SHORT REPORTS

Age distribution of cancer of the cervix uteri

The most recent cancer registration data for England and Wales, relating to 1971,¹ show that the peak for invasive carcinoma of the cervix occurs in the age group 50-54 years. Since early diagnosis of this disease affects prognosis, we studied more recent registration data to see whether there has been a trend towards presentation at an earlier age, and whether we need to screen younger women than the 1971 data would suggest.

Material, methods, and results

We used cancer registration data for patients treated from 1975 to 1978 in hospitals in the North-west Thames Region. The number of registrations for invasive carcinoma of the cervix was similar for the four years studied—306 in 1975, 310 in 1976, 281 in 1977, and 278 in 1978. Even though registration is not complete in this region, these annual figures can be considered random samples since any bias in the completeness of registration is a function not of the patient's age but of the efficiency of the hospital's cancer registry.

The age distribution of the patients is similar for the individual years 1975-8, and the combined data on 1175 registrations are compared in the table with the data for England and Wales in 1971. The basis of comparison is the percentage of the total registrations in each age group—in this instance age-specific rates are not appropriate since many patients with cancer treated in the North-west Thames Region do not live in the region. Indeed, the extent to which patients move across some regional boundaries for treatment is not always realised, with the result that statistics based on region of residence are sometimes assumed incorrectly to be accurate statistics on region of treatment.

When compared with the 1971 national data, the North-west Thames regional figures show a trend towards an increased proportion of registrations in the 20-29 and 30-39 age groups and a corresponding reduced proportion in the 40-49 and 50-59 age groups. This is most noticeable for invasive cancer, but there is a similar trend for carcinoma in situ. Of the regional registrations for carcinoma in situ, 25% were in the age group 28-31 years and only 12% at 24-27 and 18% at 32-35 years.

Comment

The age distribution of a given cancer may be the result of a complex interaction of factors and a definite explanation of empirical observations cannot always be given. One factor, however, that could give rise to the different distributions seen in the table would be a significantly younger female population in the North-west Thames Region than in the country as a whole. Nationally, women in their 20s, 30s, 40s, and 50s formed 13.7%, 11.9%, 11.1%, and 11.9% of the total female population in 1975-7 (the figures were averaged over the three years); for 1971 the corresponding percentages are 13.8%, 11.1%, 12.1%, and 12.0%. The North-west Thames age distribution for the 20s, 30s, 40s, and 50s, also averaged over 1975-7, is 15.1%, 13.0%, 11.5%, and 11.9%. These slightly higher percentages of women in their 20s and 30s in the North-west Thames Region—less than 2%—are unlikely to account for the differences seen in the table. Furthermore, the female age distribution for the other three

Registrations for carcinoma of the cervix uteri by age group for England and Wales and for the North-west Thames Region

Age group	Percentage of registrations for carcinoma of cervix			
	Invasive carcinoma (ICD No 180)		Carcinoma in situ (ICD No 234)	
	England and Wales 1971	N W Thames Region 1975-8	England and Wales 1971	N W Thames Region 1975-8
10-19	0	0.2	0.6	0
20-29	3.1	13.5	21.6	28.2
30-39	8.8	21.6	35.4	42.9
40-49	22.7	13.8	28.6	19.5
50-59	28.7	19.2	10.3	6.1
60-69	19.8	17.4	2.6	2.4
70-79	12.7	10.0	0.7	0.9
80-99	4.3	4.3	0.1	0
Total No of registrations	4090	1175	2214	574

Thames regions (NE, SW, and SE), where most of the North-west Thames extraregional patients live, does not appreciably depart from the national pattern. Factors that might have some influence on the age distribution of the patients are the possible improvement in diagnosis due to cervical cytology screening, the possibility that first coitus is occurring at earlier ages, and referral policies that might result in the treatment of more of the younger women in this region. But to explain this age trend calls for more data than are available at present, and we wonder whether the same pattern can be seen in data from other regions.

We should like to thank Miss E Kippen of the North-west Thames Cancer Registry and Dr Y Hollis for much helpful assistance with this study.

¹ Office of Population Censuses and Surveys. *Cancer statistics: registrations. Cases of diagnosed cancer registered in England and Wales, 1971. Series MB1 No 1.* London: HMSO, 1979.

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Hypoplastic anaemia associated with legionnaires' disease

Legionnaires' disease is a recently described condition, commonly presenting as acute pneumonia.¹ Other features include gastrointestinal upsets and bleeding, acute renal failure, thrombocytopenia,² and various neurological manifestations. We describe here a patient in whom legionnaires' disease was associated with hypoplastic anaemia.

Case report

A 65-year-old toolmaker was admitted on 5 October 1978 with one week's history of breathlessness, dry cough, general weakness, and poor appetite. He had no significant medical history, did not smoke, and had not been abroad. He had received co-trimoxazole and paracetamol for five days. On admission he was confused, his temperature was 38°C, pulse 110/min, and blood pressure 120/70 mm Hg. There was clinical evidence of consolidation in the left lung. His haemoglobin concentration (Hb) was 8.5 g/dl; white cell count (WCC) $2.1 \times 10^9/l$, neutrophils 87%, lymphocytes 13%, platelets $101 \times 10^9/l$; and ESR 132 mm in 1 h. Urea and serum electrolyte concentrations were normal. A chest radiograph showed woolly shadowing in the left upper lobe.

Treatment was started with parenteral ampicillin and cloxacillin. His condition remained unchanged and on the 12th day of admission he was still confused and febrile. A chest radiograph showed persisting consolidation of the left lung. Hb was 7.6 g/dl, WCC $4.3 \times 10^9/l$, and ESR 145 mm in 1 h. Legionnaires' disease was suspected and oral erythromycin was started, 1 g every six hours for 48 hours, followed by 0.5 g every six hours for seven days. Within 24 hours his temperature returned to normal and there was considerable clinical improvement. A bone marrow biopsy specimen on the 14th day showed an overall reduction in erythropoiesis and leucopoiesis with normal maturation, an increased number of immature and mature plasma cells, and normal numbers of megakaryocytes. The concentration of total globulin was 41 g/l, that of IgG 15.1 g/l, IgA 2.3 g/l, and IgM 1.05 g/l. Protein electrophoresis showed a normal pattern and urine immunoelectrophoresis showed no Bence Jones protein. Skeletal survey was normal. Serum taken on the 5th, 12th, and 22nd days of admission produced the following antibody titres for legionnaires' disease: 1/64, 1/4096 and 1/2048 respectively. The patient was discharged on 7 November 1978 with an Hb of 9.9 g/dl, WCC $6.6 \times 10^9/l$, and platelets in normal numbers. The reticulocyte count remained low throughout the illness.

During follow-up he remained well and the following results were obtained: December 1978, Hb 13.1 g/dl, WCC $4.7 \times 10^9/l$, platelets in normal numbers; April, Hb 10.1 g/dl, WCC $1.8 \times 10^9/l$, platelets $74 \times 10^9/l$; June, Hb 10.6 g/dl, WCC $2.4 \times 10^9/l$, platelets $137 \times 10^9/l$; August, Hb 11.3 g/dl, WCC $2.7 \times 10^9/l$, platelets $60 \times 10^9/l$. A bone marrow biopsy specimen in April 1979 showed decreased activity in all cell series and a relative increase in the number of immature cells.

Comment

Fraser *et al*¹ in their original description of legionnaires' disease referred to three patients out of 182 with a WCC less than $2.0 \times 10^9/l$, two of whom died. Two other patients had WCCs of less than $6.0 \times 10^9/l$.

During his acute illness our patient had pancytopenia with bone marrow depression. We can only speculate on the part played by legionnaires' disease in producing hypoplastic anaemia. A toxic effect on the marrow may explain the pancytopenia during the acute phase of the illness. Its recurrence within a few weeks of clinical recovery, however, was unexpected and difficult to explain. Marrow hypoplasia might have been present before the development of legionnaires' disease, although this seems unlikely in view of the return of an almost normal blood profile after clinical recovery.

The role of co-trimoxazole in producing the hypoplastic anaemia is probably unimportant as the blood dyscrasias of this drug are quite distinct from that seen in our patient.³

¹ Fraser DW, Tsai TR, Orenstein W, *et al*. Legionnaire's disease. *N Engl J Med* 1977;297:1189-97.

² Gasper TM, Farndon PA, Davies R. Thrombocytopenia associated with legionnaires' disease. *Br Med J* 1978;ii:1611-2.

³ Cotrimoxazole and blood. *Lancet* 1973;ii:950.

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Polyneuritis associated with azathioprine sensitivity reaction

A reaction with fever, leucocytosis, arthralgia, myalgia, and rash may occur about two weeks after taking azathioprine.¹ The mechanism of this response is unknown but the clinical pattern is similar to that of serum sickness. We report a case of reversible polyneuritis associated with other features of azathioprine sensitivity reaction.

Case report

A 40-year-old man presented with an 18-month history of weight loss, abdominal discomfort, diarrhoea without blood or mucus, aphthous ulcers, and night fever. Crohn's disease was diagnosed by finding rectal granulomata in a biopsy specimen and extensive disease throughout the small bowel on barium follow-through x-ray examination. Outpatient treatment with prednisolone 45 mg and azathioprine 125 mg (2 mg/kg body weight) daily was started. After 19 days he developed fever, arthralgia, and, within 48 hours, a rapidly progressive proximal muscle weakness such that he could not stand even with support. On admission he was febrile with a tachycardia of 140/min and blood pressure 100/50 mm Hg. There was no exacerbation of the Crohn's disease, which symptomatically had improved, but he had developed erythema nodosum over both shins. The proximal weakness was most definite in the hip girdle muscles, particularly the quadriceps (MRC grade 2), with some muscle tenderness but no fasciculation or reflex change and no sensory abnormality. He had a moderate normochromic anaemia of 11.4 g/dl, a neutrophil leucocytosis of $17.2 \times 10^9/l$ ($17\,200/mm^3$), an erythrocyte sedimentation rate of 64 mm in 1 h, a moderate hypoalbuminaemia of 25 g/l, and a serum alkaline phosphatase activity of 134 IU/l (normal 25-100 IU/l). The serum creatinine phosphokinase activity was normal. Electromyography, sampling quadriceps, showed a pattern of denervation with units of normal duration but low amplitude and moderate reduction in interference pattern. Motor conduction in the left peroneal nerve was reduced to 40 m/s (normal 42.1-63.5 m/s).

Azathioprine was stopped but prednisolone continued in the same dosage. The symptoms settled rapidly. Within four days there was no detectable weakness and the white cell count and alkaline phosphatase had returned to normal. He remained well. Five months later electromyograms were normal and conduction in the left peroneal nerve was 55 m/s.

Comment

Peripheral neuropathy has not been reported in association with Crohn's disease without secondary amyloid,² but it is a recognised complication of hypersensitivity reactions to vaccination, immunisation, and drugs such as penicillin.^{3 4} In hypersensitivity reactions a

subclinical neuropathy may be responsible for the common complaint of myalgia, and weakness may be masked by joint pain. Recognised patterns of peripheral neuropathy include mononeuritis, symmetrical motor or sensorimotor neuropathy, and brachial neuropathy, but there may also be central nervous system lesions or cranial nerve palsies, including optic neuritis. Azathioprine is now used in treating immune-mediated peripheral neuropathies and other immunological disorders of the nervous system (polymyositis, myasthenia, multiple sclerosis, polyarteritis). A drug-induced neuropathy should be considered when there is any change of neurological function associated with an azathioprine reaction. In at least one case azathioprine hypersensitivity was associated with "relapse" in a patient with dermatomyositis.⁵ The patient's serum creatinine phosphokinase activity remained normal and the increased weakness may have been due to a drug-related neuropathy.

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¹ King JO, Laver MC, Fairley KF, Ames GA. Sensitivity to azathioprine. *Med J Aust* 1972;2:939-41.

² Pallis C, Lewis PD. *The neurology of gastrointestinal diseases*. Philadelphia: WB Saunders, 1974.

³ Arnason BGW. Neuropathy of serum sickness. In: Dyck PJ, ed. *Peripheral neuropathy*. Philadelphia: WB Saunders, 1975:1104-8.

⁴ Miller HG, Stanton JB. Neurological sequelae of prophylactic inoculation. *Q J Med* 1954;87:1-44.

⁵ Goldenberg DL, Stor RA. Azathioprine hypersensitivity mimicking an acute exacerbation of dermatomyositis. *J Rheumatol* 1975;2:346-9.

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Radiological bone changes in T-cell and "common" ALL of childhood

In view of the well-known poor prognosis of T-cell acute lymphoblastic leukaemia (ALL) compared with "common" ALL¹ a difference in radiological bone changes might be expected. Analysis of recent data on incidence and width of the characteristic radiolucent metaphyseal bands in children at time of diagnosis appears to confirm this.

Patients, methods, and results

Routinely taken pretreatment skeletal survey films from 25 consecutive children diagnosed as ALL were "blindly" evaluated by one of us (EMS) and later correlated with the results of membrane marker studies of leukaemic cells aspirated from the bone marrow. The assessment of radiolucent metaphyseal bands was subjective since indefinite margins prevent exact measurement. Nevertheless, it was possible to apply the following criteria using an x-ray film centred over the knee joint in the antero-posterior position at 100-cm f c-s-film distance. Radiolucent metaphyseal bands in the femur or tibia with longitudinal dimensions up to 1 mm in width were scored as +, those between 1 and 2 mm as ++, and those over 2 mm as +++. The results are shown in the table.

Comment

The results show a significantly lower incidence and width of the characteristic radiolucent metaphyseal bands at diagnosis in children

Pretreatment radiological bone changes in 25 children diagnosed as suffering from acute lymphoblastic leukaemia (ALL)

Metaphyseal bands	"Common" ALL (n = 18)	T-cell ALL (n = 7)
None	1	6
+	3	1
++	6	—
+++	8	—

No bands vs bands +, ++, +++:
 χ^2 (Yates corr) = 12.3, $p < 0.001$ (2×2 tables).