death to give reliable results. The postmortem interval as already defined established fixed limits for the interval and avoided possible overestimation of the amino acid concentration relative to time after death.

Analysis of the results showed no evidence that a specific aminoacidopathy is implicated in the aetiology of cot death but has nevertheless improved our understanding of the biochemical background of these cases.

The baseline data for vitreous amino acid concentrations by age and postmortem interval in cot deaths may be of value to other investigators and is presented in a table that is available from the corresponding author.

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Subcutaneous rheumatoid nodules

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SUMMARY We describe seven children with subcutaneous rheumatoid nodules who had no clinical evidence of rheumatoid arthritis. Only one girl was seropositive for antinuclear factors and had a slightly raised erythrocyte sedimentation rate. Clinical aspects, risks for developing rheumatoid arthritis, and treatment of this entity are discussed.

Subcutaneous tumours that histologically resemble rheumatoid nodules are rarely encountered in healthy children—that is, those without evidence of arthritis. Unfamiliarity with these lesions often gives rise to uncertainty concerning the subsequent—possible—occurrence of rheumatoid arthritis and the treatment of the frequently appearing recurrences. In this article we review our own data and compare it with results found in the literature.

Patients and methods

We reviewed the notes of seven children who had been referred to the department of paediatric surgery at the St Radboud University Hospital in

Nijmegen between January 1970 and October 1986 with subcutaneous lesions, which were histologically undistinguishable from the nodules found in adults with rheumatoid arthritis. All children were invited to take part in a follow up examination. The response rate was 100%; the period of follow up varied from 6 months to 17 years (mean 6.3 years).

Results

At the first presentation to hospital all children were found to be healthy and none of them had a history of joint disease. Clinical details of the children are shown in the table. The group consisted of two boys and five girls, and their mean age was 5.5 years (ranging from 6 months to 10 years). A solitary nodule had been diagnosed in four children, one child had had two nodules, and two had presented with multiple nodules. Most lesions had been found in the extensor side of extremities: four pretibial, one prepatellar, one on the dorsum of the foot, and one on the extensor side of a finger. In two children the lesions had been situated on the scalp. The size of the nodules ranged from 2 mm to 4 cm. Ten of the subcutaneous nodules had been excised and histo-

Table Clinical findings

Case No	Sex	Age (years)	Number and location of nodules	Length of follow up	Observations
1	M	0.5	1, tibia	6 months	Recurrence*
2	F	2	Multiple scalp	6 years	Still recurrences
3	F	3	5, tibiae, dorsum of foot	17 years	2 recurrences†
4	F	4	2, scalp	11 years	1 year ibuprofen, no recurrence
5	M	8	1, tibia	9 months	Recurrence‡
6	F	10	1, finger	2 years	No recurrence
7	F	7	1, knee	7 years	Recurrence§

*=Recurrence still present at follow up.

†=Recurrence after re-excision of recurrence, spontaneous regression.

‡=Recurrence disappeared spontaneously.

§=Recurrence re-excised, no recurrence. This girl had a slightly raised erythrocyte sedimentation rate and was positive for antinuclear factor.

logical examination showed them all to be 'rheumatoid nodules.' One child, a 4 year old girl, had used ibuprofen for one year after the lesions had been diagnosed. Local recurrences arose in four cases; one disappeared spontaneously within five months, another had not regressed during six months of follow up. The remaining two were re-excised. One recurred, but disappeared after six months. In one patient new nodules kept developing on the scalp during the six years after the first diagnosis had been made. These lesions always regressed within two months. All unexcised nodules resolved spontaneously after a period of one month to six years.

At the time of follow up, none of the children were found to have had arthritis or any related disease. There was no evidence of rheumatoid arthritis in their family histories. No pathological murmurs were heard at cardiac auscultation and no limitations of joint movement were observed. All laboratory tests (erythrocyte sedimentation rate, white blood cell count, antistreptolysin titre, antinuclear antibodies, Latex test, and Rose's test) gave normal results except in one girl who had a slightly raised erythrocyte sedimentation rate of 13 mm in the first hour and was positive for antinuclear antibodies.

Discussion

Over 200 children with this disorder have been described. Because of the histology and clinical behaviour of the nodules they have been referred to under several different names: benign rheumatoid nodule, pseudorheumatoid nodule, non-rheumatoid rheumatoid nodule, and subcutaneous granuloma annulare. The youngest patient described with this disorder was 11 days old.¹ Some authors believe that trauma causes the nodules because there was a

history of trauma in 25% of their patients.² In our patients there was only one case where a prepatellar nodule could have been the result of trauma. Streptococcal infection has also been suggested as a causal factor.^{3,4} These nodules are seldom painful, except in areas which are susceptible to pressure. They are mostly found on the limbs, scalp, and near the eyebrows.¹⁻⁴ Their size ranges from 2 mm to 5 cm. They are nearly always joined to the underlying fascia or bones and multiple lesions are often observed. Preoperatively the diagnosis is often missed. The histological picture is identical to that which is seen in the subcutaneous nodules of adults with rheumatoid arthritis. They consist of a centre of fibrinoid necrosis surrounded by palisading fibroblasts and histiocytes, deposited in granular tissue (figure). The clinical behaviour, however, is quite different.⁵ These nodules develop in 20% of adults with rheumatoid arthritis, usually after the arthritis has manifested itself.⁵ They are mostly located on the proximal ulna, forearm, hand, pelvis, and foot. Rheumatoid nodules in adults are not painful either, but they do not regress spontaneously; their presentation implies a poorer prognosis. In children with juvenile arthritis, 6-9% develop subcutaneous nodules, but the histology is different: no central necrosis or palisading histiocytes are encountered.⁶

Some investigators have evaluated the blood test results in these children, but no definite predictive factor for subsequent rheumatoid arthritis could be established.^{3,4,6} One child has been described with a raised erythrocyte sedimentation rate and one other with positive tests for antinuclear factors at the moment the rheumatoid nodules were diagnosed: both later developed rheumatoid arthritis.^{4,6} Only one of our patients had abnormal laboratory test results (a raised erythrocyte sedimentation rate and a positive antinuclear factor) but no symptoms or

Figure Photomicrograph showing part of a pseudorheumatoid nodule: fibrinoid necrosis surrounded by palisading fibroblasts and histiocytes (haematoxylin and eosin stained, magnification $\times 200$).

signs of any rheumatoid associated disease could be found at the initial presentation or after seven years of follow up.

At least one biopsy specimen should be taken to make a proper diagnosis. If several identical nodules are present it is not necessary to excise them all

unless they are causing trouble to the patient (for example, pressure areas). The nodules will regress eventually, without any treatment.^{3,4} The same applies to the recurrences. Thus other forms of treatment such as, radiotherapy, corticosteroids or non-steroid anti-inflammatory medication (the latter was used in one of our patients) are superfluous and undesirable.³⁻⁵

The longest follow up period reported is 20 years.^{3,4} One should keep in mind that these patients are still under 30 years old; rheumatoid arthritis usually manifests itself somewhat later in life. So far four children with rheumatoid nodules have been described who have developed rheumatoid arthritis between 2 months and 18 years after the initial diagnosis.^{4,6} It seems unlikely that healthy children with rheumatoid nodules run an increased risk of developing rheumatoid arthritis later in life because the disorders have different predilection locations, the rheumatoid nodules in children regress spontaneously, and these children usually have normal blood test results. Once the diagnosis of rheumatoid nodules has been made, the parents should be reassured and their child can be discharged from follow up.

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