Failure to Thrive: The Diencephalic Syndrome of Infancy and Childhood

A Case Report*

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This case report presents an example of the enigmatic condition given the sundry names of diencephalic syndrome of infancy, inanition syndrome, athrepsia, failure to thrive, and others. It is almost invariably caused by an astrocytoma of the anterior hypothalamus and optic chiasm. Patients with this syndrome show few of the signs and symptoms usually attributed to brain tumors, optic nerve gliomas, or hypothalamic-pituitary lesions. Enough cases with similar signs and symptoms have been reported in the radiologic, pediatric, and neurologic literature in the past 7 years to form a fairly characteristic syndrome that must be considered in the differential diagnosis of emaciation in infants and children.

Case Report

History. D. C. is a white boy who was born in May, 1962. After a normal pregnancy and delivery, he did well for 9 weeks, gaining in weight from 5 lb. 14 oz. at birth to 13 lb. He then stopped gaining weight and would take only 10-16 oz. of milk and one jar of baby food a day. He was tried on many different formulas. Tests for cystic fibrosis, malabsorption syndrome, food allergy, and metabolic diseases were negative. In January, 1963, he was noted to have vertical and rotational nystagmus with no other neurologic abnormality. Skull films were normal as was lumbar puncture. A pneumoencephalogram was performed because the diencephalic syndrome was suspected, but it was interpreted as showing only mild cortical atrophy. He continued to be emaciated to a greater degree than could be explained by his caloric intake (Fig. 1) and was again hospitalized for complete metabolic and gastrointestinal studies in June and August, 1963 (aged 13-15 months).

Examination. Pituitary, thyroid, and adrenal functions were normal as shown by studies of heat and cold tolerance, serum protein bound iodine, serum electrolytes, and urinary steroids. SU-4885 studies were normal. No gastrointestinal or pancreatic dysfunction could be found. Carbohydrate and amino acid metabolism was normal as shown by glucose tolerance, insulin tolerance, adrenalin tolerance, serum glucose and galactose, and urinary amino acid studies.

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Fig. 1. Patient at the age of 15 months.

Neurologic and ophthalmologic examinations showed a bright, hyperkinetic youngster who smiled a great deal. He walked only with support and did not talk. His vision and visual fields were bilaterally normal. The optic discs and fundi were normal. He had no pupillary or extraocular muscle deficit. There was no conjugate gaze palsy. He had constant vertical nystagmus thought to be compatible with congenital nystagmus. There were no other cerebral, cerebellar, motor, sensory, or reflex abnormalities. Psychological testing demonstrated average intelligence. Skull films, electroencephalograph and spinal fluid examinations were again normal. The pneumoencephalogram performed at the age of 8 months was reviewed and thought to be compatible with an anterior third ventricular mass. Soft tissue films of the extremities showed complete absence of subcutaneous fat with relative preservation of muscle. Skeletal development was normal (Fig. 2). Films of the optic foramina revealed a markedly dilated right optic foramen. A ventriculogram demonstrated a large mass in the area of the optic chiasm and anterior
third ventricle with no obstruction of the foramina of Monro.

Operation. A right frontal craniotomy in August, 1963, (at the age of 15 months) revealed a greatly enlarged right optic nerve extending through the dilated optic foramen and extending into a massively enlarged optic chiasm. The left optic nerve was relatively normal. A biopsy taken from the optic chiasm proved to be a benign fibrous astrocytoma (optic glioma). No further removal or exploration seemed advisable or possible. The full superior and posterior extent of the tumor was not seen.

Course. He was given 4000 r tumor dose irradiation by a cobalt-60 machine through multiple ports over a 6-week period. At present (May, 1964) he is able to walk and talk, and is alert and active (Fig. 3). His vision seems intact although the nystagmus is unchanged, his appetite is fair, but he remains severely emaciated and weighs only 15 pounds. The only consistent, marked abnormality of hormones or metabolism found by laboratory tests has been a greatly elevated level of growth hormone in the serum—approximately three times maximum normal values. Extensive metabolic studies are being done and will be reported later.

Discussion

Tumors in the hypothalamic area are usually thought to cause obesity, precocious puberty, somnolence, and diabetes insipidus. Cases of emaciation and cachexia have been associated with hypothalamic tumors. Rarely, cranio-pharyngiomas cause progeria and dwarfism in children. But none of these patients demonstrated the syndrome of initial acceleration of growth followed by profound emaciation paradoxically associated with vigorous hyperactivity, eager over-alertness, and euphoria first reported by Russell in 1951 and 1957. Twenty cases with strikingly similar histories, physical findings, and pathological lesions have been reported since Russell's ten cases.

These patients are first brought to the pediatrician from the age of 3 months to 4 years with a history of failure to gain weight for several months. They may have had some vomiting and diarrhea but this is not severe enough to explain their severe emaciation. Their appetites vary from anorectic to ravenous. Examination reveals extreme cachexia with loose pale skin, but fairly good preservation of musculature. The patients usually are bright and alert with good strength and often are smiling, euphoric, and hyperactive.
Sweating may be excessive. The genitalia are normal. Neurologically, they are often normal and almost never have signs of increased intracranial pressure. Constant nystagmus similar to the congenital type is perhaps the most frequent abnormality found. Optic atrophy and ataxia are infrequent. Tests of vision have rarely been mentioned in the literature.

Laboratory tests are usually completely normal. There is no anemia in spite of the pallor. Urine volume and specific gravity are normal. All serum chemical values are normal except for occasional mild hypoglycemia. There are no abnormalities of gastrointestinal absorption or motility. Almost all endocrine evaluations have been normal except for the extremely high growth hormone levels found in the patient reported here. (No other growth hormone studies have been reported in other patients with this syndrome.) Thermodynamics and diencephalic seizures have not been noted.

Of the 33 patients reported, 26 had low grade astrocytomas involving the anterior hypothalamus. These were either intrinsic in the hypothalamus or were primary in the optic chiasm. One ependymoma and 1 oligodendroglioma were found in this area. Three tumors of the anterior third ventricle were demonstrated by air studies but not proven histologically. One patient with the syndrome had a midline cerebellar astrocytoma with marked dilatation of the third ventricle, but no evidence of hypothalamic tumor.

The pathophysiology of this syndrome is not well understood. Experimental destruction of lateral hypothalamic nuclei is said to cause emaciation while midline lesions cause obesity. Physical hyperactivity, endocrine dysfunction, malabsorption of food, and inadequate caloric intake have not been demonstrated consistently enough in these patients to explain their extreme emaciation. Poznanski and Manson have reported complete loss of fatty tissue in the limbs of their patients with anterior hypothalamic tumors. On the other hand, in children with emaciation from extracerebral malignant disease or starvation, they always found some residual fatty tissue in the limbs. A study was made of roentgenograms of the extremities of 100 emaciated patients. These showed atrophic changes of the extremities due to simple malnutrition, paraplegia associated with myelomeningocele, Morquio's syndrome, immobilization, renal osteo dystrophy, or debility associated with advanced malignancy—leukemia, neuroblastoma, rhabdomyosarcoma, lymphosarcoma, etc. Only one of these patients showed no radiographic evidence of subcutaneous fat. Thus, soft tissue roentgenograms can be of value in the differential diagnosis of children who fail to thrive. If there is complete absence of fat in the limbs, an anterior hypothalamic tumor is likely. The greatly elevated growth hormone levels found in the serum of the patient presented in this report may help to explain the paucity of fat since growth hormone is known to take part in the mobilization of fat. However, other as yet unknown factors may be of primary importance in this hypothalamic syndrome.

Summary

We have presented a case of a patient with an astrocytoma of the optic chiasm who demonstrated the features of the "diencephalic" or "failure-to-thrive" syndrome. Overactivity, overalertness and emaciation were significant symptoms in this patient. Roentgenograms characteristically demonstrate normal bone growth, good muscular outline, and absent subcutaneous fat. Increased growth hormone was found and may be a factor in the disturbed lipid metabolism.

References

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