

Neurologic Deterioration and Death in a 27-Year-Old Man with Chondrosarcoma

Stenographic reports of weekly clinicopathologic conferences held in Barnes and Wohl Hospitals are published in each issue of the *Journal*. Members of the Departments of Internal Medicine, Radiology, and Pathology of the Washington University School of Medicine participate jointly in these conferences. Kenneth M. Ludmerer, M.D., and John M. Kissane, M.D., are the editors of this feature.

A 27-year-old white man with metastatic chondrosarcoma was admitted to Barnes Hospital on October 11, 1981, after the sudden onset of headache, lethargy, combativeness, and left-sided hemiparesis. He died eight days later.

In November 1980, a diagnosis of chondrosarcoma of the right femoral head was made. Initial treatment consisted of a three-stage amputation with pelvic disarticulation. The patient did well until June 1981, when a routine checkup revealed several pulmonary nodules that were presumed to represent metastatic disease. Chemotherapy was begun, and the patient did well until the day of admission, when he suddenly lost function on his left side, and combativeness, lethargy, and a right-sided headache developed. There was no known head trauma, seizure activity, or loss of consciousness.

On admission, the patient was lethargic but responsive to vigorous verbal stimuli. He was oriented to person but not to place or time. The blood pressure was 152/90 mm Hg, the pulse rate 72 beats per minute, and the respiratory rate 16 per minute. There was no fever. The neck was supple and the chest, heart, and abdomen were normal. The right pupil reacted to light consensually but not directly. Funduscopic examination of the right eye revealed a bloodless right retina and a sharp disc margin. The patient exhibited denial of his left side and a right gaze preference. Examination of the cranial nerves was difficult, but the patient appeared to have a left field cut in the left eye. Extraocular movements were intact but dysconjugate, and the patient had left central facial palsy. Motor examination showed left hemiparesis with decreased sensation and an extensor plantar response on that side. The right upper extremity appeared normal.

Admission laboratory studies included a hemoglobin level of 11.1 g/dl, a white blood cell count of 11,400/mm³ with a normal differential, and a platelet count of 133,000/mm³. The prothrombin time and partial thromboplastin time were normal. The fibrinogen level was 414 mg/dl. A chest x-ray showed multiple nodules in both lung fields. A computed tomographic scan of the head was interpreted as normal both before and after contrast. Results of a lumbar puncture were normal, and results of cultures of the cerebrospinal fluid were negative. Results of blood cultures and urinalysis were also negative.

The admitting impression was that the patient had occlusions of the right central retinal and right middle cerebral arteries. The patient began to receive heparin, and seemed to improve slightly. A brain scan soon afterwards showed increased activity in the right frontoparietal region, and an electroencephalogram revealed a slow right hemisphere delta focus. On October 15, generalized tonic seizures developed that resolved after 1,050 mg of phenytoin was administered intravenously. Two hours later, the seizures recurred, requiring additional intravenous phenytoin as well as intravenous phenobarbital and dexamethasone for control. Heparin was discontinued. A repeat computed tomographic scan of the head was interpreted as showing a probable cerebral infarction in evolution in the right posterior frontal lobe, as well as generalized cerebral swelling of uncertain origin. The patient remained unresponsive and died on October 19.

CLINICAL DISCUSSION

Dr. Stuart Kornfeld: I would like to begin the discussion by asking Dr. Varki if he would describe the major clinical features of chondrosarcoma and the natural history of this disorder.

Dr. Ajit Varki: Before we discuss the literature on chondrosarcomas, let us consider a definition of the disease itself. A *chondrosarcoma* is defined by the World Health Organization as a "malignant tumor characterized by the formation of cartilage, but not of bone, by the tumor cells." However, mixed sarcomatous tumors are not uncommon; one can see areas of osteosarcoma or fibrosarcoma in an otherwise typical chondrosarcoma. In addition, pathologists agree that the differentiation between a benign and a malignant tumor of cartilage can be very difficult based on histologic appearance alone. For these reasons, we have to be careful when comparing studies from different institutions and different observers.

In most series, chondrosarcomas represent about 10 percent of all malignant bone tumors. Although usually a disease of the middle-aged, with a predilection for males, the tumor may occur at any age, in either sex. It usually arises in the pelvis, femur, thorax, or scapula, but it can occur in any bone that was embryologically preformed in cartilage and can sometimes even be extraosseous. Chondrosarcomas have been further subclassified based upon several features. *Primary chondrosarcomas* arise in previously normal bone and can occur in either the central or the peripheral (periosteal) regions of bone. *Secondary chondrosarcomas* arise in pre-existing benign lesions. Other subclassifications are based upon the histologic appearance, e.g., mesenchymal, clear cell. The presenting features usually relate to local symptoms that arise from bone invasion, pathologic fracture, or compression of vessels

and nerves. The clinical behavior is quite variable, ranging from a slowly growing, painless mass spanning a decade, to a rapidly expanding, painful, destructive lesion. Many of these tumors are cured by local resection; distant metastases are therefore relatively uncommon, usually occurring in cases that are not controlled locally. With regard to management, adequate surgical resection remains the only definitive approach. The tumor is not very radiosensitive, and although some chemotherapeutic drugs have been reported to be active, there is too little experience to allow the recommendation of any consistently reliable regimen. The survival of these patients is also variable, with median survivals from 25 to 75 percent being reported in different series [1-4].

One can summarize all that I have said so far about chondrosarcoma in one word: *variable*. Several investigators have therefore looked for factors that could predict the outcome of a given case of chondrosarcoma [5-8]. Once again, no single feature is an absolutely reliable predictor. The histologic grade of malignancy, as judged by such factors as the degree of nuclear atypia and the number of mitoses, is helpful. However, the intra- and interobserver and interinstitutional variability of such grading systems has not been rigorously tested. The adequacy and wideness of the surgical margins also seems to be of significance. However, while local recurrence is usually a bad prognostic sign, some patients can still be cured by a second resection. Tumors located on the extremities, hands, and feet appear to have a better prognosis; this appears to relate to both the histologic grade and the fact that a better resection may be possible in such lesions [9].

In summary, then, the clinical features and course of chondrosarcomas are extremely variable, suggesting that we may well be discussing a diverse group of diseases that look similar under the microscope.

Dr. Kornfeld: We can conclude, therefore, that while this patient's course was much more rapid and aggressive than is usually seen in patients with chondrosarcoma, similar courses have been described previously. The patient was initially treated with surgical excision of the tumor, but seven months later was noted to have several pulmonary nodules in a routine chest film. These were presumed to represent metastatic disease, and the patient began to receive combination chemotherapy. Over the next four months, he received three different regimens, but there was no evidence of a tumor response. However, he continued to do well until the morning of admission, when he had the sudden onset of left-sided weakness associated with a right-sided headache, combativeness, and lethargy. Dr. Saper, with this clinical presentation and the neurologic findings, where would you place the lesion?

Dr. Clifford Saper: The localization in this case is fairly

straightforward, although it is not quite as simple as it might appear at first. The patient had evidence of complete occlusion of the right internal carotid artery. The first branch of the affected artery was the ophthalmic artery, resulting in a bloodless retina and loss of sight in that eye. The next major branch of the internal carotid artery (after the anterior choroidal artery) is the anterior cerebral artery. When it is occluded, paresis is seen in the contralateral lower extremity and, if occlusion is proximal to the recurrent artery of Huebner, in the upper extremity as well. The superior division of the middle cerebral artery supplies the lateral surface of the frontal lobe, including the frontal eye fields. Interruption of blood flow in this artery causes inability to look to the contralateral side of space, explaining this patient's gaze paresis. The motor strip in the precentral gyrus and the primary somatosensory representation in the post central gyrus are also supplied by the superior division of the middle cerebral artery. Damage to these areas accounted for the paresis of the contralateral arm and face as well as the contralateral hemianesthesia. The inferior division of the middle cerebral artery supplies the lateral surface of the parietal and temporal lobes. This patient had evidence of parietal lobe dysfunction in the right hemisphere, in that he denied the left side of his body and the left side of space.

Two features in this patient's presentation increase the difficulty of localization. The patient's visual field cut might suggest involvement of the occipital cortex on the medial wall of the hemisphere, which is supplied by the posterior cerebral artery. However, the optic radiations traverse the parietal and temporal lobes and can be interrupted by middle cerebral artery infarction as well. In fact, if an obtunded patient is not paying attention to the left side of space and cannot see from his left eye, it is difficult to prove that there is a left visual field cut at all. A second problem in localization is the patient's dysconjugate gaze. However, if a patient cannot see from one eye, a latent exophoria will cause the eyes to become dysconjugate. Stuporous patients who are not focusing their vision often have dysconjugate gaze, and this is not necessarily a sign of oculomotor dysfunction.

Everything thus far fits with a sudden occlusion of the right internal carotid artery. The only problem with this localization is the patient's depressed level of consciousness. Right parietal lobe infarction has been reported to cause an acute confusional syndrome, presumably owing to the difficulty in directing attention, but a depressed level of consciousness indicates that there was also dysfunction in either the contralateral hemisphere or in the brain stem. There is other evidence that this patient had bilateral cerebral disease. On computed tomographic scan, there was apparently diffuse

swelling. With massive infarction of one hemisphere, one would expect that there would be swelling in that hemisphere and displacement of the midline toward the other side. Computed tomographic evidence of diffuse edema suggested that there was not only a right internal carotid artery occlusion but also left hemisphere ischemia as well. This could occur in one of two ways. If there was a pre-existing lesion of the left carotid system, the left hemisphere might derive a major portion of its blood supply, via the circle of Willis, from the right carotid circulation. Occlusion of the right internal carotid artery would therefore cause left hemisphere ischemia as well. However, under these circumstances the occlusion of the right internal carotid artery would cause maximal dysfunction in its most distal distribution, the left hemisphere. It is more likely that occlusive disease in the left carotid distribution also simultaneously developed in this patient. The occlusions probably were multifocal and small rather than central and large, because of the relative preservation of the left hemisphere function. The most likely cause of multifocal, sudden vascular occlusions would be multiple cerebral emboli.

Dr. Kornfeld: You are confident that the patient had emboli rather than a thrombosis?

Dr. Saper: Yes. The reason for that is the sudden occurrence of multiple neurologic defects in this patient.

Dr. Kornfeld: I would agree with that. The question we have to address, then, is the source of the emboli. I think we can rapidly exclude most of the usual causes. Rheumatic heart disease is very unlikely in this patient, who had no history of heart disease, no murmurs, and no atrial fibrillation. Myocardial infarction is unlikely in view of the patient's age and the lack of chest pain. Atherosclerotic emboli are also unlikely in this young patient. The possibility of paradoxical embolism deserves some consideration. That is a situation in which a thrombus originates in the venous circulation, usually in the lower extremities or the pelvis, and then enters the right heart and then the left heart via a patent foramen ovale. The thrombus can then lodge in the cerebral circulation. Paradoxical emboli are frequently seen in association with recurrent pulmonary emboli that lead to the development of increased pulmonary arterial pressure and elevated pressure in the right atrium. This, in turn, allows shunting to occur from the right atrium to the left atrium. The patient had no evidence of deep vein thrombosis in his remaining leg and no signs or symptoms of pulmonary emboli, making this diagnosis unlikely. On the other hand, another cause of paradoxical emboli is tumor emboli. This occurs very rarely, but is a possible diagnosis in this case that I'd like to come back to later. The diagnosis of subacute bacterial endocarditis can be excluded because of the lack of

fever, the lack of heart murmurs, and the negative blood culture results. We can also exclude fat embolism and air embolus because of the clinical setting.

That leaves us with two major possibilities, non-bacterial thrombotic endocarditis and tumor emboli, both of which are associated with malignancies. Non-bacterial thrombotic endocarditis is found in approximately 0.4 percent of general autopsy series and in about 1 percent of cancer patients who undergo autopsy. Approximately one third of all patients with nonbacterial thrombotic endocarditis have underlying cancer. Most patients are greater than 40 years old, but there have been cases in younger persons. The condition is characterized by the presence of single or multiple verrucous lesions that range in size from 1 to 15 mm and that usually involve the aortic and/or the mitral valve. Only rarely are the pulmonic and tricuspid valves involved. The lesions are composed of fibrin and platelets present on uninflamed, nonulcerated valve leaflets. The affected valves often show some underlying scarring. Nonbacterial thrombotic endocarditis is most commonly associated with adenocarcinomas of the lung, pancreas, and stomach. It has also been seen with many other cancers, but is extremely rare in patients with sarcomas. I was unable to find any reported cases of nonbacterial thrombotic endocarditis in association with chondrosarcoma. Arterial emboli occur in about one half of the patients with this disorder. The emboli are usually multiple and particularly involve the brain, spleen, and kidneys. The emboli may cause gross infarcts, with 10 to 20 percent of patients with this disorder having cerebral infarcts. The disorder is also associated with venous thromboses, clinical thrombophlebitis, and recurrent pulmonary emboli. This association has led a number of investigators to postulate that nonbacterial thrombotic endocarditis is a component of a generalized hypercoagulable state or an ongoing "chronic" disseminated intravascular coagulopathy.

The diagnosis of nonbacterial thrombotic endocarditis is rarely made prior to autopsy. Since only about a third of patients with autopsy-demonstrable nonbacterial thrombotic endocarditis have murmurs, the lack of a murmur does not exclude this disorder. Another approach to the evaluation of cardiac valves is echocardiography. Dr. Geltman, would you review the echocardiographic study that was performed in this case, and discuss the usefulness of this procedure in evaluating heart valves and making the diagnosis of nonbacterial thrombotic endocarditis?

Dr. Edward Geltman: Echocardiography is an extremely valuable tool for the assessment of cardiac structure and function. The two forms of echocardiography that are employed clinically, M-mode and two-dimensional, are complimentary procedures, each with

its strengths and limitations. M-mode echocardiography is very useful for tracking the motion of cardiac structures because of its excellent temporal resolution, which permits the assessment of rapid cardiac motion, and its excellent resolution of depth. However, M-mode echocardiography has only modest lateral resolution and limited capabilities for the delineation of complex structural relationships. In contrast, two-dimensional echocardiography has limited temporal resolution, good depth resolution, but provides excellent spatial resolution, permitting superior assessment of cardiac anatomy, especially for the detection of intracardiac masses and for the description of complex congenital cardiac malformations.

When employing echocardiography for the assessment of patients with suspected systemic embolization or suspected endocarditis (either bacterial or marantic), M-mode and two-dimensional echocardiography are complimentary. M-mode echocardiography is superior for the assessment of aortic insufficiency, because the attendant fluttering of the anterior mitral valve leaflet is too rapid for detection with two-dimensional echocardiography. However, two-dimensional echocardiography is clearly a superior technique for the detection of intracardiac masses (e.g., left atrial myxoma, mural thrombus, or valvular vegetations). In M-mode echocardiograms, valvular vegetations generally appear as a nonspecific thickening of the leaflets or as an indistinct echo-dense mass moving with the valve leaflets. In two-dimensional echocardiograms, valvular vegetations are often recognizable as distinct mobile masses attached to the leaflets, although nonspecific leaflet thickening may also be seen. Overall, 13 to 68 percent of patients with documented bacterial endocarditis have valvular vegetations detected by M-mode echocardiography, but two-dimensional echocardiography is more sensitive, detecting 43 to 79 percent of such patients [10].

Unfortunately, echocardiographic detection of marantic endocarditis has only been reported in two patients [11,12], and in one of these patients an M-mode echocardiogram early in the patient's course did not reveal an apparent vegetation [11]. The size of vegetations found at postmortem with marantic endocarditis varies from 3 mm (the lower limit of the resolution of vegetations by echocardiography) to 1.5 cm or larger [13]. Therefore, it is likely that vegetations should be found by echocardiography in patients with marantic endocarditis with sensitivity comparable to that described for patients with bacterial endocarditis.

The echocardiogram performed in this patient was an M-mode study. Both the aortic and mitral valves were normal in structure and motion. Left and right ventricular sizes were normal and left ventricular posterior wall and interventricular septal motion were normal. These data

make endocarditis or marantic endocarditis unlikely but certainly do not exclude this possibility. Normal septal motion and normal pulmonic valve motion make pulmonary hypertension with subsequent paradoxical embolization also unlikely. No evidence of a left atrial mass was seen, but M-mode echocardiography alone is of limited sensitivity for the detection of left atrial tumor or thrombus. Thus, it is unlikely that there was a cardiac source for systemic embolization in this patient.

Dr. Kornfeld: Thank you. At this point I'd like to summarize the data that are available concerning the possibility that the patient under discussion had nonbacterial thrombotic endocarditis. In favor of the diagnosis is the fact that nonbacterial thrombotic endocarditis is a well-established cause of cerebral artery emboli in cancer patients. However, the following points are against the diagnosis: (1) nonbacterial thrombotic endocarditis is a very rare complication in patients with sarcomas; (2) there was no evidence of ongoing disseminated intravascular coagulation or other thrombotic or hemorrhagic phenomenon; (3) there was no evidence of emboli to other organs; (4) there was no detectable heart murmur; and (5) results of the echocardiogram were negative. I believe we must conclude, therefore, that although the diagnosis of nonbacterial thrombotic endocarditis cannot be excluded, it is not very likely.

This leaves us with the possibility of tumor emboli. The most common way that metastatic cancer involves the brain is by the formation of metastatic nodules in the brain parenchyma or by spread to the meninges. However, tumor embolization with occlusion of cerebral vessels is a rare but well-described entity. One situation in which this occurs is in association with thoracic surgery. Twelve cases here have been reported where major arterial tumor embolization occurred after pulmonary resection. One well-documented case was reported by the thoracic surgery group here at the Washington University Medical Center [14]. The patient was a 70-year-old woman with a fibroliposarcoma that had metastasized to the right lower lobe, near to the inferior pulmonary vein. The patient underwent a thoracotomy for resection of this metastatic nodule and during surgery had a myocardial infarction and died shortly afterwards. At autopsy, there were large tumor emboli present in all branches of the aorta with occlusion of the vessels of the arch and the vessels leading to the kidney, the mesentery, and the liver. Microscopic tumor emboli were present in the coronary arteries. It was postulated that the tumor had invaded the inferior pulmonary vein and grown centrally into the left atrium, and at surgery, when the pulmonary vessel was clamped, a piece of the tumor broke off, giving rise to these emboli. A similar syndrome has been described in the other patients. In seven of the 12 cases, emboli

to cerebral vessels occurred. Two of these patients had sarcomas. Spontaneous tumor emboli, other than from atrial myxomas, are even rarer. There are a few reports of spontaneous tumor emboli in patients with lung cancer. In addition, there have been reports of patients with abdominal tumors and cerebral vascular occlusions due to tumor emboli, presumably representing paradoxical emboli.

At this point I'd like to ask Dr. Varki if he would tell us about the typical patterns of spread of metastatic chondrosarcoma and whether he thinks that tumor emboli were likely to have occurred in this patient.

Dr. Varki: As I pointed out earlier, there is considerable variation in the metastatic potential of chondrosarcomas. Distant metastases are uncommon; when they do occur, by hematogenous seeding, the lungs are usually involved. Lymphatic spread is quite rare. In addition to conventional hematogenous seeding, however, there are many anecdotal reports of a rather peculiar form of spread of chondrosarcoma. I quote to you from several sources: "In some instances autopsy reveals a continuous intravascular growth of tumor which may extend to the right side of the heart, or even into the pulmonary arteries . . ." [1]; ". . . show extensive invasion of regional veins, and large intravascular masses may extend for long distances within the lumen, in continuity with the primary tumor" [2]; ". . . it tends to break into the regional venous channels and by intravascular growth and extension, without necessarily adhering to even the vessel walls may reach the heart and lungs. . ." [3]. In a recent textbook on bone tumors, Huvos [4] pointed out that such cases were first reported in the old German literature by Virchow, Weber, and others; he also pointed out a recent case report in the German literature in which a chondrosarcoma metastatic to the lung had undergone direct extension via the pulmonary veins to the left atrium.

Now what is the incidence of this bizarre tumor growth pattern in chondrosarcoma? This is extremely hard to deduce, since most of the large series did not include many autopsies. Regardless, if we consider that this patient may have had such intravascular tumor masses, there are two possible way in which we could explain the cerebral emboli. First, the chondrosarcoma may have grown directly into the right side of the heart, causing pulmonary embolism, pulmonary hypertension, and a patent foramen ovale, resulting eventually in "paradoxical" tumor embolism. Alternatively, the pulmonary metastases may have grown into the pulmonary veins by direct extension and then released tumor emboli directly into the arterial circulation.

Dr. Kornfeld: I believe that this is as far as we can go with the available information. The patient had a very rare tumor, a chondrosarcoma, and a rare complication, the thrombosis of the internal carotid artery and multiple



Figure 1. Numerous pulmonary metastases from the chondrosarcoma are seen. Some of the latter extend into the pulmonary veins.

cerebral vessels. The most logical diagnosis in this case is that the emboli were in fact tumor emboli, most likely arising from the pulmonary metastases that invaded the pulmonary vein. Alternatively, they might have arisen as paradoxical emboli, but I think the data in support of this possibility are not strong. Although we cannot rule

out the diagnosis of nonbacterial thrombotic endocarditis, I think that this is the less likely diagnosis in this patient. Dr. Bobzien will discuss the pathologic findings.

PATHOLOGIC DISCUSSION

Dr. Bonnie Bobzien: This case demonstrates a straightforward but unusual complication of chondrosarcoma. The propensity of chondrosarcoma to invade vessels and grow intravascularly has been well documented. Borzotta and co-workers [15] described a 19-year-old man with a pelvic chondrosarcoma that had invaded the right common iliac vein and its tributaries. At necropsy, tumor emboli were found in the hepatic vein, right atrium, and right ventricle. Shields [16] reported a case of a 32-year-old man with a chondrosarcoma of the left sacroiliac joint. The tumor invaded the left hypogastric vein and extended from there into the inferior vena cava. Tumor emboli were found in the left pulmonary artery at necropsy. However, vascular extension usually occurs through the venous system [17]. What makes our case unusual is the presence of multiple arterial emboli, including emboli to the cerebral vessels with subsequent cerebral infarction.

The postmortem examination showed multiple gelatinous, white nodules scattered throughout both lungs. The metastases of the chondrosarcoma invaded the pulmonary veins and obstructed the vascular lumens (Figures 1 and 2). Microscopic examination of the neoplasm showed plump cells with large nuclei containing vesicular chromatin. The neoplastic cells were dispersed in a myxoid stroma. Scattered mitotic figures were present. The lungs also contained scattered foci of bronchopneumonia.

Presumably, it was the tumor invasion of the pul-

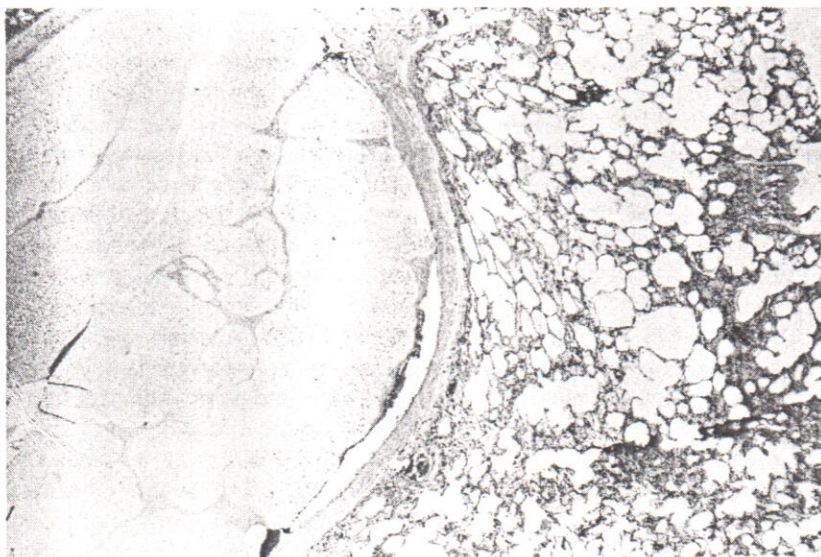


Figure 2. Lobulated masses of tumor completely occlude the lumens of some pulmonary vessels (hematoxylin and eosin; original magnification X 20, reduced by 4 percent).

monary veins that allowed access to the systemic circulation, with embolization and subsequent infarction in numerous organs including the brain, the eye, the right kidney, and the spleen.

The right kidney, weighing 120 grams, contained numerous metastases throughout the cortex and medulla. The spleen weighed 460 grams and contained similar metastatic lesions. In both these organs, the tumor was primarily located within vascular lumens. The surrounding parenchyma exhibited hemorrhagic infarction.

Examination of the brain showed a large, relatively acute infarct of the right posterior frontal lobe. This lesion would correspond with the patient's left hemiparesis. A subacute infarct, present in the lateral medulla, may explain the patient's symptoms of nausea and vertigo. This latter infarct most likely resulted from the occlusion of the right vertebral artery. A large tumor embolus completely filled the lumen of this vessel. Multiple small infarcts, both hemorrhagic and ischemic, involved the basal ganglia, cerebral cortices, and white matter bilaterally (Figure 3). These infarcts ranged in diameter from 1 mm to 1.5 cm. They ranged in age from recent to several weeks old, with most being less than two weeks of age. Associated with the infarcts were plugs of chondrosarcoma, which obstructed the lumens of the leptomeningeal and intraparenchymal vessels (Figure 4). Fibrin thrombi were present in both carotid arteries. However, they did not completely occlude the vascular lumens. No tumor emboli were found in either carotids. Finally, a 1.5 cm diameter metastasis was found in the right occipital lobe.

In regard to the possibility of nonbacterial thrombotic

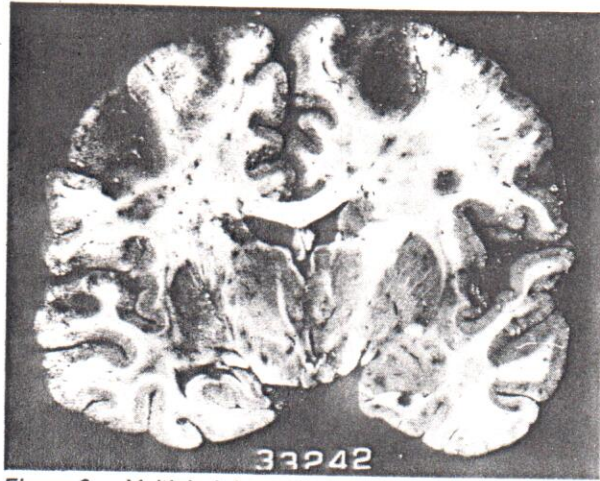


Figure 3. Multiple infarcts involve the basal ganglia, cerebral cortices, and white matter bilaterally.

endocarditis, the examination of the heart was unremarkable.

This case demonstrates two unusual features. First, sarcoma rarely metastasizes to the brain. In the study by Gercovich et al [18], of 456 patients with metastatic sarcoma, only 1.3 percent had cerebral metastases, as documented by brain scan. Støier [19] reported no sarcoma in his autopsy series of secondary cerebral neoplasms. In the former study, the patients were treated with combination chemotherapy regimens containing doxorubicin hydrochloride. Fourteen patients relapsed after an initial response or stabilization of at least six months. In five (36 percent) of these patients, the cause of the relapse was the development of ce-



Figure 4. Tumor emboli occlude the lumen of leptomeningeal and intraparenchymal cerebral vessels (hematoxylin and eosin; original magnification X 40, reduced by 4 percent).

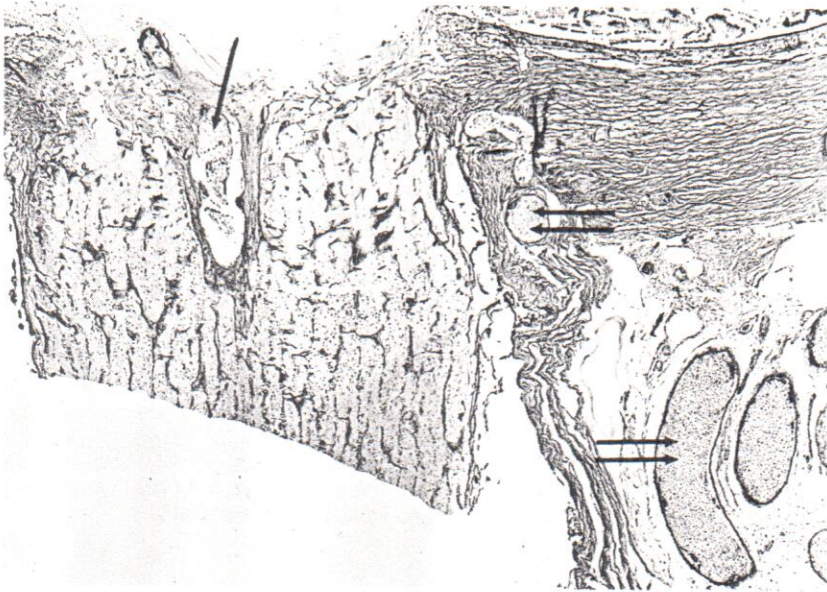


Figure 5. The central retinal artery (single arrow) and the short posterior ciliary arteries (double arrows) are filled with tumor emboli.

rebral metastases. One of the patients who relapsed was a 54-year-old man with chondrosarcoma of the ileum. The investigators suggested that prolonged survival with chemotherapy may have altered the metastatic pattern of the disease.

In the patients with metastatic chondrosarcoma, the presence of tumor emboli in the cerebral vessels was not specifically mentioned. The presence of the latter in our patient is the second unusual feature. The occurrence of cerebral infarction secondary to tumor emboli is a rarely reported phenomenon. The most frequent site of obstruction in this circumstance is the middle cerebral artery or one of its branches [20].

Dr. Smith will now discuss the ocular pathologic findings.

Dr. Morton Smith: I would like to point out that when this patient was seen by the ophthalmologist, it was emphasized that there was no "cherry red spot" in the fundus of the right eye; in other words, it appeared that both the retinal and choroidal circulation were occluded.

We can see by the histopathologic features of the right eye that the clinical diagnosis was correct. All of the posterior ciliary arteries were filled with chondrosarcoma emboli (Figure 5). A portion of the optical nerve was infarcted. The central artery showed chondrosarcoma emboli within the lumen. A portion of the choroid and the overlying retina showed evidence of acute necrosis. Farther forward on the eye, there was disruption of the pigment epithelium of the pars plicata and pars plana, which denotes involvement of the long posterior ciliary artery. The left eye showed less involvement.

Final pathologic diagnosis: Chondrosarcoma, right hip, resected November 1980; multiple bilateral pulmonary metastases with invasion of pulmonary veins; multiple infarcts, large and small, of cerebral cortex and brain stem, associated with tumor emboli in leptomeningeal vessels and with total occlusion of right vertebral artery by tumor embolus; metastatic chondrosarcoma to the right occipital lobe, kidney, and spleen.

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