is likely that the aberrations are the result of a major 'catastrophe' in meiosis in one of the parents, rather than a long series of independent aberrations.

According to our interpretation, two chromosomes 22 have participated in the formation of the marker chromosomes M1 and M2, so that the patient has chromosome 22 material partly in triplicate and partly in quadruplicate. At least one chromosome 22 must be involved, otherwise the patient would have monosomy 22, which as far as we know at present is not compatible with life.⁶

Most of the chromosome material that we assume that our patient has in quadruplicate consists of constitutive heterochromatin and satellites which are reported to be inactive.⁷ Therefore, the clinical manifestations should arise mainly from the partial trisomy for the long arm of 22. Certain features have been reported to be characteristic of partial trisomy 22.⁴ Our patient has some of these characteristics including mental retardation, growth retardation, antimongoloid slanting of the eyes, frontal bossing, broad nose, downturned mouth, micrognathia, large low-set ears with preauricular sinuses, and a striking resemblance to the patient described by Garlinger *et al.*⁴ Thus, these clinical features support our interpretation of the marker chromosomes in the patient.

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Concurrence of anorexia nervosa and yellow mutant albinism

SUMMARY A review of published clinical reports shows that anorexia nervosa has been found in association with several genetic anomalies, principally gonosomal aneuploidy. An additional, and unique, association is described here: a case of anorexia nervosa in a patient with the yellow mutant form of oculocutaneous albinism and no other apparent chromosomal abnormalities. While the concurrence of these two disorders in a single person is apparently a chance phenomenon, our review of experimental publications shows that feeding disturbances also occur in yellow mutant mice. Such complementary findings suggest the need for continuing investigation of the genetic foundations of eating behaviour.

Anorexia nervosa is a feeding disorder occurring primarily in adolescent women and is apparently increasing in incidence.¹ Primary symptoms include severe self-induced malnutrition with weight loss exceeding 25%, distorted bodily perceptions, or implacable attitudes towards food, weight, and eating. These symptoms occur in the absence of other physical or psychiatric illness that would account for this.² Frequent secondary manifestations include amenorrhoea, bradycardia, lanugo hair, hyperactivity, bulimia, and vomiting. Current theories regarding the aetiology of anorexia nervosa postulate intrafamilial, psychodynamic, genetic, or hypothalamic factors. Although no genetic basis for the disease has been clearly established, at least ten cases in association with gonosomal aneuploidy (Turner's syndrome) have been reported since 1963.³⁻¹³ Halmi and associates have argued persuasively that these cases reflect a much greater than chance concurrent incidence of XO gonosome abnormality and anorexia nervosa.^{5,6} On the other hand, Walinder and Mellbin¹⁴ found normal karyotypes in all 30 anorexic patients they observed.

Because of the epidemiological implications of a potential linkage between gonadal dysgenesis and anorexia nervosa, we have been conducting genetic, gynaecological, and urological studies as part of the medical work-up of anorexic patients receiving treatment at University of Minnesota Hospitals during the past several years. Results of these studies will be reported elsewhere; to date they show no significant incidence of sex chromosome anomalies in this patient population. One exceptional case,

however, does present another genetic anomaly in connection with anorexia nervosa. The case reported here is the first, to our knowledge, of anorexia nervosa in a patient with the yellow mutant form of oculocutaneous albinism.

Case report

The proband is a Caucasian American female with normal birth and childhood medical history. Menarche occurred at the age of 13 with normal flow every 30 to 35 days. Height was 162.5 cm and weight was 67 kg at the age of 18 when her medical problems began after a back injury. Repeated orthopaedic and neurosurgical examinations could show no explanation for her continuing pain, muscle spasm, weakness, and numbness. After a 3-month stay in hospital she was discharged weighing 53 kg and later fell to 45.5 kg. Over the next year her menses became irregular and finally stopped when she was 20 years old. Extensive testing failed to identify a pituitary or adrenal abnormality. Gynaecological examination for defeminisation was unrevealing. Multiple parameters of thyroid function indicated a borderline-low circulating level of thyroxine, a very low uptake of radioactive iodine, and a normal response to administration of thyroid stimulating hormone (TSH). Hypothyroidism was diagnosed on the basis of these results and the patient's recurrent complaints of amenorrhoea, chronic fatigue, and intermittent water retention with oedema (presenting with an unexplained rise in blood urea nitrogen (BUN) and multiple gastrointestinal problems). Daily treatment with 0.3 mg l-thyrosine, with diazepam for muscle spasm, continued for the next few years.

A diagnosis of anorexia nervosa was first made when the patient was 25 years old, on the basis of her continued weight loss (to 38.6 kg), amenorrhoea, hypotension, weakness, vomiting, food aversion, and laxative abuse. Six months of hospital treatment including force feeding, psychotherapy, and a behaviour modification approach had only temporary effects. She was last seen at the age of 28. Her weight had stabilised between 36 and 41 kg, unexplained back pains persisted, and hyponatraemia, hypovolaemia, hypokalaemia, and raised BUN, all secondary to dehydration, had led to prerenal azotaemia. Treatment with tranquillisers, dietary recommendations, and thyroid extract continued.

GENETIC FINDINGS

Of particular interest in this anorexic patient is the occurrence of oculocutaneous albinism of the yellow mutant type, as described by Nance *et al.*¹⁵ No other

FIG 1 Photograph of patient's left optic disc and fundus, cf albino fundus and blonde fundi in Hodes BL. The fundus of the eye. *Postgrad Med* 1975;58:155-8.

members of the patient's family had albinism, but her light complexion, yellow-brown hair, and pale fundi (fig 1) prompted further testing, the results of which are all consistent with this diagnosis. Hair bulbs incubated in tyrosine or dopa failed to form increased black eumelanin. When cysteine was added to the incubating solution, the yellow colour intensified, apparently because of the production of pheomelanin. Electron microscopy of the ultrastructure of the hair bulbs showed normal number and morphology of melanocytes. Melanosomes were relatively unpigmented with many in the premelanosome stage. Results of platelet studies were normal. Chromosomal analysis showed from 2 to 12% chromatid breaks on various occasions and a normal karyotype. When tested for visually evoked cortical potentials, the patient showed the markedly asymmetrical response pattern (fig 2) characteristic of a high percentage of human albinos.¹⁶

Discussion

In the past 15 years several cases of anorexia nervosa have been reported in conjunction with hereditary disorders, mostly Turner's syndrome, urogenital malformations, XO-XX mosaicism, and chromatid breakage.^{5,6} With these findings and our patient's longstanding amenorrhoea in mind, we examined her extensively, finding (1) a normal urogenital tract as determined by pelvic examination, culdoscopy,

FIG 2 Visually evoked potentials recorded from both hemispheres under conditions of binocular and monocular illumination. (Courtesy of Don L Creel.)

intravenous pyelogram, and cytосcopy, and (2) normal karyotype with some chromatid breakage and retardation of leucocyte response to mitogenic (phytohaemagglutinin) stimulation. The unusual genetic condition concurrent with this case of anorexia nervosa is the yellow mutant form of oculocutaneous albinism. This condition causes less photophobia and social reaction than other types of albinism, but may involve subclinical perceptual or visual system anomalies. At present we

are not proposing an aetiological relationship between these two disorders. We are merely reporting the association since we know of no other such report. Indeed, there may be no reason to regard their concurrence in a single person as anything more than a random event. On the other hand, Fuller's experimental evidence¹⁷ that yellow mutant mice have higher proportions of body fat, and gain weight earlier and faster than their non-yellow littermates parallels a hypothesis put forward by Crisp.¹⁸ Crisp's notion is that the aetiology of anorexia nervosa is related somehow to high birthweight (thus its absence in developing countries), higher proportions of body fat (thus females are at greater risk than males), and premorbid obesity. Such a conjunction of laboratory evidence from animal studies and patterns emerging from retrospective studies of humans should motivate continued investigation of possible inherited controls over eating behaviour.

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