts. (Growth charts according to Wong HB *et al.*).^{11,12}

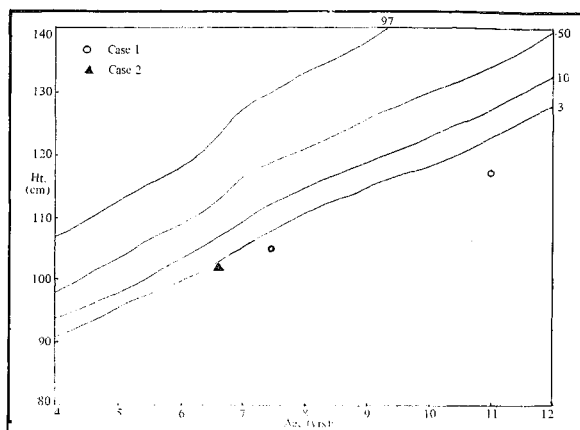


Fig. 3 Heights of patients in relation to percentile charts. (Growth charts according to Wong HB *et al.*).^{11,12}

At age 11½ years, Case 1 was glaringly stunted when compared with his twin brother who was of normal height and weight (Fig. 4).

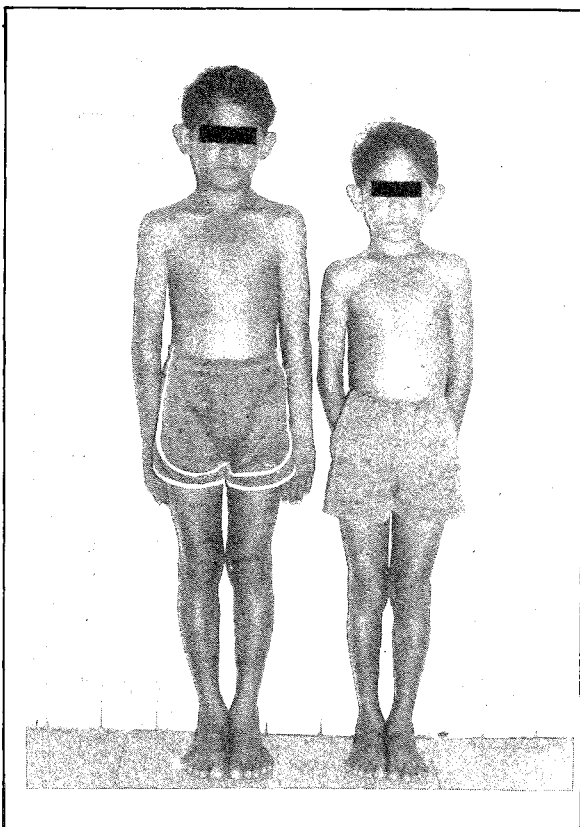


Fig. 4 Gross stunting in Case 1 (right) compared to his twin brother of normal height and weight.

CASE REPORT 2

R.L., a six-and-a-half-year-old Kadazan boy was first seen at the age of four years nine months, with a low-grade fever and painful neck movements. On admission, he weighed 13.0 kg. Height was not measured. His symptoms subsided spontaneously soon after admission. Cervical spine, hands and feet X-rays were normal and no diagnosis was made at that time.

At the age of five years three months, he returned with fever, generalised arthralgia and difficulty with walking. Clinical examination revealed warm tender neck, elbow, wrist, knee and ankle joints with splenomegaly. Repeat X-rays showed soft tissue swelling of the ankle joints, the rest of the radiological films were normal.

Investigations included the following: ESR 70, ASOT — not raised; RA factor — positive; anti-nuclear antibody — negative; LE cells — negative. The HLA typing was not done. Haemoglobin 10.5 g/100ml, serum albumin 3.4 g/100ml.

He was started on 1.2 g of Aspirin daily with little improvement and a fortnight later, Prednisolone (15 mg daily) was added. Over the next fifteen months, his disease following a polyarticular pattern⁴ with two severe relapses. His maintenance dose of Prednisolone was never at any time less than 5 mg daily. He was seen by five successive doctors in the 15 months of follow-up after being started on Prednisolone.

The relevant data are presented diagrammatically in Fig. 5.

Weights at 4½ and 6½ years were 13.0 kg and 13.3 kg; height at age 6½ years was 102cm. These are represented on growth charts in Figs. 2 and 3. The thoracolumbar spine X-ray at age 6½ years showed severe osteoporosis with collapse of multiple thoracic and lumbar vertebrae (Fig. 6).

The hands showed marked soft tissue-swelling of the proximal interphalangeal and wrist joints. There was also swelling of the knees and ankles.

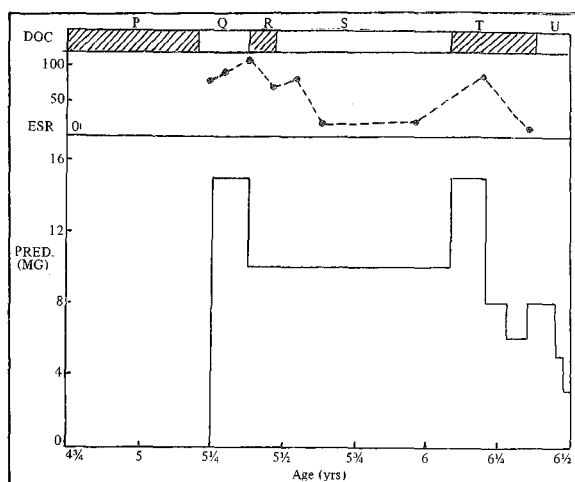


Fig. 5 Follow-up history of Case 2 showing dose of steroids at various times of follow-up. Disease activity is indicated by ESR values. Doctors involved are indicated by alphabets.

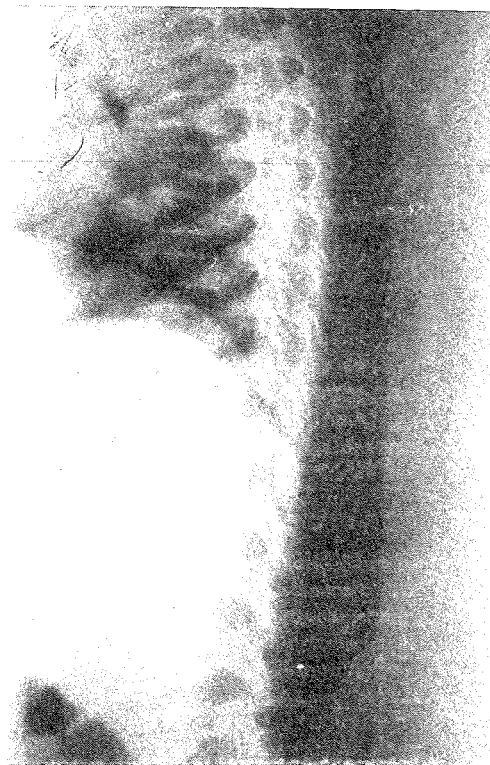


Fig. 6 Case 2. Lateral X-ray of thoracolumbar spine. There is gross osteoporosis with collapse of multiple thoracic and lumbar vertebrae.

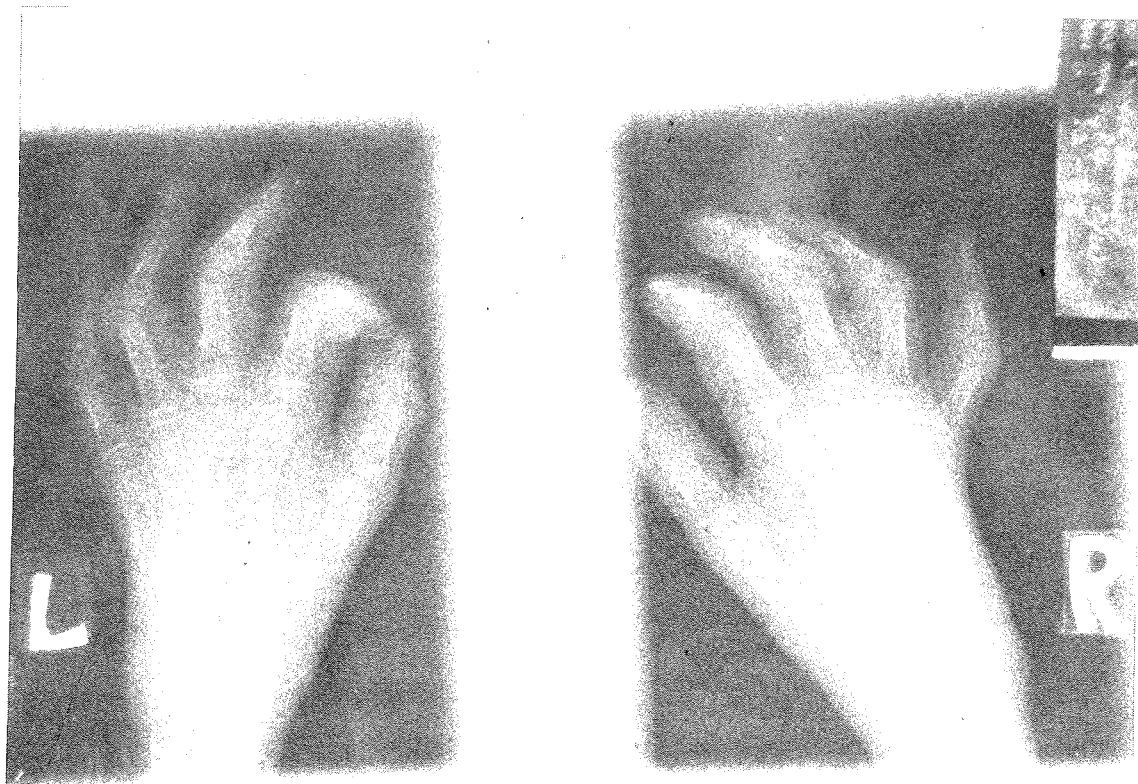


Fig. 7 Case 2. X-ray of hands showing soft tissue swelling with juxta-articular osteoporosis.

X-ray of the hands and wrists showed rheumatoid deformity with marked juxta-articular osteoporosis and soft tissue swelling (Fig. 7).

DISCUSSION

Case 1 was on an average of 4.8mg of Prednisolone daily for most of the five-and-a-half years. Case 2 was on nearly twice that dose — an average of 8.9mg daily without interruption for fifteen months. While it is true that growth may be slowed by the disease process itself,⁵ it is probable that growth suppression in these two cases was due largely to steroids for the following reasons.

In Case 1, the disease itself was relatively mild but the dose of Prednisolone was maintained more or less continuously at a high average dose of 4.8mg daily for over five years. That this affected growth was already evident after the first year. His weight

had fallen from above the tenth percentile at the onset of the disease to below the tenth percentile mark by age 7½ and markedly below the third percentile by age 11½ years. Height at age 7½ and 11½ years were also below normal. Growth suppression was more marked at age 11½ years than at 7½ years.

In Case 2, although the disease had been present for a shorter time, it was more severe and the average maintenance dose of Prednisolone was much higher, (8.9mg daily). Steroid side-effects were marked: he had gross osteoporotic changes with collapsed vertebrae and marked wasting of his proximal limb muscles. His weight at presentation (age 4¾ years) was just above the tenth percentile, but by 6½ years of age the weight had fallen below the third percentile mark. Although there was no previous height for comparison, it is likely that the steroid-related osteoporosis with multiple vertebral

collapse contributed significantly to reducing his height below the third percentile at age 6½ years.

Other factors which might affect child growth also need to be considered, the two most important being diet and previous infections.⁶ Diet was probably adequate in Case 1 as his twin brother was of normal height and weight (Fig. 4). *Ascaris* ova were detected in the stools of Case 1 on admission; he was treated, and repeated stool examinations on subsequent hospital visits were negative. There was nothing in the past history to suggest other severe infections.

The evaluation of the part played by malnutrition in growth suppression in Case 2 is more difficult. Case 2 came from a rural background and had a normocytic anaemia (Hb 10.5 g/dl) with reduced serum albumin (3.5 g/100ml) on admission. He responded partially to a blood transfusion, with folate and iron supplements. His serum albumin returned to normal on his next visit, and he maintained a haemoglobin concentration of between 11–12 g/dl on subsequent visits. Repeated serum iron and total iron binding capacity were both reduced, suggesting this was an anaemia of chronic disorder. Stool examination for ova and cysts were repeatedly negative.

Although malnutrition cannot be excluded as a contributory factor to growth retardation before the onset of the disease in Case 2, its effect was minimised during the follow-up period by vitamin supplements and dietary advice to his parents.

The overall prognosis for JRA in general is known to be fairly good. At least 75% enter long-term remission without residual deformity or functional deficit.⁷ Treatment is therefore primarily symptomatic and is directed towards reducing joint inflammation and keeping therapeutic harm to a minimum. Corticosteroids are known not to reduce the duration of activity of the disease or to affect long term prognosis.⁸ Thus if corticosteroids are used at all, they should be for cases with severe systemic or ocular manifestations or those with acute arthritis which do not respond adequately to high dose Aspirin or other non-steroidal anti-inflammatory drugs.⁹

The maximum recommended dose of Aspirin for acute childhood rheumatic arthralgia is 125mg/kg/day, i.e., approximately 1.9 g for Case 1 and 1.7 g for Case 2.¹⁰ Thus in neither case was Aspirin given to its maximum dose before Prednisolone was added. Even when corticosteroids are used, it is generally accepted that they should only be given for short periods during uncontrollable relapses and tailed off rapidly after a few weeks. This practice may prove hazardous especially when the 'tailing off' falls under the care of a rapid turnover of doctors during outpatients follow-up as occurred in these two cases.

Often, lack of time for a new doctor to familiarise himself with a case in a busy follow-up clinic, failure to appreciate the length of time a patient has been on steroids, coupled with a fear of relapse if steroids are stopped may all combine to prolong a doctor's 'tailing off' regime of the drug. A study of Figs. 1 and 5 seems to support this view. Doctors taking over a patient's follow-up tended on the whole to keep the patient on his previous dose of steroids or to increase it for a period. This period was highly variable and ranged from two weeks to eight months. Children with JRA on steroids (either long or short term) may therefore be amongst those potentially at risk in busy hospital follow-up clinics where the turnover of junior doctors is high.

It is important that such children are followed up by a more permanently based clinician who will already be familiar with the case. In hospital practice, this would probably mean the consultant or perhaps the registrar. A simple 'steroid chart' with details of existing and previous steroid dosages should be tabulated and incorporated in the case notes so that such vital information can be quickly gleaned in the clinic. This will reduce further the chances of oversight. A wary eye must be kept on the child's weight and height at all times and admission for control of relapses should be considered if outpatients' management becomes unsatisfactory.

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REFERENCES

- ¹ Still G F. On a form of chronic joint disease in children – reprinted (1897). *Arch Dis Childhood* 1941; 16:156.
- ² Ansell B M, Bywaters E G L. Rheumatoid arthritis (Still's Disease). *Paed Clin N America* 1963;10:921.
- ³ Schaller J G. Juvenile rheumatoid arthritis – A review. *Paediatrics* 1972;50:940.
- ⁴ Schaller J G *et al.* The diversity of juvenile rheumatoid arthritis: A 1976 look at the subgroups of chronic childhood arthritis. *Arthritis Rheum* 1977;20:6.
- ⁶ Ansell B M, Bywaters E G L. *Textbook of rheumatic diseases*. Copeman W S C (ed). E & L Livingstone: Edinburgh, 1969.
- ⁶ Chen P C Y. Ecological factors influencing the growth of the Child. *Med J Malaysia* 1979;34:6–11.
- ⁷ Schaller J G, Wedgwood R J. *Nelson textbook of paediatrics*. Behrman R E & Vaughn V C (ed), 12th edition. WB Saunders & Co., 1983:569-570.
- ⁸ Ansell B M. *J Roy Coll of Physicians* 1970; 4:49.
- ⁹ Calabro J J. Management of juvenile rheumatoid arthritis. *J. Paed* 1970; 77:355.
- ¹⁰ Goodman L S, Gilman A G. *The pharmacological basis of therapeutics*. Gilman A (ed) 6th edition. New York: MacMillan Pub Co. 1980:691-698.
- ¹¹ Wong H B, Tye C Y, Quek K M. Anthropometric charts based on measurements. *J Singapore Paed Soc* 1972.
- ¹² Wong H B, Tay J S H. *J Singapore Paed Soc* 1975.