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Hemangiopericytoma of the heart following treatment of Hodgkin's disease

A case report

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Summary. During the autopsy of a 24 year old woman, who died of cardiorespiratory insufficiency a large solitary tumour was found extending into the right ventricle of the heart and obstructing the pulmonary valve subtotally. Histologically the tumour showed a vascular pattern of differentiation typical of a hemangiopericytoma with almost uniform cellularity and a dense reticulin meshwork surrounding the individual tumour cells. Ten years before death the patient had been diagnosed as having Hodgkin's disease treated with an unusually high dose of radiotherapy combined with chemotherapy. Although tumours have been known to arise following radiation and chemotherapy and hemangiopericytomas of almost all parts of the body have been described, to our knowledge this is the first case of an (iatrogenically induced) hemangiopericytoma of the heart.

Key words: Hemangiopericytoma – Heart – Radiation – Chemotherapy – Tumour induction

Introduction

Hemangiopericytoma was first described and named in 1942 by Stout and Murray. However, it had been accepted as a unique well-defined entity only in the last few years (Enzinger and Smith 1976).

The basic cells of the tumour are the ubiquitously present pericytes of Zimmermann (1923). Not surprisingly therefore, hemangiopericytoma has been observed to arise in almost all parts of the body. Nevertheless, it is an uncommon neoplasm and the prediction of its clinical behaviour is tentative. Patients with hemangiopericytoma range in age from infants and small children to 92 years (Kaufmann and Stout 1960; Angervall et al. 1978) there being no significant difference in the sex related incidences (McMaster et al. 1975; Enzinger and Smith 1976; Neumann 1983). Most publications on hemangiopericytomas are case reports and there are only a few papers describing series of cases (Stout 1949; McMaster et al. 1975; Enzinger and Smith 1976). Pericytes do not possess readily identifiable cellular features and they are difficult to distinguish from histiocytes, fibroblasts and endothelial cells. Thus, the only criterion for the diagnosis of a hemangiopericytoma under the light microscope is its architectural pattern. Electronmicroscopical examination is often found to be essential in diagnosis.

In this case report we describe a hemangiopericytoma found during autopsy in the heart of a 24 year old female patient who died from cardiorespiratory insufficiency. The tumour had probably developed after radiation and chemotherapy given for Hodgkin's disease ten years before death. To our knowledge solitary manifestation of hemangiopericytoma in the heart has not been previously described.

Case report

Hodgkin's disease (Lymphocytic-Histiocytic predominance type) of the anterior mediastinum was diagnosed in a 14 year old female patient in 1972. The staging of Hodgkin's disease showed stage IIIB according to the Ann Arbor classification (Carbone et al. 1971). Complete remission was reached by three cycles of COPP (Young et al. 1972) and radiation therapy (104 GY upper-mantle irradiation and 29 GY to the paraortic field). Six years after treatment, contraction of the right lung

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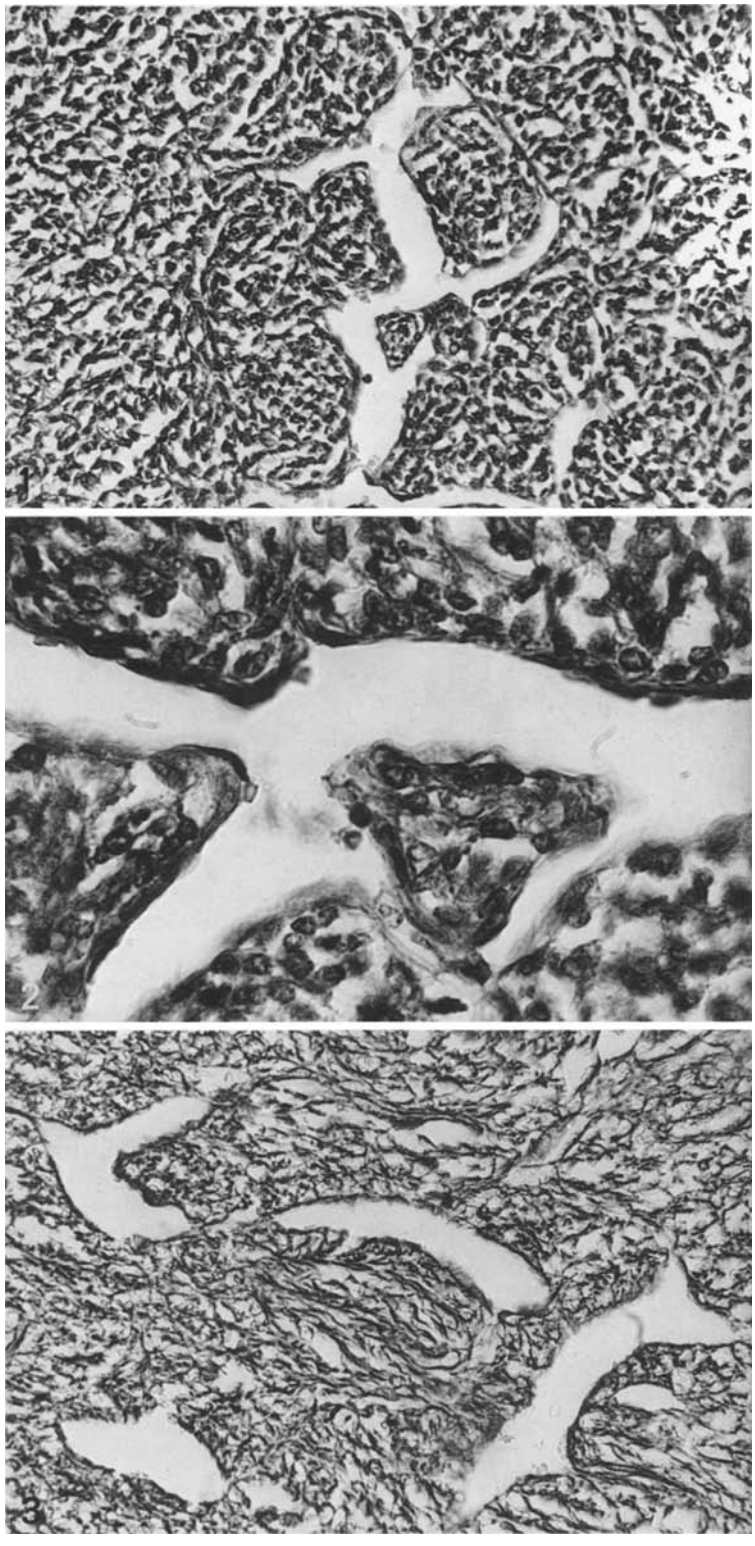

Fig. 1. Characteristic "staghorn" configuration of a sinusoidal vessel. The vessels are surrounded by uniform tightly packed tumour cells (H and E, × 213)

Fig. 2. Higher magnification of the sinusoidal vessel shown in Fig. 1 (H and E, × 553)

Fig. 3. Reticulin preparation outlining the basement membrane of the vascular spaces and the reticulin meshwork surrounding the individual tumour cells (Gomori-silver-stain, × 213)

as a radiation effect, exudative pleuritis and spontaneous pneumothorax were noted. Furthermore, supraventricular tachycardia was documented. Three years later pleurectomy and decortication of the right lung had to be done because of continuing discomfort and recurrent exudative pleuritis and bronchitis. Nevertheless, pleural effusion continued and had to be tapped. Two years before death a complete cardiological examination, including echo-cardiography, showed no evidence of heart disease (valvular deformities or tumour).

Ten years after the diagnosis of Hodgkin's disease the patient died with symptoms of progressive pleural effusion (500–1,000 ml/day), orthopnea and right heart failure but without any signs of recurrence of Hodgkin's disease.

During the autopsy a sessile tumour measuring $7 \times 6 \times 4$ cm was found in the right ventricle of the heart arising from the cardiac septum and obstructing the pulmonary valve subtotally. The cut surface was described as fleshy, had a red-brown to greyish-white colour and showed vascular spaces. In addition areas of haemorrhage and necrosis were observed. There was no evidence of metastases. Contraction of the upper lobe of the right lung and fibrosis of the mediastinum were noted due to radiation effects following the treatment of Hodgkin's disease 10 years before. No evidence for recurrent Hodgkin's disease was found. The patient had evidently died of cardiorespiratory insufficiency.

The tumour was fixed in 10% buffered formalin, paraffin embedded and stained with Hematoxilin-eosin, by the Gomori-silver-staining technique, Masson-trichrome and antibodies against Factor VIII related antigen (PAP immunoperoxidase technique), cytokeratin, vimentin, desmin (indirect immunoperoxidase technique) and Ulex europaeus agglutinin 1 (indirect method, using a goat-anti-UEA 1 antibody). Unfortunately, no tissue had been embedded for ultrastructural investigation. Re-embedding for EM of paraffin-embedded material provided unsatisfactory electronmicroscopical results.

The tumour, which infiltrated the cardiac muscle for not more than 3 mm, was composed of tumour cells around endothelium lined vascular channels, ranging from large, sinusoidal spaces to capillaries. The sinusoidal vessel profiles depicted the characteristic "staghorn" pattern of a hemangiopericytoma (Fig. 1). The tumour cells around the vessels were plump and thightly packed (Fig. 2). Variable size nuclei and a few mitoses (less than 4/10 HPF) were found. There were two small foci depicting calcification and a fibro-sarcoma like pattern, respectively. Gomori-silver-staining technique showed reticulin fibrils between the long, extending processes of the pericytes (Fig. 3). No intracellular myofibrils were demonstrated with the Masson-trichrome staining. Immunostaining for Factor VIII related antigen and staining for UEA 1 was negative in the tumour itself but positive in endothelial cells lining the vascular channels. The tumour was moderately positive for vimentin in immunohistochemical staining, whereas no positivity could be demonstrated with cytokeratin and desmin.

Discussion

For many years hemangiopericytoma has been a controversial entity. In the last few years however, the knowledge of its morphological variations and ultrastructural investigations (Kuhn and Rosai 1969; Battifora 1973; Nunnery et al. 1981) as well as clinicopathological studies have helped to define hemangiopericytoma more clearly. As a result of its various patterns and the difficulty to distinguish hemangiopericytoma from other richly vascular tumours hemangiopericytoma has often been misdiagnosed or misinterpreted (Jensen et al. 1966; Pitkethly et al. 1970). In our case hemangioendothelioma, fibrous histiocytoma, extraskeletal mesenchymal chondrosarcoma and synovial sarcoma were taken into differential diagnostic consideration, because all of them (in particular the latter two) show a vascular pericytoma-like pattern. Hemangioendothelioma is readily recognised in the Gomori-silver-stain because of the proliferation of endothelial cells. Furthermore, the staining reaction for Factor VIII related antigen was negative in our case. Fibrous histiocytoma may cause considerable difficulties to distinguish from hemangiopericytoma. Showing a storiform and cartwheel pattern, the vascular network is not so clearly pronounced as in hemangiopericytoma. Focal vascular patterns imitating hemangiopericytoma can also be seen in fibroxanthosarcomas. Extraskeletal mesenchymal chondrosarcoma consists of poorly differential small or oval tumour cells in addition to hemangiopericytoid foci and islands of cartilage and sometimes osteoid and bone (Dahlin and Henderson 1962).

Irregular vascular spaces, sometimes pericytoma-like in pattern, multinodular tumour areas with fibrosarcoma-like spindle cell areas and small foci of calcification and a biphasic cellular pattern with the typical slits and gland-like spaces are findings in poorly differentiated synovial sarcoma. A case of synovial sarcoma in the heart which extended into the right ventricle, obstructing the pulmonary valve, was published by Hagensen and Stout in 1944.

Although no electronmicroscopical investigation was possible in our case the almost uniform cellularity, the vascular pattern and the dense reticulin meshwork surrounding the individual cells of this tumour led us to the diagnosis of a hemangioperiytoma.

The development of a second primary neoplasm ten years after the diagnosis of a Hodgkin's disease is of special interest. It is well recognised that patients with cancer are at increased risk of developing subsequent neoplasms (Moertel et al. 1961). Despite this, Holm et al. (1976) discussed the role of a depression of cell mediated immunity in patients with Hodgkin's disease. However, the question of second malignancies being causes by chemotherapy has been discussed (Kyle 1982). The incidence of second neoplasms is higher in patients treated with radiotherapy and cytostatic agents than either modality alone (Valagussa et al. 1968). In their study of 764 patients with Hodgkin's dis-

ease, treated either with radio- or chemotherapy or both, the overall incidence of solid second tumours was 7.3% within ten years of initial treatment. In one third of the patients the tumour occured in the irradiated areas.

To what extent radiotherapy and/or chemotherapy can be responsible for the induction of hemangiopericytoma is difficult to judge and there is little information in the literature on this particular field. Treatment with unusually high doses of radiation and concomitant chemotherapy might have led to the development of a hemangiopericytoma in our case. The late manifestation of the hemangiopericytoma is not an argument against therapy induced neoplasm. Although there is no clear answer as to whether therapy caused the hemangiopericytoma or not our case demonstrates that the normally great benefit of tumour treatment has to be weighed carefully against its carcinogenic potential.

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References

Angervall L, Kindblom LG, Nielson JM, Steiner B, Svendsen P (1978) Hemangiopericytoma. Cancer 42:2412–2427

Battifora H (1973) Hemangiopericytoma: Ultrastructural study of five cases. Cancer 31:1418–1432

Carbone PP, Kaplan HS, Musshoff K, Smithers DW, Tubiana M (1971) Report of the comittee on Hodgkin's disease staging classification. Cancer Res 31:1860–1867

Dahlin DC, Henderson ED (1962) Mesenchymal chondrosarcoma: further observations on a new entity. Cancer 15:410–417

Enzinger FM, Smith BH (1976) Hemangiopericytoma, an analysis of 106 cases. Human Pathol 7:61–82

Haagensen CD, Stout AP (1944) Synovial sarcoma. Ann Surg 120:826–842

Holm B, Mellstedt H, Bjorkholm M, Johansson B, Killander D, Sundblat R, Soderberg G (1976) Lymphocyte abnormalities in untreated patients with Hodgkin's disease. Cancer 37:751–762

Jensen PA, Dockerty MB, Symmonds RE, Wilson RB (1966) Endometroid sarcoma ("stromal endometriosis"): report of 15 cases including 5 with metastases. Am J Obstet Gynecol 95:79–90

Kaufmann SL, Stout AP (1960) Hemangiopericytoma in children. Cancer 13:695–710

Kuhn C III, Rosai J (1969) Tumors arising from pericytes: ultrastructure and organ culture of a case. Arch Pathol 88:653–663

Kyle RA (1982) Second malignancies associated with chemotherapeutic agents. Seminars in Onoclogy 9/1:131

McMaster MJ, Soule EH, Ivins JC (1975) Hemangiopericytoma. A clinicopathologic study and long term follow up of 60 patients. Cancer 36:2232–2244

Moertel CG, Dockerty MB, Baggenstoss AH (1961) Multiple primary malignant neoplasms. First introduction and presentation of data. Cancer 14:221

Neumann H (1983) Morphologie und Klinik des Haemangiopericytoms. Pathologe 4:64–71

Nunnery EW, Kahn LB, Reddick RL, Lipper S (1981) Hemangiopericytoma. A light and ultrastructural study. Cancer 97:906–914

Pitkethly DT, Hardman JM, Kempe LG, Earle KM (1970) Angioplastic meningiomas: clinicopathologic study of 81 cases. J Neurosurg 32:539–544

Stout AP, Murray MP (1942) Hemangiopericytoma: a vascular tumor featuring Zimmermann's pericytes. Ann Surg 116:26–33

Stout AP (1949) Hemangiopericytoma: a study of twenty-five new cases. Cancer 2:1027–1035

Valagussa P, Santoro A, Kenda R, Fossati-Bellani F, Franchi F, Banfi A, Rilke F, Bonadonna G (1980) Second malignancies in Hodgkin's disease: a complication of certain forms of treatment. Brit Med J 280:216–219

Young RC, DeVita VT, Johnson RE (1973) Hodgkin's disease in childhood. Blood 42:163–174

Zimmermann KW (1923) Der feine Bau der Blutkapillaren. Z Anat Entwicklungsgesch 68:29–36

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