TERATOMATOUS CYSTS WITHIN THE VERTEBRAL CANAL¹

OBSERVATIONS ON THE OCCURRENCE OF SEX CHROMATIN

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Among the space-occupying lesions within the vertebral canal, intradural extramedullary cysts of abnormal developmental origin are uncommon. In this paper, we report the occurrence of such a cyst in a young girl and review comparable lesions, cited in the literature, which caused symptoms similar to those in our case. In addition, observations are described on the presence of nuclear sex chromatin (Barr-chromatin) in the cells of such cysts and the significance of this finding with reference to the nature and origin of some of these cystic structures.

CASE REPORT

A 6-year-old girl was admitted to the Neurological Unit, Boston City Hospital, in March 1955 because of pain in the back of the neck for four days. The pain had started suddenly without known preceding trauma. Episodes of relative comfort alternated with bouts of severe pain in the neck and upper back. There was no weakness of the arms, no gait disturbance, and no difficulties with bowel or bladder.

The past medical history, growth and development, family history, and review of systems were normal.

Physical examination on admission revealed an alert, well-built girl with normal vital signs. The child appeared anxious and uncomfortable, complaining of diffuse pain in the posterior part of the neck with the midscapular region and the inferior lateral portion of the right scapula as the areas of severest spontaneous pain. The pain had no definite pattern of radiation. The head was held stiffly, retracted and rotated to the right.

General physical examination was unremarkable.

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The cranium and cranial nerves were normal. There was no tenderness over the vertebral spinous processes. The patient resisted any attempt to active or passive motion of the cervical spine because of pain; attempted flexion of the neck caused considerable distress.

The gait was abnormal with unsteadiness, absent associated movements of the arms, an increased lumbar lordosis, and a thoracic scoliosis with convexity to the left. There was some dragging of the right foot with circumduction. Muscle strength appeared considerably reduced in the right hand and fingers, right foot and toes, with weak dorsiflexion at right ankle and wrist. The right arm could not be raised above the shoulder level because of pain. There was normal resistance to passive movement in the extremities. The deep tendon reflexes were all present, somewhat more active on the right side. The abdominal reflexes were present. There was no ankle clonus. The plantar response was extensor on the right and flexor on the left. No abnormalities were found on sensory examination; there was no evidence of meningeal irritation, rectal, or urinary difficulties.

Radiological studies of the chest and skull were normal. The cervical spine showed loss of the normal curvature, the odontoid process was in the normal position, and there was no evidence of fracture. There was no evidence of anterior or posterior spina bifida.

The following laboratory studies were normal: urine analysis, haemoglobin, white blood count and differential count, sickle cell preparation, sedimentation rate; Hinton, tuberculin skin test. The throat culture grew beta haemolytic streptococci.

Results of three lumbar punctures during the patient's hospital stay gave the results shown below.

Manometric studies during the third lumbar puncture were normal; flexion of the neck during this procedure, however, was limited because of pain. Cultures of the spinal fluid were negative.

Hospital Day	Opening Pressure	Closing Pressure	Fluid	Polymorphs	Lymphocytes	Pandy Reaction	Protein (mg. %)	Sugar (mg. %)
1	200	115	Clear	0	2	Negative	12	60
5	150	100	Clear	0	3	Negative	11	68
11	150	150	Clear	1	2	Negative	13	62

During the patient's first week in hospital, the right-sided weakness progressed to a hemiplegia with increased deep tendon reflexes and an extensor plantar response. At no time could a sensory defect be demonstrated. Gradually, during the remainder of the hospital stay, the right hemiplegia cleared and the child was discharged on the twenty-ninth hospital day with minimal residual weakness. The back pain had slowly diminished until the tenth hospital day when the child was free of pain. Follow-up examinations during the next half year gave consistently normal findings on general physical examination and neurological evaluation. There was no evidence of weakness or muscle atrophy and the plantar responses were flexor bilaterally. There was no complaint of pain and the child led a normally active life.

The patient was not seen again until June 1958 when she was admitted for the second time with pains in the upper back, both shoulders, and left wrist of approximately two weeks' duration. The pain was severe with brief episodes of amelioration; there was no relief from salicylates. On this second admission, the patient was afebrile and the general examination was normal. The child complained of severe pain in both shoulders and upper back. There was also some pain in the left wrist. The neck was held stiffly and any attempt to flex or

extend it was vigorously resisted. Palpation of the axillae and the right scapula evoked severe pain. Muscle strength in arms and legs was normal. There was no muscle atrophy, local swelling, heat, redness, or tenderness on percussion of the vertebral spinous processes. The gait was unsteady without evidence of weakness. There was a thoracic scoliosis with the convexity to the left and an increase in the lumbar lordosis. The deep tendon reflexes and superficial reflexes were normal. The plantar responses were flexor. There were no abnormalities on sensory examination. The clinical picture did not change until the sixth hospital day when weakness developed in the left hand. On the seventh day, the deep tendon reflexes were symmetrically hypoactive in the arms and hyperactive in the legs. The plantar responses were extensor for the first time since admission and there appeared to be diminished sensation to pinprick below the nipple line and along the distribution of the C8 dermatome of the left hand. Shortly afterwards, weakness developed in the left leg and the weakness of the left arm became complete and more severe.

Laboratory work on admission gave normal results for urine analysis, haemoglobin, white cell count, throat culture, and tuberculin skin testing. A lumbar puncture on admission revealed an opening pressure of 140 and a

FIG. 1. Photomicrograph of section of one of the cysts from the case of this report. Fibrous cyst wall with columnar and rarely pseudostratified epithelium. Occasional papillary folds. (Haematoxylin and eosin $\times 54$.)

FIG. 2. Same as Fig. 1, showing columnar epithelium with ciliated cells. (Haematoxylin and eosin $\times 540$.)

closing pressure of 100. The fluid was clear and did not contain cells; the Pandy reaction was faintly positive and the total protein was 53 mg. %. The sugar content was 50 mg. %. Smear and culture were negative. Manometric studies gave normal results. A repeat lumbar puncture on the tenth hospital day, at the time when the patient had developed a left hemiplegia in addition to weakness of the right leg, showed a pressure varying between 240 and 210. The fluid was slightly xanthochromic. There were no cells; the Pandy reaction was positive and the total protein was 220 mg. %. The sugar content was 50 mg. %. Smear and culture were negative. Manometric studies showed the presence of a complete block, which a myelogram localized at the level of C6.

A laminectomy of the cervico-dorsal region was performed on the tenth hospital day. The cord was found to be compressed at the level of C5 and C6 by three separate, transparent leptomeningeal cysts, displacing the cord dorsally and laterally, left to right. The grape-like cysts were each about 10 to 15 mm. in diameter. They appeared to originate from the inner aspect of the dural membrane, and were not attached to the cord. The cysts were removed.

The post-operative course was uneventful and the patient rapidly returned to a normal neurological status and the pain disappeared. Post-operative studies of the

lumbar spinal fluid gave normal findings. Regular clinical follow-ups during the three years after laminectomy showed the child to be free of complaints and to have a normal general and neurological examination.

Microscopic examination of the cysts removed at operation showed a uniform appearance throughout. The cyst wall was thin and composed of fibrous tissue without recognizable smooth muscle. The epithelium was of a single-layered tall columnar type with rare ciliated cells (Figs. 1 and 2). Many epithelial cells contained fine granules which stained with P.A.S. and Alcian blue as though composed of mucoproteins. In some areas, small papillary folds projected into the lumen of the cyst; in others, the more prevalent epithelium was replaced by a flat type. This had the appearance of squamous epithelium with rare intercellular bridges and it was interpreted as representing squamous metaplasia. Keratin was not present. The fibrous and epithelial cells contained typical sex chromatin bodies.

DISCUSSION

Comparable intradural extramedullary cystic structures within the vertebral canal have been reported by Kubie and Fulton (1928), Hosoi (1931), Puussepp

TABLE I

Author(s)	Sex	Age in Years at First Symptoms	Age in Years at Operation	Location to Spinal Cord	Extent	Attachment of Cyst
Kubie and Fulton Case 1	M	2 2/12	2 5/12	Dorsal	D9-L1	Spinal cord
Kubie and Fulton Case 2	F	2 6/12	27	Dorsal	C3-C4	Spinal cord
Hosoi	M	Childhood	24	Dorsal	L2-L3	Spinal cord
Puussepp	M	5	27	Dorsal	C3	Dura
Bucy and Buchanan	M	1 4/12	2 10/12	Dorsal	D11-L4	Spinal cord
Masten	F	5	5	Dorsal	C4-D1	Spinal cord
Adams and Wegner Case 1	M	28	41	Dorsal	D10-L2	Spinal cord
Adams and Wegner Case 2	M	23	29	Dorso-lateral	C4	Dura
Harriman	M	5	20	Ventral	D3-D4	Dura
Adams	M	28	33	Ventral	C4-C5	Pia
Present case	F	6	9 3/12	Ventral	C5-C6	Dura

(1934), Bucy and Buchanan (1935), Masten (1940), Adams and Wegner (1947), Harriman (1958), and Adams (1960). Some pertinent features of these cases have been summarized in Table I. Despite differences in the histology of the individual cysts, their main clinical manifestation was uniformly that of intermittent spinal cord compression. The virtual complete clearing of signs and symptoms between these episodes of neurological disease could account for the often long interval between first symptoms and operation. The majority of the cysts have been found dorsal or dorso-lateral to the spinal cord; in our case the cysts were located ventral to the spinal cord and this was true in the cases of Harriman (1958) and Adams (1960). Radiological findings in the cases cited were limited to widening of the vertebral canal and thinning of pedicles at the respective levels of the vertebral column.

Histologically, the lining of the cysts was most commonly composed of a simple low cuboidal to high columnar ciliated epithelium with areas of pseudostratified epithelium interspersed. The cyst walls and, when present, a mural nodule, have been shown to contain either collagenous fibrous tissue only or, in addition to it, other tissues such as smooth and striated muscle, mucous and serous glands, cartilage, bone, myelinated fibres, fat cells, paccinian corpuscles, ganglion cells, and glial tissue.

The varied nomenclature for these cysts reflects the uncertainty regarding their nature and origin. Kubie and Fulton (1928) called the lesions 'teratomatous cysts' and regarded them as 'ependymal diverticula of the central canal of the spinal cord'. Hosoi (1931) and Bucy and Buchanan (1935) spoke of the 'teratoid', *i.e.*, of bidermal origin, lacking elements of the third germinal layer, the endoderm. It is now agreed, however, that in the reported cases, elements of endodermal origin were present and that the term 'teratoid' should be avoided (Willis, 1953). Puussepp (1934), Masten (1940), and Adams and Wegner (1947) spoke of 'teratomas'. Harriman (1958)

referred to 'intraspinous enterogenous cysts' and Rhaney and Barclay (1959) discussed this group under the heading 'cysts of endodermal structure'. The principal difference of opinion as to the nature and origin of the cysts under discussion was well expressed by Bucy and Buchanan (1935), who concluded that the structures 'are probably not to be explained by a simple embryological malformation such as gives rise to dermoid and epidermoid cysts, or congenital dermal sinuses', but that they probably arose from a maldevelopment of the ovum, the misplacement of some multipotential germinal cells early in embryonic development'.

In recent publications (McLetchie, Purves, and Saunders, 1954; Knight, Griffiths, and Williams, 1955; Bentley and Smith, 1960) attempts have been made to define a common pathogenic mechanism for a group of congenital anomalies involving, in varying degrees of severity, combined midline defects of the vertebral column, spinal cord, and meninges, mediastinal, intestinal, and genito-urinary structures, and the superficial tissues overlying the neuraxis. Prominent among these theories is the one stressing that early in embryonic life the anlage of the notochord (notochordal plate) becomes, for a brief period of time, part of the roof of the anlage of the primitive gut; this process is called 'incalation' (Fallon, Gordon, and Lendrum, 1954). Subsequently, the notochordal plate separates again from the endoderm ('excalation') to form the notochord between neuroectoderm and primitive foregut. Incomplete or faulty excalation is thought to lead to diverticula or cysts of endodermal nature in addition to abnormalities of the vertebral column, the formation of which is dependent on the notochord.

Another theory postulates the persistence of adhesions between neuro-ectoderm and endoderm after the close contact between these two layers early in embryonic life; this contact is normally completely broken (Bentley and Smith, 1960). Such adhesions

are thought to form an obstruction in the path of the cephalad growing notochord leading to a cleft in this structure ('split notochord') in addition to inclusion of endodermal elements within parts derived from ectodermal and mesodermal layers.

Rhaney and Barclay (1959) have re-evaluated these theories of abnormal separation of germ layers in early embryonic development and conclude that the origin of those enterogenous cysts within the vertebral canal, that are located ventral to the spinal cord, can be explained by these theories, even in the absence of concomitant anomalies of the vertebral column itself. In contrast, however, cysts found dorsal to the spinal cord are thought to be 'analogous with dermoid cysts within the vertebral canal and are really congenital malformations, or heterotopias' and not teratomas. To explain the presence of derivatives of the endoderm in the dorsally-located cysts, Rhaney and Barclay offer the suggestion 'that the ectoderm of the primitive streak is probably capable of forming both endoderm and paraxial mesoderm, and if this be so, then detachment of cells from Hensen's node during its caudal migration could well be the origin of these cysts'.

The alternate hypothesis that cysts of this nature arise in a teratoma-like fashion has been advanced previously (Bucy and Buchanan, 1935); this theory postulates that germ cells displaced toward the midline during their migration from the endoderm to the gonadal ridges subsequently either remain dormant or resume proliferative activity through haploid division and endomitosis or fertilization of locally derived gametes. At present, this is a plausible way to account for the occurrence of teratomas in the midline of such structures as brain and mediastinum. The lack of representation of all germ layers in such tumours is not necessarily evidence against their origin from primordial germ cells. Thus, the common ovarian 'dermoid' (cystic teratoma) often contains only derivatives of skin anlage but must still be considered to have arisen in a way similar to the tumours of a more complex composition.

Determination of nuclear sex by the method of Barr (1959) has advanced the knowledge of the nature and origin of teratomas. The original observations of Hunter and Lennox (1954) that the cells of teratomas in women always contain sex chromatin while the cells of teratomas in males may or may not have it, have been repeatedly confirmed. We have attempted similar 'sexing' of the cysts under discussion. It is clear that for this purpose only tumours occurring in males can be of help.

Through the courtesy of the respective authors, microscopic slides have been examined of the following cases previously reported: Adams and Wegner, cases 1 and 2 (1947), Harriman (1958), and Adams

(1960); the descriptions of these patients are not repeated here. The results of nuclear sex determination in these cases and the case of this report are summarized in Table II.

TABLE II

RESULTS OF NUCLEAR SEX DETERMINATION OF FOUR CYSTS PREVIOUSLY REPORTED IN THE LITERATURE AND OF THE ONE DESCRIBED IN THIS PAPER

Author(s)	Sex of Patient	'Sex' of Cyst
Adams and Wegner (1947)		
Case 1	Male	Female
Case 2	Male	Female
Harriman (1958)	Male	Male
Adams (1960)	Male	Male
Present case	Female	Female

The cells of the cysts reported by Harriman (1958) and by Adams (1960) were clearly chromatin negative. Many cells of the epithelial lining of the cysts described by Adams and Wegner (1947) were chromatin positive (Fig. 3). An accurate count of the percentage of cells containing nuclear sex

FIG. 3. Epithelial cells in Case 1 of Adams and Wegner (1947). Typical nuclear sex chromatin body of cell in centre (arrow). Other arrows point to sex chromatin, slightly out of focus, in the other cells. (Haematoxylin and eosin $\times 1,900$.)

chromatin was not possible because of the thickness of the sections available for examination. In Case 1 of Adams and Wegner (1947), the cyst wall consisted of elements resembling bronchus; nuclear sex chromatin was present in epithelial and smooth muscle cells but it was not found in the cells of cartilage and adjacent fibrous tissue. The cyst of the second case of Adams and Wegner (1947) was lined with keratinizing squamous epithelium, glandular and ciliated columnar epithelium. In this case too, nuclear sex chromatin was only present in the cells of the epithelial tissues; the chromatin negative surrounding tissues in both cases probably represented 'host' tissue. The second patient of Adams and Wegner (1947) was examined by us in 1961, 15 years after the operation for intraspinal cyst. The physical examination in general was normal; the testes were of normal size, the pattern of pubic and axillary hair was normal, and there was no gynecomastia. The cells of a buccal smear preparation of this patient were chromatin negative.

Because the cells of the fibrous capsular tissues in these cysts did not show nuclear sex chromatin in contrast to the chromatin-positive cells of their epithelial lining, a teratomatous nature of the cysts has to be considered. The first patient had no clinical evidence of Klinefelter's syndrome at the time of operation and the second patient showed no clinical or cytological features of this syndrome. The only alternative could be to consider heteroploidy of the tissues examined; this is currently thought to be rarely the cause of chromatin-positive nuclei in the cells of malignant tumours in males (Moore and Barr, 1957). Clinically and histologically, there was no evidence of malignant behaviour of the structures under discussion.

To our knowledge, this is the first time that an attempt has been made to determine the nuclear sex of the cells of spinal teratomatous cysts and the suggestion is made that comparable tumours in the future be studied in a similar manner. Only when

the true chromosome complement, determined by tissue culture, in a number of such tumours becomes known, will it be possible to suggest the true origin of these interesting structures.

SUMMARY

The occurrence of intradural extramedullary cysts in a young girl is described. Comparable cases from the literature have been reviewed.

Observations are reported on the significance of the presence of nuclear sex chromatin in the cells of such cysts for the understanding of their nature and origin.

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