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BIOCHEMICAL AND AUTORADIOGRAPHIC STUDIES IN A CASE OF FULMINANT, METASTATIC CHONDROSARCOMA UNSUCCESSFULLY TREATED WITH ^{35}S-SULFATE

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In two recent papers in this journal (Boström et al. 1968a, b) the need for new methods of treatment of chondrosarcoma was discussed and the principles of therapy with ^{35}S-sulfate outlined. One of these papers dealt with the *in vitro* incorporation of ^{35}S-sulfate in samples from two surgically removed chondrosarcomas of long bones. The other paper described a case of chondrosarcoma, with pulmonary and skeletal metastases, occurring after hemipelvectomy, in which ^{35}S-treatment was successfully applied.

The purpose of the present paper is to report another case of chondrosarcoma treated with the same isotope. In this case, which had a fulminant course, ^{35}S-therapy was instituted as a last resort and was unsuccessful. However, because of the detailed biochemical and autoradiographic observations, we believe that a separate presentation of the case is warranted.

CASE REPORT

Male, 43 years of age. Previous history of periods of low back pain necessitating brace-treatment for immediately preceding 3 years. In April 1966 pains along the left iliac crest radiating to the lower left part of the abdomen. Increasing pains both on weight-bearing and at rest, and a slight swelling of the soft tissues in the proximal-medial part of the left gluteal region brought the patient to examination. In May 1966 roentgenological examination showed an irregular osteolytic lesion in the medial and cranial part of the left iliac bone. At a control in July 1966 this lesion had grown considerably (Figure 1). A biopsy was then performed. At

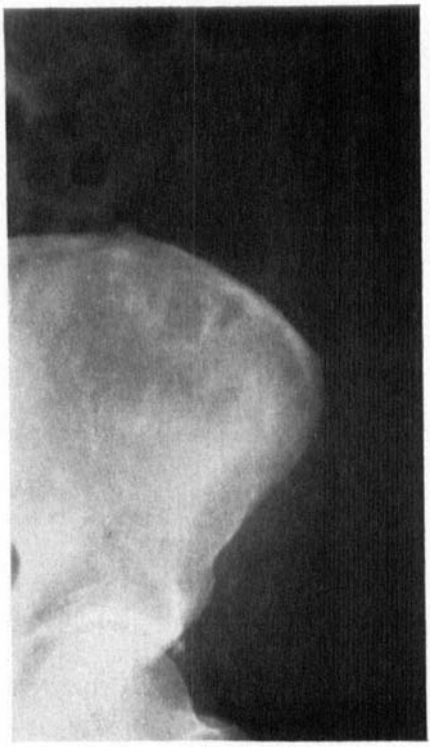

Figure 1. Osteolytic destruction in the upper part of the left iliac wing, showing the size of the chondrosarcoma in July 1966.

operation an egg-sized, soft tumor was found adhering to the exterior part of the left iliac bone. The same soft, grayish tissue also grew in the cystic lesion of the bone. The histologic diagnosis was *chondroma.* The patient was discharged, but asked to return for checkups.

In August 1966 the pains again increased, now also radiating into the left thigh. Paresthesia developed in the left leg. The severe pains resulted in an almost fixed flexion contracture of 45 degrees of the left hip. There was also a recurrence of the tumor, which had a diameter of about 15 cm, protruding into both the pelvis and the left gluteal region. Another biopsy was performed in September 1966. The histologic diagnosis was now *chondrosarcoma;* and the patient was referred to the Department of Orthopedic Surgery, Norrbackainstitutet.

On palpation the tumor was found to extend into the lower left part of the abdomen and the left gluteal region, continuing almost up to the twelfth rib on the left side. Roentgenological examinations showed marked destruction of the left iliac bone (Figure 2), and protrusion of the tumor in accordance with the clinical findings (Figure 3). The left ureter was dislocated almost to the mid-line of the pelvis. The left colon and the left common iliac vessels were also dislocated medially. There were no signs, however, of tumor infiltration into the structures examined, the tumor apparently having an encapsulated growth. No metastases were observed either clinically or roentgenologically.

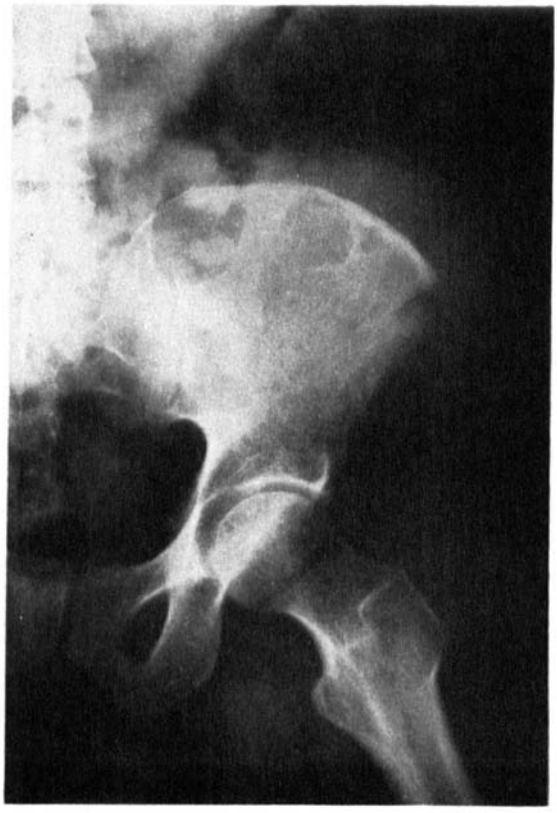

Figure 2. Marked progressive destruction of the iliac bone, especially in the region of the anterior superior iliac spine in Sept. 1966.

In the middle of September 1966 a left hemipelvectomy was performed. At operation the encapsulated growth of the tumor was confirmed. Removal of the huge tumor was considered radical, as judged by macroscopic and microscopic examinations. The osteotomies were done through the left sacro-iliac joint and close to the symphysis. Because of the expansion of the tumor the gluteus maximus muscle had to be removed. When suturing the soft tissues of the stump, this defect was closed by a tantalum net. The histologic diagnosis of chondrosarcoma was confirmed.

The postoperative course was complicated by anemia, which could not be fully corrected by blood transfusions. Moreover, the patient developed pains in the lower part of the thoracic cage of both sides. On 2 November 1966, multiple pulmonary metastases were demonstrated at roentgenologic examination (Figure 4). The general condition of the patient was poor. Obviously, the prognosis was unfavorable; and it was decided to make a last effort to stop the progression of the tumor by treatment with ^{35}S-sulfate. The patient was therefore transferred to the metabolic ward of the Medical Clinic at the Serafimer hospital. On 21 November a last roentgenologic examination was made prior to initiation of ^{35}S-treatment.

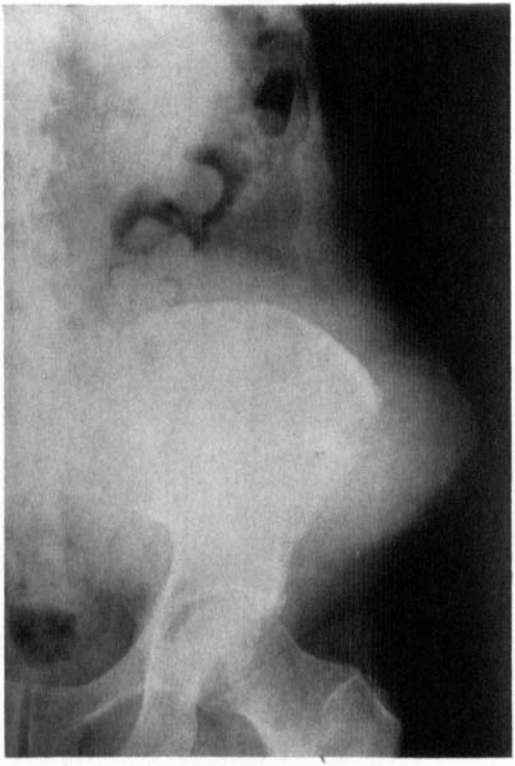

Figure 3. Roentgenogram to show the size of the expanding tumor growing into the soft tissues both medially and laterally to the iliac bone, cf. Figure 2.

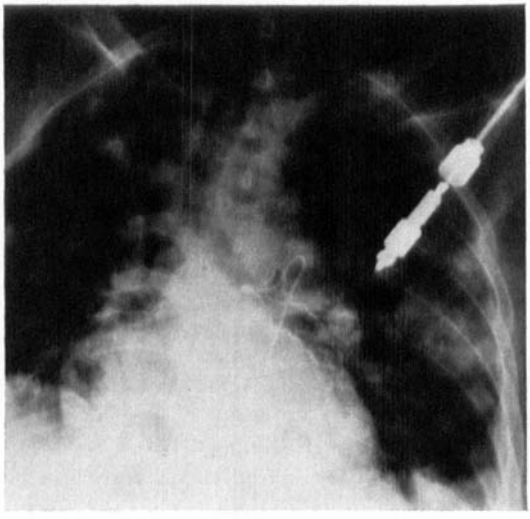

Figure 4. Roentgenogram showing the catheter placed in position for administration of radiosulfate in the bronchial arteries. Vessels visualized by injection of a few ml of contrast solution. Multiple metastases in both lungs. 24 Nov. 1966.

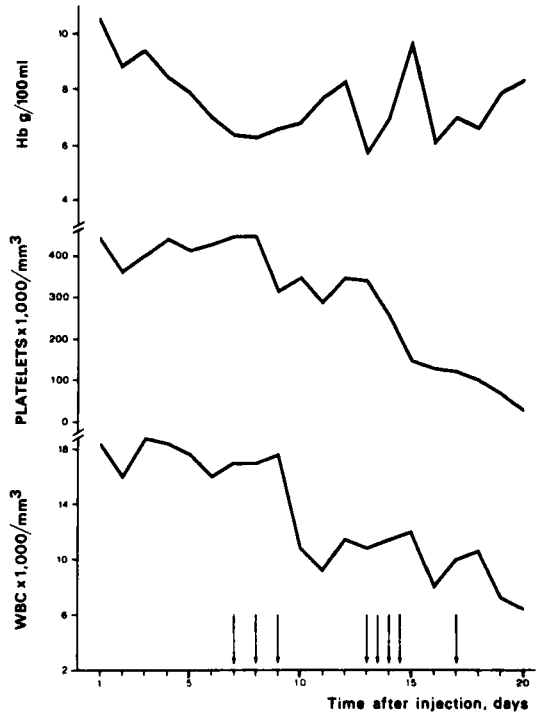

Figure 5. Levels of hemoglobin, platelets, and white blood cells after administration of a single dose of radiosulfate. Arrows indicate blood transfusions.

This examination showed an increase in both the number and the size of the pulmonary metastases.

The isotope was administered on 24 November in the following way[1]: A catheter was introduced into a femoral artery and placed in the aorta with its tip in the bronchial artery. The correct position of the catheter was checked by the injection of a few ml of contrast solution (Figure 4). In all, 406 mC of ^{35}S were administered, as carrier-free $Na_2{}^{35}SO_4$ in 12 ml of saline, through the catheter by the rapid injection of 2 ml portions. After the last dose had been given the position of the catheter was checked once more by means of contrast solution; it was found to be in its initial position.

A pulmonary roentgen examination on 1 December did not show any change in the metastases. At this time, however, there was a recurrence of the primary tumor, which could be palpated in the abdomen. The size of the tumor rapidly increased during the two weeks that the patient remained alive.

Thus, the patient's general condition steadily deteriorated. He ran a fever of septic type with peaks up to 39.5° C. Repeated cultures on blood and urine were always negative. However, intravenous treatment with 12 g methicillin daily, as well as 1 g streptomycin sulfate i.m. daily, was started on 28 November on the

[1] The same procedures were used as outlined by Boström et al. (1968b), for the handling of the radioactive material and the management of the patient.

basis of the cultures made on secreta from the partly unhealed surgical wound. The antibiotic treatment was combined with the daily administration of 200 mg hydrocortisone acetate. This treatment slightly reduced his fever, but could not prevent the fatal outcome on 14 December.

The thrombocyte count was around 400,000/mm^3 at the start of ^{35}S-treatment, but decreased rapidly during the last days before death, and on 14 December it was 25,000/mm^3 (Figure 5). Concomitantly, the white blood cell count fell from 18,000 to 6,300/mm^3. The hemoglobin level declined rapidly until the institution of transfusion therapy, and was then maintained at about 8 g/100 ml.

Autopsy showed the presence of an enormous, extraperitoneal tumor mass expanding in all directions from the left lateral part of the sacrum. Its weight was estimated at 7 to 8 kg. Several metastases of varying sizes were found in the pleurae, lungs, kidneys, and cerebrum including the choroid plexus. Metastatic growth also occurred in mesenteric vessels with segmental infarction of the ileum.

EXPERIMENTAL

Histologic and Autoradiographic Studies

Specimens were taken at autopsy—in addition to those withdrawn for routine histopathological examination—from the extraperitoneal tumor mass and from lungs, kidneys, adrenal, and brain. Tissues were fixed in alcohol-formalin (3 + 1 parts) and embedded in paraffin. Semiserial sections were cut at 5 μm and mounted on glass slides.

Coated autoradiograms were prepared by a modification of the Messier & Leblond (1957) method. Ilford K5 nuclear emulsion was used, diluted with two parts of water. Exposures lasted from 8 to 86 days. The autoradiograms were developed in Kodak D19b, coverslipped, and examined by light and by phase-contrast microscopy, with qualitative evaluation of density.

The autoradiograms were stained with hematoxylin and eosin or with toluidine blue. In addition, some uncoated slides were stained with various connective tissue stains.

The histologic examination showed that the recurrent, extraperitoneal tumor was a moderately to rather highly differentiated chondrosarcoma. It had the same appearance as the tumor material examined after the hemipelvectomy and at the preceding biopsy. The greater part of the tumor was composed of rounded areas with abundant metachromatic matrix of a myxomatous to chondroid appearance. These "areas" were delineated by strands of connective tissue with a fibrous matrix, sometimes forming rather solid capsules. In the connective tissue small clusters of tumor cells occurred with a scant, mostly non-

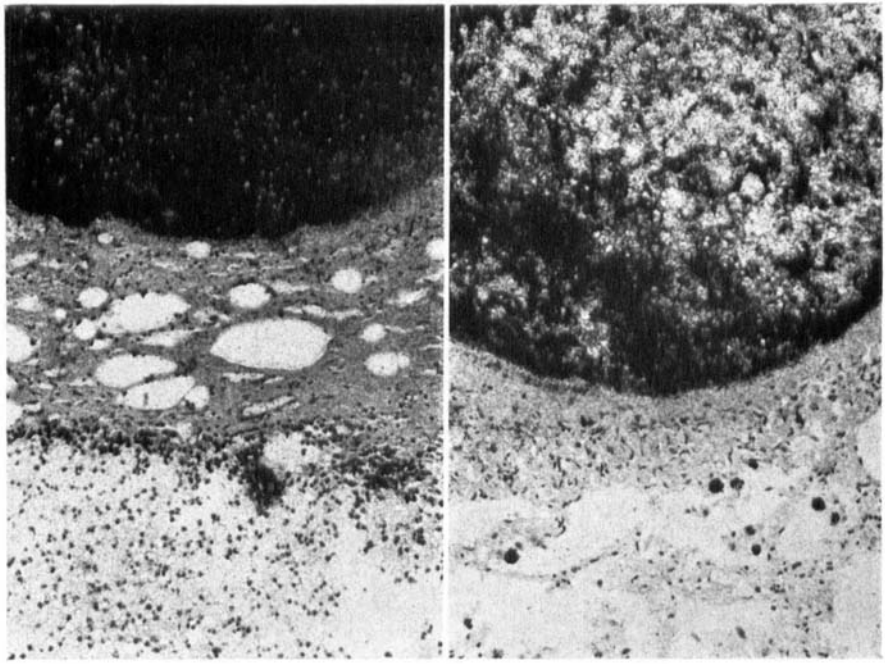

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Figure 6. Coated autoradiograms, exposure 86 days, hematoxylin and eosin. A: Recurrent tumor, × 200. Intense ^{35}S-activity in tumor "area" (top); no activity in connective tissue strand (center) or in—presumably newly formed—"area" (bottom). B: Lung, × 200. Intense ^{35}S-activity in metastatic "area" (top).

metachromatic, matrix. Formation of intramembranous bone was observed in some sections. Necrotic "areas" were occasionally noted.

Metastases with similar histologic appearance were found in the lungs, kidneys (Figure 7A), cerebrum, and choroid plexus; there were no metastases in the adrenals. Osteogenesis did not occur in the metastases.

In the autoradiograms of both recurrent tumor and metastases, moderate to strong ^{35}S-activity was observed in the greater part of the above-mentioned metachromatic "areas" (Figures 6A, 6B and 7B). This occurrence of the isotope contrasted strikingly with the very low ^{35}S-activity that was observed in normal bronchial cartilage present in some of the lung sections. The isotope was predominantly located in the matrix. The distribution within the "areas" varied from one "area" to another. Frequently, the ^{35}S-activity was most marked in the center of an "area", diminishing towards the periphery. In other "areas" the

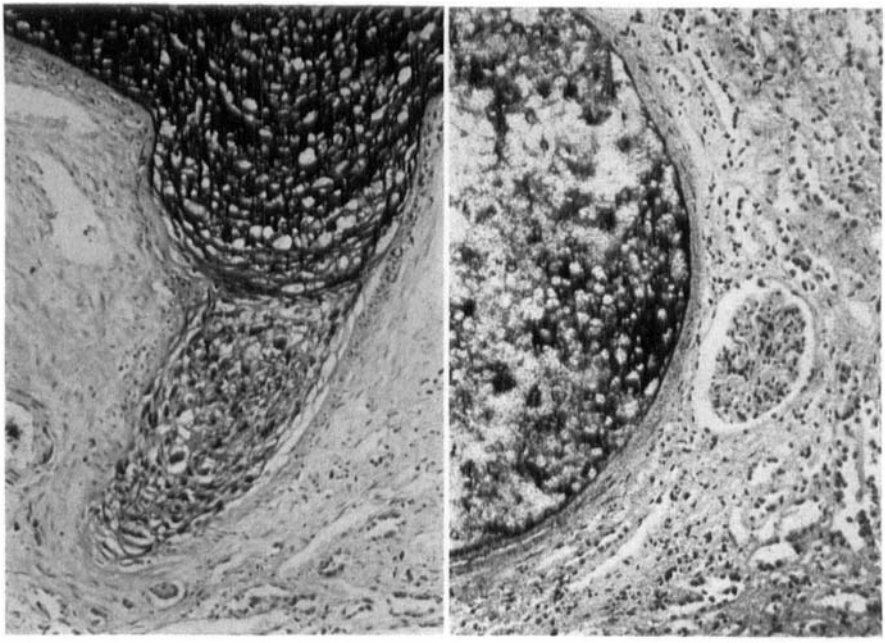

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Figure 7. A: Kidney, × 200. Marked toluidine blue metachromasia in tumor "area" (top). A non-metachromatic cell nest has broken through the thin capsule (center). B: Kidney, × 200. Coated autoradiogram. Varying ^{35}S-activity in metastasis (left). Note distinctly intercellular location of the radioisotope. Exposure 86 days. Hematoxylin and eosin.

radioactivity was distributed in a spotty or streaked manner. Like most of the cell clusters in the connective tissue, some "areas" were nonradioactive. In the connective tissue matrix ^{35}S-activity was low.

Biochemical Analyses and Radioassays

Analysis of tissue samples. Specimens of 5 to 100 g wet weight were obtained at autopsy from normal lung and rib cartilage, from the recurrent tumor mass, and from metastases in the lungs and cerebrum. The cartilage was cut into small pieces. Soft tissues were homogenized in a Virtis homogenizer. The different preparations were then dried with acetone and kept as dry powder at + 4° C for further studies.

For the radioassays 1 mg of the dry material, weighed on a Cahn microbalance, was digested with pronase.[1]

[1] Calbiochem, Los Angeles, Cal., U.S.A.

Table 1. Chemical analyses and radioassays of tissue samples.

Tissue	Total N % of dry weight	Hexosamine N % of total N	Hexosamine % of dry weight	CPM/mg dry weight	CPM/μmole hexosamine	Uronic acid % of dry weight	Hexosamine/ uronic acid
Rib cartilage	11.8	5.85	8.8	27	54	2.0	4.4
Recurrent tumor	11.8	3.47	5.3	283	949	1.53	3.5
Normal lung tissue	12.0	1.42	2.2	12	90	0.56	3.9
Pulmonary metastasis I	11.5	2.96	4.3	95	394	2.8	1.5
Pulmonary metastasis II	11.8	1.95	2.9	105	644	1.6	1.8
Brain metastasis I	7.2	1.11	1.0	17	304	0.3	3.3
Brain metastasis II	7.5	1.06	1.0	20	358	0.42	2.4

Complete solubilization of the material was obtained. Aliquots from the digested samples were plated and counted at infinite thinness in a Geiger-Müller counter with an 1.9 mg/cm^2 end-window tube. Radioactivity was expressed as counts per minute (cpm) per mg of dry tissue.

Total nitrogen of the various samples was determined according to Kjeldahl's micro method, total hexosamines according to Elson & Morgan (1934), and uronic acid according to Dische (1947).

The results of the above-mentioned analyses are presented in Table 1. The hexosamine content of the recurrent pelvic tumor was almost two-thirds of that of rib cartilage, whereas the hexosamine content of pulmonary metastases was markedly increased compared with that of normal lung tissue. The radioactivity of the recurrent tumor, expressed as cpm per mg of dry tissue, was about ten times that of rib cartilage, and about 18 times greater when expressed as cpm per μmole of hexosamine. In comparison with normal lung tissue, the corresponding values for lung metastases were respectively from eight to nine times and from four to seven times greater.

Fractionation of glycosaminoglycans. In order to determine the incorporation of the isotope into individual glycosaminoglycan fractions, a 20 mg sample of acetone-dried powder from the recurrent tumor was digested with papain in a 2 ml volume, according to Antonopoulos et al. (1964). The hexosamine content in 100 μl of the digest, determined according to Boas (1953), was found to be 37.8 μg, corresponding to a hexosamine content of 3.8 per cent on a dry weight basis. This

Table 2. Fractionation of the glycosaminoglycans from the recurrent tumor on cetylpyridinium chloride-cellulose columns.

Fraction	μg hexosamine	% of total	CPM	% of total	CPM/μmole hexosamine	Corresponds to
1 % CPC	13.4	40.2	60	10.7	—	Glycoproteins and keratan sulfate (?)
0.3M NaCl	6.1	18.6	20	3.6	—	Hyaluronic acid
0.6M $MgCl_2$	12.1	36.8	427	76.8	6300	Galactosaminoglycans
6M HCl	1.4	4.4	50	8.9	1146	?
Total	33.0		557			

100 microliters of tissue digest was applied to each column. The columns (5 × 60 mm) were eluted with 2 ml of each solution. The given values are the means of three columns.

value is somewhat lower than that given in Table 1, but represents a different sample of the recurrent tumor. That considerable regional variations may occur in a chondrosarcoma, in both morphology and metabolism, is evident from the study by Boström et al. (1968a). The radioactivity of an aliquot of the same size was 578 cpm, as determined in a Packard liquid scintillation counter. For the fractionation of the glycosaminoglycans the cetylpyridinium chloride (CPC)-cellulose column technique of Antonopoulos & Gardell (1963), Antonopoulos et al. (1964), and the ECTEOLA-cellulose column technique of Antonopoulos et al. (1967) were used. Aliquots from the different fractions were taken for determination of hexosamine content and for radioassay in the liquid scintillation counter. The results are given in Tables 2–4. Hexosamine values and radioactivities indicate a recovery of approximately 90 per cent in the micro-column procedures.

For the further characterization of the glycosaminoglycan fractions a 120 mg sample from the recurrent tumor was digested with papain in a 5 ml volume according to Antonopoulos et al. (1964). The glycosaminoglycans were then fractionated and isolated by the large scale CPC-cellulose technique described by Antonopoulos (1965). The 0.6 M $MgCl_2$ fraction was subjected to infra-red analysis in KBr pellet with a Unicam SP 200 photometer. This fraction showed absorption bands characteristic of a mixture of chondroitin-4- and chondroitin-6-sulfates in about equal proportions (Mathews 1958). The fractions obtained with 0.3 M NaCl and 2 M $MgCl_2$ did not contain enough material for infra-red

Table 3. Fractionation of the glycosaminoglycans from the recurrent tumor on cetylpyridinium chloride-cellulose columns.

Fraction	μg hexosamine	% of total	CPM	% of total	CPM/μmole hexosamine	Corresponds to
1 % CPC	12.7	41.2	50	9.8	—	Glycoproteins and keratan sulfate (?)
0.3M NaCl	5.2	16.8	16	3.1	—	Hyaluronic acid
P/M*	6.1	19.8	237	46.3	6972	Chondroitin-4-sulfate
0.75M $MgCl_2$ in 0.1M HAc	5.8	18.8	189	37.0	5815	Chondroitin-6-sulfate
0.75M $MgCl_2$	0.7	2.2	16	3.1	—	—
6M HCl	0.4	1.2	4	0.7	—	—
Total	30.9		512			

100 microliters of tissue digest was applied to each column. The columns (5 × 60 mm) were eluted with 2 ml of each solution. The given values are the means of three columns.

* A mixture of propanol 40 per cent v/v, methanol 20 per cent v/v, glacial acetic acid 1.5 per cent v/v and water 38.5 per cent v/v and containing 0.4 per cent w/v of cetylpyridinium chloride.

Table 4. Fractionation of the glycosaminoglycans from the recurrent tumor on ECTEOLA-cellulose columns.

Fraction	μg hexosamine	% of total	CPM	% of total	CPM/μmole hexosamine	Corresponds to
H_2O	5.7	16.9	3	0.5	—	Glycoproteins
0.02M HCl	3.3	9.7	5	1.0	—	Glycoproteins
1.0M HCOONa	8.4	24.9	46	8.7	—	Hyaluronic acid
1.5M HCOONa	1.7	5.1	27	5.1	2828	Galactosaminoglycans
2.0M HCOONa	4.8	14.2	158	29.9	5889	Galactosaminoglycans
2.5M HCOONa	5.8	17.3	230	43.5	7088	Galactosaminoglycans
6M HCl	4.0	11.9	60	11.3	2685	Keratan sulfate (?)
Total	33.7		529			

100 microliters of tissue digest was applied to each column. The columns (4 × 40 mm) were eluted with 2 ml of each solution. The given values are the means of three columns.

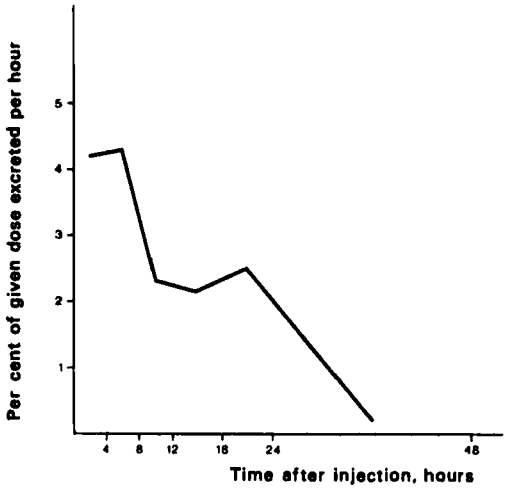

Figure 8. Urinary excretion rate of radioactivity during the first two days after injection of ^{35}S-sulfate.

analysis. Instead, glucosamine and galactosamine were separated according to Antonopoulos (1966). The former fraction contained approximately 91 per cent glucosamine, whereas in the latter fraction galactosamine accounted for approximately 94 per cent of the total hexosamine content.

Urinary radioassay. The urine was collected quantitatively by means of an indwelling urethral catheter during the 20 days that the patient stayed alive after the institution of ^{35}S-treatment. The excretion of the radioisotope into the urine was examined in samples obtained at scheduled times, as described by Boström et al. (1968b). The excretion rate was highest during the first few hours, with a maximum at about 4 hours after injection (Figure 8). About 71 per cent of the given dose was excreted in the urine during the first 24 hours after ^{35}S-injection. Another 5 per cent was excreted during the following 24-hour period. The urinary isotope recovery over the total 20-day period was 86.5 per cent of the given dose.

DISCUSSION

This case of chondrosarcoma is strikingly different in its clinical course from the one described recently (Boström et al. 1968b), which was also treated with ^{35}S-sulfate. In the latter the disease progressed slowly, which is typical of most chondrosarcomas. In the present case, the fulminant development of the malignancy rapidly caused a fatal outcome despite all therapeutic measures. This aggressive behavior

of the tumor is unusual in chondrosarcoma. The swift spread of the disease, with the emergence of multiple metastases in different parenchymatous organs, is also exceptional. Lichtenstein (1965) states that "metastases elsewhere than in the lungs are uncommon in connection with chondrosarcoma". The morphological appearance of the tumor, as shown by routine histopathological examination, did not correspond to the clinical findings. The tumor was described as a predominantly well-differentiated chondrosarcoma. In fact, the tumor was even thought to be a chondroma at the first biopsy. Thus, this case illustrates the recognized fact that the aggressive character of chondromatous tumors is often underestimated owing to their rather innocuous histologic appearance. Special caution should always be taken as regards chondromatous tumors in the pelvic bones, which are nearly always true chondrosarcoma. Hence, in such cases, radical surgery should be resorted to without delay.

The treatment with ^{35}S-sulfate was not able to stop the progressive development of the malignant disease in this case. In view of the excessive amounts of chondrosarcomatous tissue in different parts of the body this is not surprising. Moreover, in the previously described case (Boström et al. 1968b), signs of arrest of tumor growth were not evident until several weeks after institution of ^{35}S-therapy. It could be argued that the isotope treatment should have been started already at the time of the hemipelvectomy. On the other hand, the tumor was then thought to be radically extirpated both macroscopically and microscopically. Furthermore, the prognosis in pelvic chondrosarcoma treated by hemipelvectomy is not unfavorable, a 30 per cent ten-year-cure rate was reported by Troup & Bickel (1960).

Total resistance to ^{35}S-sulfate treatment was also reported by Botstein & Marcus (1963) in a case of recurrent chondrosarcoma of the facial bones, though this case was not of the same fulminant nature as the present one. Apparently there is a great need for better diagnostic criteria—clinical, histologic, and metabolic—in the evaluation of cases of chondrosarcoma suitable for ^{35}S-sulfate treatment.

Following institution of ^{35}S-treatment there was a more pronounced drop in blood corpuscular levels than in our previous case. This may represent a greater radiosensitivity of the bone marrow in the present case. At least to some extent, however, it may also reflect the rapid progression of the malignant growth.

In spite of the rather innocuous histopathological findings referred to above, the rapid growth and spread of the malignancy was evident

in the histologic and autoradiographic preparations made in this study. Although the main part of the recurrent tumor and the metastases had a well-differentiated appearance, protrusion of cell nests, through surrounding connective-tissue strands and capsules, was frequently seen (Figure 7A). In the autoradiograms there was also evidence of rapid new formation of chondrosarcomatous tissue, viz. in the marked variation in ^{35}S-activity between different tumor portions. It seems reasonable to interpret metachromatic "areas" with marked ^{35}S-activity as having been labeled at the time of the isotope injection. On the other hand, nonradioactive tumor zones, observed, e.g., in the periphery of labeled "areas" or in protruding cell nests, presumably were formed well after the injection of the isotope. It is justifiable to make such an assumption, since the ^{35}S-activity in blood—and hence the availability of the isotope—falls rapidly during the first few days after injection.

No systematic investigation on the occurrence of different mucopolysaccharides in a large material of chondromatous tumors has been reported in the literature. However, the presence of certain glycosaminoglycans has been demonstrated in a few separate cases. Meyer et al. (1956) studied two chondrosarcomata and one chordoma. One chondrosarcoma yielded chondroitin-4-sulfate as the only glycosaminoglycan, whereas the other two tumors contained only chondroitin-6-sulfate. These authors suggested that tumors of mesodermal origin produce only a single type of mucopolysaccharide. Hasegawa et al. (1961) found only chondroitin-6-sulfate in the extract of a human chondrosarcoma. The presence of chondroitin-4-sulfate, and the absence of keratan sulfate, in one human chondrosarcoma was reported by Adams (1963). Anderson et al. (1963) studied one case of human scapular chondrosarcoma. The tumor yielded chondroitin-6-sulfate as the sole mucopolysaccharide.

These investigations have thus shown that chondroitin sulfates regularly occur in chondrosarcomatous tissues. On the other hand, they have failed to disclose the presence of hyaluronic acid and keratan sulfate. However, this failure may have been due to limitations in the analytical procedures then available.

In spite of the results of the aforementioned studies, it nevertheless seems reasonable to expect the neoplastic chondrocytes to be able to simultaneously produce more than one kind of glycosaminoglycan. Mesenchymal tissues normally contain a mixture of these substances; and more specifically, both chondroitin sulfates and keratan sulfate occur in hyaline cartilage. The presence of both hyaluronic acid and

chondroitin sulfate in a case of mandibular myxoma was reported recently by Prout & Hodson (1968). The occurrence of both chondroitin sulfate(s) and keratan sulfate in a case of human chondrosarcoma was suggested by Boström et al. (1968a). Thus, the present chemical analyses were made on the assumption that the tumor might contain more than one type of glycosaminoglycan.

Because of the difficulties involved in the separation of individual glycosaminoglycans from a complex mixture, several different fractionation procedures were employed. On the basis of the analytical findings reported above, it is possible to conclude that the tumor produced the following hexosamine-containing substances: a glycoprotein fraction, hyaluronic acid, chondroitin-4-sulfate, and chondroitin-6-sulfate. The presence of keratan sulfate was suggested by the appearance of hexosamine in the 6 M HCl fraction from the ECTEOLA-cellulose column. The occurrence of keratan sulfate could also explain the difference in hexosamine content between the 1 per cent CPC fractions (Tables 2, 3), on the one hand, and the water plus 0.02 M HCl fractions (Table 4), on the other. If it is assumed that the 1 per cent CPC fractions did contain approximately 12 per cent of keratan sulfate, a specific activity of about 2440 cpm/μmole hexosamine can be calculated. This value is comparable with that of the 6 M HCl fraction reported in Table 4. Further work to establish the exact nature of the latter fraction is in progress and will be reported elsewhere. Whether or not the continued studies will confirm the presence of keratan sulfate, the findings reported substantiate the working hypothesis.

The radioactivity measurements indicated that the different samples of chondrosarcomatous tissue contained up to 10 times the amounts of ^{35}S present in normal tissues. Similar values were reported in the *in vitro* study by Boström et al. (1968a). In the individual glycosaminoglycan fractions the highest "specific activities", expressed as cpm/μmole of hexosamine, occurred in the fractions representing chondroitin-4- and chondroitin-6-sulfate. It is not possible, however, to draw any conclusions, from the radioactivity measurements, concerning the metabolic rates of the various glycosaminoglycans. This would require measurements after different intervals of time following injection.

SUMMARY

A case is described of fulminant chondrosarcoma, with local recurrence, and pulmonary, renal, and cerebral metastases occurring after hemi-

pelvectomy. The case was unsuccessfully treated with ^{35}S-sulfate. It was concluded that the failure of isotope treatment was due to the advanced growth of the tumor.

Autoradiographic studies gave evidence of rapid new formation of chondrosarcomatous tissue. Biochemical analyses indicated that this tumor produced at least three glycosaminoglycans, namely chondroitin-4- and chondroitin-6-sulfate, and hyaluronic acid.

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