Case Reports

EXOPHTHALMIC GOITER IN A BOY TWO AND ONE-HALF YEARS OF AGE

REVIEW OF THE LITERATURE

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In 1923 Cowden [1] was unable to find in the literature a report of hyperthyroidism in a boy under 10 years of age, but since that time several such reports have appeared. Helmholtz [2] cited the case of a boy aged 3 years who had had symptoms of hyperthyroidism since the age of 11 months. The same author, in reporting 30 cases of exophthalmic goiter in children under 14 years of age, found that the incidence in boys was extremely low as compared with that in girls. In his series there were only 4 boys as compared with 26 girls.

Elliot [3] reported hyperthyroidism in a girl 2½ years old on whom an operation was performed at the age of 2 years and 10 months. After preliminary ligations, a right subtotal lobectomy was successfully performed, and the patient obtained complete relief from all symptoms. The onset of hyperthyroidism had been at the age of 1 year. Braid and Neale [4] reported a fatal outcome in a case of hyperthyroidism in a girl 2½ years of age. At this time they were able to find only 2 cases of recovery in children under 5 years. The first was Dreschfeld's,[5] in which a child 3 years of age recovered after the use of belladonna and a pancreatic emulsion. It is difficult to estimate the severity of the disease in this case. The second was that of the child of 3 years, previously referred to, in Helmholtz' series.

1. Cowden, Charles: Exophthalmic Goiter in the Child, Tr. South. S. A. **36**:75-83, 1923.

2. Helmholtz, H. F.: Exophthalmic Goiter in Childhood, J. A. M. A. **87**: 157-162 (July 17) 1926.

3. Elliot, P. C.: Exophthalmic Goiter Before One Year of Age, J. Pediat. **6**:204-210 (Feb.) 1935.

4. Braid, F., and Neale, A. V.: Case of Exophthalmic Goiter, Arch. Dis. Childhood **5**:229-232 (June) 1930.

5. Dreschfeld, J.: Notes on Graves' Disease, Practitioner **57**:135, 1896.

Stephen [6] reported a case of hyperthyroidism in a girl 3½ years of age. The onset of the disease was placed at the age of 2½ years, and although definite hyperthyroidism was present, the child recovered without an operation.

Kerley [7] reported a case of exophthalmic goiter in a girl of 3½ years. The diagnosis was apparently perfectly clear, but the disease subsided spontaneously after rest and treatment with solution of potassium arsenite and iron.

In Dinsmore's series,[8] 48 cases of hyperthyroidism in children under 14 years of age were reported, but there was no case in a boy under 5 years. In the case of a girl of 7, the onset of the disease was placed at the age of 2½ years.

White [9] reported the presence of exophthalmic goiter and tachycardia in an infant born of a mother who had active hyperthyroidism. The child lived only thirty-five hours. The thyroid gland showed hyperplasia. Although this is the youngest patient with hyperthyroidism whose case appears in the literature, it is extremely difficult to determine, in view of the fact that the mother had exophthalmic goiter, whether the child had acquired the disease independently or from the mother through the blood stream.

Helmholtz [2] quoted Sattler, who had reported 184 cases of hyperthyroidism in children, representing an incidence of 5.3 per cent of his total of 3,477 cases of hyperthyroidism. This unusually high incidence of hyperthyroidism in children and the fact that the symptoms listed were less severe in every respect than in the cases recorded by Helmholtz, Dinsmore and others in the American literature lead us to believe that the disease is somewhat less severe in Germany. It is interesting to note that the incidence of hyperthyroidism in Sattler's series was more equally distributed between the sexes, there being 4 boys to 7 girls in the age group of from 1 to 5 years. Therefore, it is not improbable that some of these cases represented the thyroid hyperplasia of iodine deficiency rather than true exophthalmic goiter.

Ochsner and Thompson [10] described exophthalmos in a boy 5 weeks of age. This child had a turret head, and no mention was made of

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6. Stephen, E. H. M.: Exophthalmic Goiter in Girl Aged Two Years, M. J. Australia **1**:29-30 (Jan. 7) 1933.

7. Kerley, C. G.: Exophthalmic Goiter in Girl Three and One-Half Years of Age, Arch. Pediat. **48**:61-62 (Jan.) 1931.

8. Dinsmore, R. S.: Hyperthyroidism in Children, Surg., Gynec. & Obst. **42**:172-176 (Feb.) 1926.

9. White, Clifford: A Foetus with Congenital Hereditary Graves' Disease, J. Obst. & Gynaec. Brit. Emp. **21**:231-233, 1912.

10. Ochsner, Albert J., and Thompson, Ralph L.: The Surgery and Pathology of the Thyroid and Parathyroid Glands, St. Louis, C. V. Mosby Company, 1910, p. 193.

the pulse rate or of diagnostic studies. Patterson [11] reported the case of a girl with hyperthyroidism which dated from the age of 4 months. The child was, however, 14 years old when she first came under Dr. Patterson's observation. Exophthalmos was the chief sign of hyperthyroidism, and the early history was somewhat obscure.

Lahey [12] mentioned that he performed a thyroidectomy on a child of 3 years, but the sex of this child was not stated.

Beilby and Carlton [13] reviewed the literature in 1931 and found reports of 8 cases of hyperthyroidism in children under 5 years of age. Two of these were from the Mayo Clinic series (ages, 5 and 3 years), 1 from the Lahey Clinic (age, 3 years), 1 reported by Braid (age, 2½ years), 1 reported by Barrett (age, 2½ years), 1 reported by Schkarin (age, 4½ years) and 1 reported by Klaus (age, 9 months). In the report of the last case the sex of the patient was not stated, nor were any convincing diagnostic tests made in that case; the disease disappeared without an operation. Sherman's case of hyperthyroidism in a girl of 2½ years was also mentioned. This child was later seen at the Cleveland Clinic; she recovered without an operation. Beilby and Carlton reported a case of active hyperthyroidism in a girl of 2 years and 9 months. Thyroidectomy was performed in one stage at the age of 2 years and 10 months, and the postoperative course was entirely uneventful.

In a series of 4,300 cases of exophthalmic goiter, Bram [14] found 102 cases in children. Only 5 of these were in boys. Two patients were from 2 to 3 years old; 3, from 3 to 4, and 5, from 4 to 5. No mention was made of the sex of the children in the age group of from 2 to 3 years, nor was there any report that operations were performed.

It is apparent that, while a number of cases of hyperthyroidism in children appear in the literature, proved hyperthyroidism before the age of 5 years is extremely rare. Only 7 patients—those of Helmholtz, Braid and Neale, Lahey, Stephen, Beilby and Carlton, Kerley and Elliot—were carefully observed, fully reported on in the literature and shown to have had unquestionable hyperthyroidism before the age of 5 years (table). The following case is unique in that the patient is the youngest boy with active hyperthyroidism yet reported on. Although

11. Patterson, Donald: Hyperthyroidism Dating from Infancy, Proc. Roy. Soc. Med. **28**:832-833 (May) 1935.

12. Lahey, F. H.: Primary Hyperthyroidism in Children, S. Clin. North America **9**:1327-1330 (Dec.) 1929.

13. Beilby, G. E., and Carlton, J. G.: Exophthalmic Goitre in Children, New York State J. Med. **31**:1329-1332 (Nov. 1) 1931.

14. Bram, I.: Exophthalmic Goiter in Children of Ten and Under, Pennsylvania M. J. **37**:45-48, 1934.

Helmholtz dated the onset of symptoms in his patient at the age of 11 months, the child was not seen or observed until the age of 3 years. The case reported here is also unique in that the patient is the youngest child described in the literature on whom successful thyroidectomy has been performed.

REPORT OF CASE

The child was born on Aug. 30, 1933. He was a full term infant, and delivery was normal, labor lasting seven hours. The mother vomited during the entire pregnancy, but there were no postnatal complications. The child cried well at birth. No cyanosis, convulsions or nursing difficulties occurred, and no hemorrhage, paralysis or deformity was evident. The weight at birth was 10 pounds (4,535 Gm.).

The family history was entirely irrelevant, neither the mother nor the father having had any evidence of goiter. There were no other children. There was no family history of tuberculosis, syphilis, allergy, diabetes, goiter or nervous disease. The child did well on breast milk for one year and was then weaned to cow's milk. Solid foods were added between the ages of 9 months and 1 year.

Cases of Proved Hyperthyroidism in Children Under 5 Years of Age Reported in the Literature Written in English

Author	Age	Sex	Treatment	Outcome
Helmholtz	3	M	Thyroidectomy	Cure
Braid and Neale	2½	F	Thyroidectomy	Operative death
Lahey	3	Not stated	Thyroidectomy	Cure
Stephen	2	F	Conservative	Cure
Beilby and Carlton	2¾	F	Thyroidectomy	Cure
Kerley	3½	F	Conservative	Cure
Elliot	2½	F	Thyroidectomy	Cure

He sat up at 6 months, walked at 8½ months and talked at 1 year. The teeth appeared early, at approximately 6 months. The second year was normal with the exception of several instances of gastro-intestinal disturbance and a few uncomplicated head colds. No immunization was carried out. On Aug. 1, 1935, at the age of 23 months the child had an attack of dysentery characterized by frequent bloody stools. His height at that time was 38 inches (96 cm.) and his weight 30 pounds (13.6 Kg.). He was considerably dehydrated, but there was evidence of hyperthyroidism.

On April 1, 1936, at the age of 2 years and 7 months, the child was examined by one of us (J. L. B.) because of abdominal pain and nervousness. For the previous five days he had complained of abdominal pain and had been vomiting. He had no appetite. The stools were normal. He was extremely nervous, and this condition had been present for about six months. He slept poorly, but he never had slept well. He had not gained in weight since the attack of diarrhea seven months previously. The mother stated that he perspired excessively and was easily excited. His appetite until five days before had been good.

Physical examination showed the temperature to be 102 F. by rectum, the height 40½ inches (103 cm.) and the weight 31½ pounds (14.3 Kg.). The normal weight at this age is 37 pounds (16.8 Kg.). The child was extremely nervous and apprehensive, sweating profusely and crying constantly. There was definite exophthalmos of both eyes. Both ear drums were dull. The nostrils were open, and there was no discharge. The mouth was normal, but the tongue was heavily coated.

The throat was red, and there was a postnasal discharge. The submaxillary and axillary lymph nodes were palpable. There were visible pulsations over the carotid artery, and the thyroid gland was large and soft. The chest was normal in shape. The respirations were rapid. The lungs were clear; the heart was observed by percussion to be slightly enlarged; the pulse rate was 150, and the blood pressure was 120 systolic and 60 diastolic. There was a systolic apical murmur which was not transmitted. The abdomen was soft; the edge of the liver was palpable 3 fingerbreadths below the costal margin on the right side. The spleen, likewise, was palpable. The genitalia and the extremities were normal. There was marked tremor of the extended fingers. The child's parents stated that although some months previously he could walk quite well without falling, recently he had appeared weak and had stumbled, staggered and fallen a great deal. In addition, they thought that his speech was more unintelligible than formerly. The development of speech, which had begun at the age of about 1 year, had not progressed as rapidly as they had expected, but it was extremely difficult to tell anything about the child's speech because he was crying constantly. There was no weakness of the muscles of the back, but the child stood up only with considerable difficulty, and there seemed to be definite weakness of the quadriceps muscles. The coordination of the hands was good, and the awkwardness, stumbling and peculiar gait could all be attributed to weakness of the legs.

Urinalysis at this time gave entirely negative results. The child was sent home, put to bed and given 1/8 grain (0.008 Gm.) of soluble phenobarbital and 3 grains (0.195 Gm.) of acetylsalicylic acid in syrup every four hours. The diet was modified, and the parents were instructed to return in one week.

On April 12 the acute nasopharyngitis had cleared up, but the child was still extremely nervous and slept poorly. The appetite was excellent again. He continued to sweat freely and was easily frightened. The weight was 30½ pounds (13.8 Kg.), and the temperature was 99.2 F. by rectum. In view of these findings, a diagnosis of hyperthyroidism was made, and the patient was referred to the Cleveland Clinic.

On examination at the clinic, approximately the same findings were noted except that the child was utterly unmanageable (fig. 1). The excitement of the trip and the unfamiliar surroundings made him cry constantly, and at any attempt to approach or examine him he screamed and resisted. The edge of the liver could be felt. Examination was extremely unsatisfactory because of the lack of cooperation. On admittance to the hospital, the pulse rate was consistently 160.

Laboratory Studies.—Urinalysis gave entirely normal findings. Examination of the blood showed 6,070,000 red cells, 78 per cent hemoglobin, 13,100 white cells, 42 per cent neutrophils, 1 per cent eosinophils and 57 per cent lymphocytes. The sugar content of the blood was 182 mg. per hundred cubic centimeters during fasting, and the cholesterol content was 136 mg. The Wassermann and Kahn reactions were negative. A twenty-four hour specimen of urine showed a total excretion of creatinine of 0.108 Gm. The excretion of creatine during the same period was 0.152 Gm. A recheck of the blood cholesterol several days later again showed 136 mg., and a second test of the blood sugar during fasting showed 139 mg. A negative Friedman test indicated that there was no excess of gonadotropic substance in the urine. The blood iodine content was 14.9 micrograms per hundred cubic centimeters, a figure just above the upper limit of normal. Roentgen examination of the epiphyses of the wrist showed development of the bones approximating that of a 5 year old child. A roentgenogram showed the sella turcica to be normal in size and shape. The skull showed no evidence of increased intracranial pressure and no other abnormality. Roentgen examination

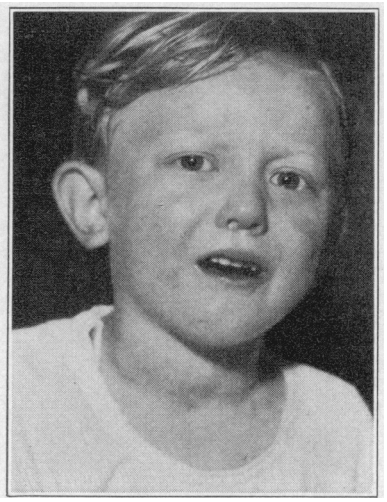

Fig. 1.—A photograph of the patient before the operation. Emotional strain is evident. Exophthalmos is not evident in this photograph because the patient was crying and the eyes were half closed.

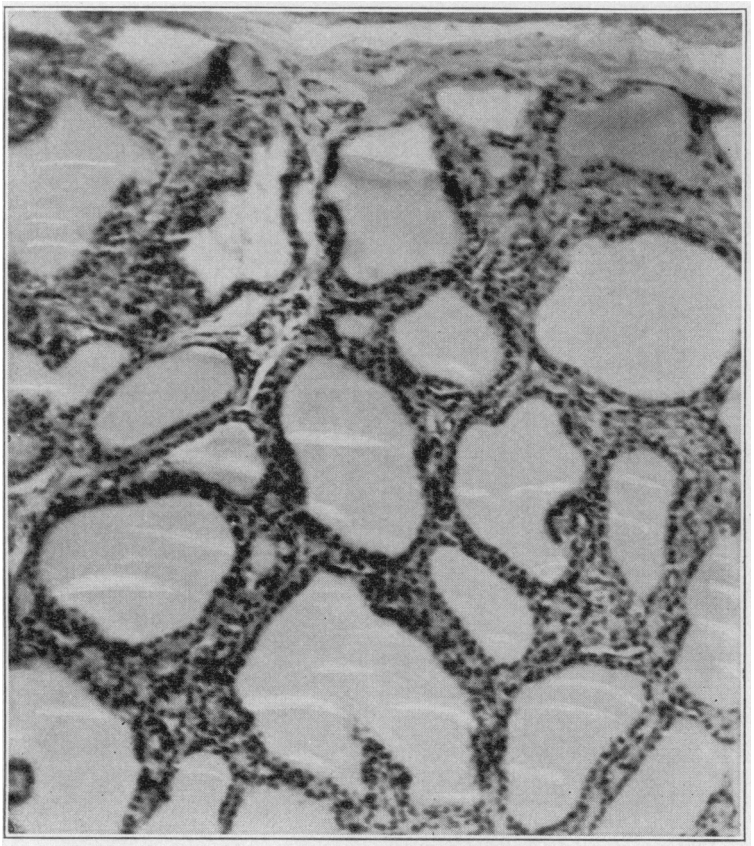

Fig. 2.—A photomicrograph of the tissue removed (× 150).

of the chest showed no abnormality. Examination of the eyes showed widened palpebral fissures and early exophthalmos. Actual measurements were impossible owing to lack of cooperation. Dental examination showed all the deciduous teeth to be present. The physiologic age as shown by the teeth was estimated to be from 3 to 3½ years. There was no dental caries.

Course.—The child was given 4 minims (0.24 cc.) of compound solution of iodine three times daily and 5 grains (0.325 Gm.) of sodium bromide three times daily. His weight at entry was 36½ pounds (16.5 Kg.); it had fallen to 35 pounds (15.9 Kg.) at the end of the fifth day, but on the twelfth day of hospitalization it had risen to 38 pounds (17.2 Kg.). The pulse rate, which was 160 at entry, fell gradually over a period of twelve days to 120 and remained stabilized at about that level. On May 15, when the child was 2 years and 8½ months old, a subtotal thyroidectomy was performed by Dr. George Crile Sr., with the patient under anesthesia induced by tribromethanol, 100 mg. per kilogram of body weight being given. The gland was about five times the normal size. It was extremely vascular and somewhat friable. The major portion of both lobes was removed, the weight of the tissue removed being 33 Gm.

The pathologic diagnosis was hyperplastic and moderately involuting goiter. There was little increase in stroma and little lymphoid tissue (fig. 2). No adenomas and no parathyroid glands were present in the specimen removed.

The immediate postoperative course was stormy, the temperature rising to 105 F. and the pulse rate to 170. The temperature, however, was always controllable by the administration of 5 grains (0.325 Gm.) of acetylsalicylic acid, and the child remained conscious and took fluids throughout the entire postoperative period. The oxygen tent was used constantly for several days. On the third day postoperatively, acute infection of the respiratory tract and acute follicular tonsillitis developed. The temperature again rose to 105 F., but the pulse rate did not rise above 160. After this the temperature rapidly returned to normal.

The child was discharged on the seventeenth postoperative day, the pulse rate at this time varying between 95 and 110. He was still nervous and apprehensive but was more quiet than at the time of his entry to the hospital. Several months after his discharge he was gaining weight and strength, was less nervous and was improving steadily in every way.

COMMENT

Although the finding of persistent tachycardia, nervousness, loss of weight, sweating, tremor, exophthalmos and goiter established the diagnosis of hyperthyroidism beyond any question, the clinical picture was somewhat obscured by the marked muscular weakness. This weakness was so pronounced that the patient walked with a stagger and frequently fell. In addition, the extreme nervousness and apprehension left the child in constant fear, so that it appeared as if there were definite mental retardation. Because these neurologic signs were not clearly understood, a roentgen examination of the skull was made to rule out the possible presence of increased intracranial pressure. The high blood iodine level and the low cholesterol level were findings perfectly consistent with hyperthyroidism. It is a well known fact that epiphysial closure is delayed in hypothyroidism during childhood, and it is hence interesting to note that the development of the bones of this

2½ year old child was estimated from a study of the epiphyses to be that of a 5 year old child. Likewise, the dental development was somewhat advanced for the age.

Another interesting feature of this case is the fact that a dose of 100 mg. of tribromethanol per kilogram of body weight quieted the child for only about three quarters of an hour, at the end of which time he asked for candy. When severe hyperthyroidism is superimposed on the normally high metabolism of children, they are remarkably tolerant of depressive drugs. Morphine sulfate in doses of ⅛ grain (0.008 Gm.) was given hypodermically during the postoperative period, but practically no depression of respiration was noted.

SUMMARY

Seven cases of clearcut hyperthyroidism in children under 5 years of age have been reported in the American literature.

A case of hyperthyroidism in a boy 2½ years of age is reported.

A review of the literature shows that there is no report of a case of hyperthyroidism in a younger boy in which a diagnosis was made and confirmed by adequate clinical and laboratory investigation.

Our patient is also the youngest child for whom a successful thyroidectomy for hyperthyroidism has been reported.