TWELVE CASES OF LYMPHOBLASTOMATA IN CHILDREN

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The primary purpose of this paper is to illustrate the protean symptomatology of a group of growths known collectively as the malignant lymphomata or lymphoblastomata. Much discussion centres on the exact nomenclature of these conditions, and no attempt is made here to elucidate this matter. Gall and Mallory (1942) discuss the problems involved, and suggest a cytological basis for subdivision; Custer and Bernhard (1948) point out that the cellular structure of lymphatic tumours is extremely labile, and that transition from one apparently distinct type to another is frequently seen, so that an absolute cytological diagnosis by biopsy may be very difficult.

From the descriptive standpoint, with the exception perhaps of Hodgkin's disease, these conditions are relegated to small sections of the average paediatric textbook, emphasis generally being placed on enlargement of lymph nodes in the symptomatology. Arey (1949) does not discuss Hodgkin's disease or lymphosarcoma, stating that they have their counterparts in adult life. Dargeon (1947) states that the physical signs and symptoms of lymphosarcoma will depend on the anatomical site of the affected structures, and says that the nasopharynx, the tonsil and the cervical, or any other group of nodes, may be involved. In a later study (1953), however, he describes more specific cases, and emphasizes the difficulty of diagnosis and management.

Material

The cases are drawn from the practice of the University hospitals of the University of Wisconsin. In all 12 cases the diagnosis was established by biopsy, at necropsy, or by both means. The cytological diagnosis was variously stated to be lymphoblastoma, lymphosarcoma or reticulum-cell sarcoma, each thus being included in the lymphomata as described by Gall and Mallory, or represented in the lymphoblastomata of Custer and Bernhard.

Case Histories

Case 1. This 4-year-old white boy was admitted with a mass on the left cheek which had begun as a small spot

10 weeks earlier and had rapidly increased in size. Sweating at night was an early feature, and shortly before admission deafness in the left ear and epistaxes had occurred. Examination showed a hard, painless mass 4×5 cm., anterior to the left ear, involving the tragus and almost closing the auditory canal. The post-auricular, left anterior cervical and axillary nodes were also involved. The other systems were devoid of pathology.

A biopsy suggested lymphoblastoma.

X-ray therapy was begun, but the mass did not regress, the left face being ultimately partially paralysed. A course of nitrogen mustard reduced the size of the mass and nodes, and relieved the facial palsy. Review three months after the initial examination showed recurrence of the original mass and glandular involvement. The patient did not return for further review.

Case 2. This 3-year-old white boy had a history of falling and cutting the inside of the right upper lip. Three weeks later on the outer surface of the same lip a reddish lump appeared, and was thought to be a boil coming to a head. It was reduced in size by hot fomentations, but rapidly grew again. It was incised, but only a small amount of bloody fluid was obtained. It was then excised totally, but the mass recurred. The child was soon afterwards sent to the hospital where examination revealed a large mass involving the right upper lip and extending upwards almost to the zygoma. It was hard and painless and distorted the whole right face. The right sub-maxillary gland was also affected.

A biopsy suggested a reticulum-cell sarcoma.

Fever was a prominent symptom, but there was no clinical or radiological evidence of spread to other systems. Treatment by x rays was begun, and rapidly reduced the size of the facial lesion. He was seen six months later, when the tumour of the lip was greatly reduced, though the sub-maxillary glandular enlargement was still present. The patient did not report thereafter.

Case 3. This 9-year-old white boy had developed a swelling of the left lower jaw some two months before admission. Initially it was regarded as a dental infection, and treated by penicillin. This failing, surgical drainage was carried out, without relief of the pain and swelling. Therefore, a 'cyst' was removed from the outside of the jaw. At the time of admission here, a swelling the size of a grape-fruit involved the left lower jaw and face. Purulent granulations covered the site of the previous incision. Nutrition was unimpaired; a moderate anaemia

present. A clinical diagnosis of actinomycosis was made, but radiographs revealed a destructive lesion of the left mandible and suggested a neoplasm. A biopsy specimen was unsuitable for a full diagnosis.

X-ray therapy was begun, and the mandibular lesion completely disappeared. Three months after the first admission, swellings had appeared in the long bones of the legs, and the child rapidly lost weight. Examination revealed a pallid, cachectic boy, with tumour masses palpable in many parts of the body. Most were attached to bone, a few enlarged lymph nodes were present, the liver and spleen were involved, as were both testicles. Radiographs confirmed widespread metastases to almost all the long bones and the pelvis. He was discharged in a terminal state.

A second biopsy showed a reticulum-cell sarcoma.

Case 4. This 15-month-old white girl was admitted with a history of bruising the right lower chest some two months before. The resultant lump had grown slowly and painlessly. Three weeks before admission, small swellings had appeared in the skin behind the left ear and on the right occiput. Thereafter small painless masses varying in size from pinhead to 0.3 cm. in diameter had appeared in the skin. The mother had been told that they were 'mosquito bites'. Examination showed a well nourished child who played actively, and whose only remarkable features were a hard, painless mass over the right lower ribs, and a multitude of small reddish plaques of varying size in the skin of the scalp, trunk, limbs and labia (Fig. 1). The blood count was at this time normal. A biopsy of one of the skin lesions suggested a lymphoblastoma. Her course was rapidly downhill. The skin lesions increased in size and number, and a terminal leukaemic reaction with a severe anaemia became evident. Treatment with cortisone and T.E.M. (triethylene-melamine) was without avail and the child died at home one week after discharge. Further biopsy of a lymph node again suggested lymphoblastoma.

Case 5. This 3-year-old white boy was well until one week before admission, when the parents noted rapid swelling of the abdomen, failure of appetite, and night sweats. Examination showed an irritable, fevered boy with gross ascites, though a doughy sensation was felt through the fluid collection. A clinical diagnosis of tuberculous peritonitis was considered, but tapping the effusion gave a 'tomato-juice' specimen. This was negative for tumour cells. Soon afterwards signs of fluid in the right pleural cavity appeared, and a mass was felt in the right hypochondrium. A laparotomy was carried out, and the child died suddenly shortly after the operation, at which a large mass involving the intestine and mesenteric glands was found.

Necropsy revealed a tumour, identified microscopically as a lymphosarcoma, involving the peribronchial, mediastinal, mesenteric, omental and retroperitoneal nodes. The lungs, pericardium, pancreas, stomach, small intestine and appendix were invaded. The adrenals were infiltrated, and the diaphragm was encased in neoplasm.

Case 6. This 4-year-old boy had been well until two months before admission here. He then lost his appetite

and became pale and listless; there was intermittent looseness of the bowels and constipation. A mass was felt in the right lower quadrant, and a laparotomy was carried out in another hospital. This showed enlargement of all the mesenteric lymph nodes, and a biopsy suggested malignancy.

On admission he was pale and emaciated, the abdomen was protuberant, and a mass 10 cm. wide extended from above the umbilicus to the pelvis. It was firm and pain-

FIG. 1.—The skin lesions in Case 4.

less. A few slightly enlarged glands were palpable in the groins and axillae. The child had a 'coffee-ground' vomit, apparently inhaled some of this, and died after a grand-mal convulsion.

At necropsy it was seen that the small intestine was encased in firm, white, nodular tumour as were the sigmoid, rectum and bladder. The neck of the gall-bladder was similarly involved, and the omenta (gastro-hepatic and colic), and splenic capsule were heavily infiltrated. Several tumour nodules were seen on the liver. The surfaces of the kidneys were studded with whitish masses of irregular shape and size, which involved the cortex but not the medulla. Numerous lesions were present in the anterior part of the costo-phrenic sulcus. The cytological diagnosis was lymphosarcoma.

Case 7. Two weeks before admission this boy, 8 years old and a microcephalic idiot, became ill with fever, listlessness, pallor and some looseness of the stools. A few days after the onset, the left cervical nodes enlarged, and the liver and spleen became palpable and enlarged rapidly. Examination at admission showed a pale, orthopnoeic boy with a distended abdomen due to a grossly enlarged liver and spleen. Both organs were very hard but not tender. A firm glandular mass was present in the right neck, and there was lesser involvement of the axillary and inguinal groups. The child was febrile, and there were signs of a left pleural effusion and of bronchial compression. A radiograph confirmed the mediastinal involvement. The blood at this time showed anaemia with a normal white and differential count. The condition rapidly deteriorated in spite of x-ray therapy. The glandular masses increased, and the blood picture 10 days after admission suggested leukaemia, though a previous gland biopsy showed lymphoblastoma. Death occurred after 14 days in hospital. Permission for necropsy was denied.

Case 8. An 11-year-old white boy had a laparotomy for acute appendicitis, from which he made a good recovery. Two and a half months later he felt weak and listless, and he himself found a lump in his abdomen. There was rapid loss of weight thereafter, and six weeks later he was admitted to this unit. Examination revealed a hard, left-sided, abdominal mass, which moved slightly on respiration, and was painless. The submaxillary, cervical, axillary and inguinal nodes were bilaterally enlarged, as were the epitrochlears. The abdominal swelling had some of the characters of a renal tumour, but pyelography and barium enema showed that it was extra-renal and extra-colic. Biopsy of a mesenteric gland showed lymphosarcoma. The boy died soon afterwards.

Case 9. The complaint in this case was of the appearance of a hard, painless, abdominal swelling in an otherwise healthy 18-month-old girl. The process had lasted for three weeks before admission. Fever, anorexia, listlessness and insomnia had been noted, but all urinary and gastro-intestinal symptoms were absent. Examination showed a coconut-sized mass stretching from the left upper quadrant to the left iliac fossa. The liver was also felt and was thought to contain nodular masses.

Radiotherapy was begun, causing rapid diminution of the abdominal tumour, and laparotomy was carried out. This revealed a retroperitoneal mass not involving the adrenals or kidneys. She was readmitted four months later, and the previously noted mass was felt only with difficulty, and the liver was thought to be smaller. A 'brassy cough' suggested mediastinal involvement, and radiographs confirmed this. Soon afterwards the abdominal tumour increased, gross anaemia occurred, and the child died.

Necropsy revealed a retroperitoneal mass displacing the stomach, spleen and pancreas. The liver was heavily infiltrated with tumour metastases, as were the anterior and superior mediastina. The pre-aortic lymphatics were also heavily involved. Microscopy confirmed the diagnosis of lymphosarcoma.

Case 10. This white girl, age 8 years, had bruised her left groin. Fever followed, and a lymphatic swelling was discovered. A biopsy was done, and revealed a 'small-cell lymphoblastoma'. She was seen in this unit three months after the onset of symptoms, and after radiotherapy had been begun. The residua of the enlarged nodes were palpable, but there was no evidence of further involvement. Six months later the nodes of the left anterior triangle and supraclavicular areas were enlarged and the spleen was felt. There was local recurrence in the left inguinal region. Four months later, that is one year after the onset, she was rapidly deteriorating in spite of further x-ray therapy. Thereafter she was lost sight of, but her local physician was of the opinion that she was in the 'terminal' stages of the illness one month after final discharge.

Case 11. This 9-year-old white girl became ill 3 months before admission here. The initial symptoms were of fever and swelling of the glands in the left neck. These were reddened, somewhat tender, and adherent to the deeper structures. A diagnosis of tuberculous lymphadenitis being made, the child was admitted to a sanatorium. There a negative tuberculin test led to the removal of a node, and microscopy suggested a reticulum-cell sarcoma. Examination revealed a pallid, listless child. The left cervical nodes were enlarged and slightly tender. The corresponding nodes on the right were also involved as were those of the right axilla. The spleen was felt 6 cm. below the costal margin, being firm and not tender. There was a hypochromic anaemia, with a normal white and differential count. Enquiry failed to elucidate her further course.

Case 12. This girl, 2 years old, was seen in the eye department with a 2×3 mm. mass in the inner canthus of the right eye which had been present for one month. It did not seem inflammatory, and obscured the caruncle without interfering with lacrimal drainage. The mass was removed, and section showed it to be a lymphoblastoma. Follow-up over a period of two years, with extensive clinical and x-ray surveys, has failed to show evidence of local recurrence or metastatic spread.

Clinical Features

The clinical features are summarized in Table 1, and the relevant haematological detail is given in Table 2. A great variation in the clinical picture, quite unrelated to a fairly constant cytological pattern, is seen. Thus the initial symptom in three cases (Cases 6, 8, 9) was of a painless intra-abdominal mass, and in two (Cases 10 and 11), enlargement of lymph nodes. Three cases (Cases 1, 2 and 3) each presented with a mass on the face. In Case 5 there was a rapid onset of ascitic swelling of the abdomen, clinically simulating an acute tuberculous peritonitis, the true diagnosis only being considered when a blood-stained effusion was found. Similarly in Case 11, the onset of fever and painful swelling of the neck nodes led to an erroneous

TABLE 1
SYMPTOMATOLOGY

Case	Initial Symptom	Fever	Pallor	Anorexia and Listlessness	Lymph Node Involvement (Clinical)	Duration before Admission to Hospital	Total Duration
1	Swelling of face	no	no	no	yes	10 weeks	Followed for 4 months
2	Mass on right upper lip	yes	no	no	yes	1 month	Followed for 6 months
3	Swelling of left jaw	yes	yes (in later stages) not initially	In later stages	yes	2 months	Terminal after 3 months
4	Mass on right lower chest with skin lesions	yes (later stage)	no	no	yes	2 months	Died after 4 months
5	Swelling of abdomen (acute)	yes	no	Anorexia only	no	1 week	Died after 1 week
6	Swelling in abdomen, gastro-intestinal upset	no	yes	In later stage	no	2 months	Died (inhalation) after 2 months
7	Fever: gastro-intestinal upset, gland swelling	yes	yes	yes	yes	2 weeks	Died after 1 month
8	Localized mass in abdomen	no	yes	yes	yes	4 months	Lost sight of
9	Mass in abdomen	yes	no	yes	no	3 weeks	Died after 5 months
10	Swelling of groin glands	yes	no	Later stage	yes	3 months	Terminal after 8 months
11	Swelling of neck glands	yes	yes	yes	yes	3 months	Lost sight of
12	Small growth inner canthus right eye	no	no	no	no	1 month	Alive after 2 years

diagnosis of tuberculous lymphadenitis. The patient was confined to a sanatorium for two months before biopsy clarified the condition. The history and early clinical course in Case 3 were most misleading, and actinomycosis was the clinical diagnosis; radiographs, however, showed widespread mandibular destruction suggestive of neoplasia. Pallor, anorexia and listlessness were common features. In Cases 7, 10 and 11, a prominent, or in Case 7, the only, initial complaint was fever. Trauma was an associated factor in Cases 2, 4 and 10, and in two instances seemed definitely to have preceded the appearance of the primary lesion. Case 4 was referred initially as a dermatological problem, the lesions having previously been dismissed as mosquito bites. The course in Case 7, with massive glandular

enlargement and hepatosplenomegaly, was perhaps more suggestive. Case 12 was diagnosed only by biopsy.

The paucity of symptoms in relation to widespread anatomical lesions is very striking in Cases 5, 6 and 9. The first two reflect the condition reported by Guthrie (1948) in describing a case with similar necropsy findings.

The table of haematological findings shows that a severe hypochromic anaemia was the usual state. In this connexion Sugarbaker and Craver (1940) in reviewing a series of adult cases, state that the blood picture is non-specific in lymphosarcoma, 70% of their patients having a haemoglobin level of 80% or more.

Two cases (4 and 7) showed a leukaemic picture

TABLE 2
BLOOD FINDINGS

Case	Hb (g. %)	R.B.C. (millions)	W.B.C. (thousands)	Differential White Count
1	12.3	3.93	4.85	Normal
2	8.4	3.0	6.9	Normal
3	10.0	3.5	8.1	Normal
4	Initial 5.1	1.9	6.05	Normal
4	Terminal 11.3	3.92	8.0	Normal
5	Initial 8.5	3.48	151.0	Abnormal—leukaemic picture
5	Terminal 12.5	4.5	10.6	Polymorph response
6	9.0	3.8	6.5	Normal
7	Initial 12.0	4.85	7.3	Normal
7	Terminal 8.4	2.5	18.65	Abnormal lymphocyte response—leukaemia
8	8.4	3.64	8.7	Normal
9	8.0	3.9	18.0	Normal
10	11.4	4.2	2.8	Normal (x-ray therapy)
11	10.0	4.4	8.5	Normal
12	13.5	5.1	8.3	Normal

Hb = Haemoglobin.
R.B.C. = Red blood count.
W.B.C. = White blood count.

after a relatively short time. The bone-marrow biopsy in the latter was not, however, typical of acute leukaemia. This phenomenon of transformation does not necessarily negate a diagnosis of lymphoblastoma, having been previously observed by Custer and Bernhard (1948) and by Warthin (1931). The latter noted leukaemic transition in nine of 134 cases of lymphosarcoma, and observes that mycosis fungoides, of which Case 4 might be a variety, could become leukaemic terminally. Fraser (1925), however, demonstrated mycosis fungoides as a type of lymphosarcoma.

Table 1 shows that the course was fulminant in many cases, though full information on this point is lacking in view of the incomplete follow-up. However, of those where definite information was available, the majority were dead, in spite of treatment, in six months, and in five cases the disease was fatal in four months or less.

Treatment

Radiotherapy was tried in all cases, except in Case 12, where only simple excision was used. In addition, Case 7, and Cases 1 and 10 received

T.E.M. (tri-ethylene-melamine) and nitrogen mustard therapy respectively. The response was disappointing, though temporary benefit was occasionally seen.

Summary

Twelve cases of lymphoblastoma in children are presented; none was thought to be of the Hodgkin variety. The symptoms and physical signs are seen to be protean, and in some cases bear no relation to widespread anatomical lesions. The process in the majority is rapidly fatal. The difficulties of diagnosis are discussed, the initial picture being misleading, here varying from actinomycosis of the jaw, tuberculous peritonitis, and benign lesion of the caruncle, to scrofula.

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