Virchows Arch. A Path. Anat. and Histol. 370, 41—54 (1976)

Comparison of Histologic Types of Primary Testicular Germ Cell Tumors with Their Metastases

Consequences for the WHO and the British Nomenclatures?

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Received December 22, 1975

Summary. 61 autopsy cases with malignant germ cell testis tumors were examined. Both the primary tumors and their metastases were classified histologically according to the nomenclature of the WHO Panel on Testicular Tumours and to the modified nomenclature of the British Testicular Tumour Panel. The classification of the primary and metastatic tumor tissues is relatively easy to handle with both nomenclatures. The comparison of histological structures of the primary tumors with their metastases evoked a variety of deviations, depending on the tumor categories investigated and the nomenclature applied. The seminomas are a very homogenous tumor category usually metastasizing as seminoma. However, anaplastic seminomas can be indistinguishable from solid embryonal carcinomas. The distinct seminomas combined with nonseminomatous germ cell tumors do not seem to metastasize. From the point of view of histologic patterns of metastases and primary tumors, the embryonal carcinoma combined with teratoma i.e. teratocarcinoma (malignant teratoma intermediate) and the pure embryonal carcinoma (malignant teratoma undifferentiated) are not distinct entities. The term of malignant teratoma for these tumor types used by the British authors interprets these events more adequately, reflecting the occurrence of transitional types between teratoma and embryonal carcinoma supported by the appearance of different histologic types of metastases. Pure forms of choriocarcinoma are extremely rare. Yet in our cases of choriocarcinoma combined with other types, the metastases are always of the pure choriocarcinomatous type, and clinical courses were rapidly fatal in less than one year. The distinction of pure forms from combined forms of choriocarcinoma is not of great clinical relevance. 10% of our patients with metastatic germ cell tumor disease revealed testicular lesions referred to as so-called "burned-out" testis tumors. A tumor category of "burned-out" testis tumors is proposed.

Key words: Testicular neoplasms — Nomenclature.

Zusammenfassung. Bei 61 Autopsiefällen mit metastasierenden malignen Keimzelltumoren der Hoden wurden sowohl die Primärtumoren als auch die Metastasen histologisch nachkontrolliert und nach den Nomenklaturen des "WHO Panel on Testicular Tumours" und des "British Testicular Tumour Panel" klassifiziert. Beide Nomenklaturen sind in Bezug auf die Einteilung der Primärgeschwülste und der Metastasen relativ einfach anwendbar. Der Vergleich der histologischen Strukturen der Primärtumoren mit denjenigen der zugehörigen Metastasen ergibt aber gewisse strukturelle Abweichungen, die je nach Tumorkategorie verschieden ausgeprägt sind. Seminome bilden eine anscheinend recht einheitliche Gruppe; sie metastasieren in der Regel auch als Seminome. Anaplastische Seminome können aber unter Umständen nicht von ausgesprochen solid wachsenden embryonalen Karzinomen unterschieden werden. Der Seminomanteil innerhalb kombinierter Tumoren scheint in der Regel nicht zu metastasieren. Die Betrachtung des histologischen Aufbaus der Metastasen und der Primärtumoren der embryonalen Karzinome kombiniert mit Teratom (maligne Teratome, Intermediärtyp nach der englischen Nomenklatur) und der reinen embryonalen

Karzinome (maligne Teratome, undifferenzierter Typ) ergibt, daß diese beiden Tumorformen keinen eigenständigen Kategorien entsprechen. Der Überbegriff des malignen Teratoms der Briten trägt dieser Tatsache Rechnung, umfaßt er doch auch diese Übergangsformen zwischen Teratomen und embryonalen Karzinomen. Reine Choriokarzinome sind ausgesprochen seltene Hodengeschwülste. Unsere Patienten mit primären Choriokarzinomen im Rahmen von Teratomen, also Choriokarzinome kombiniert mit anderen histologischen Tumortypen, wiesen jedoch ebenfalls nur Metastasen von rein choriokarzinomatöser Struktur auf. Sie starben zudem alle innerhalb eines Jahres an ihren Metastasen. Die Unterscheidung reiner und kombinierter Formen von Choriokarzinomen, wie das die WHO vorschlägt, ist deshalb klinisch ohne Bedeutung. 10% unserer Patienten mit metastasierenden Keimzellgeschwülsten wiesen Hodenläsionen auf, die als sogenannte ausgebrannte Hodentumoren bezeichnet werden. Eine entsprechende Tumorkategorie fehlt in beiden Nomenklaturen.

Introduction

Testicular tumors are mainly classified according to the nomenclatures of the Armed Forces Institute of Pathology (A.F.I.P.) presented by Mostofi and Price Jr. (1973) or of the British Testicular Tumour Panel (BrTTP) (Collins and Pugh, 1964). A reliable new classification is being prepared by the WHO Panel on Testicular Tumours under the direction of Mostofi and will be published in the near future. Its actual outline is similar to the classification of the A.F.I.P. Concerning the germ cell testis tumors, the small number of tumor categories and the relatively simple application of the histological criteria required are common features of these three classifications. The heterogenous tissue composition of germ cell tumors of the testis however, is a challenge to any classification providing simplifying groups. The term malignant teratoma used by the British authors for the embryonal carcinoma, the different groups of teratoma, and the choriocarcinoma already gives rise to discussions. Furthermore, the British authors still reject the separation of "pure choriocarcinoma" and "choriocarcinoma and any other type". They use a single category: malignant teratoma trophoblastic. The American authors (Mostofi and Price Jr., 1973) however, distinguish between pure and mixed types, because pure choriocarcinoma almost invariably adopts a rapidly fatal course, whereas the mixed types may not. Finally, in metastases deviations of histologic structure are to be expected (Friedman and Moore, 1946; Dixon and Moore, 1952, 1953; Collins and Pugh, 1964; Snyder, 1969; Willis and Hajdu, 1973; Mostofi and Price Jr., 1973).

The present investigation of 61 autopsy cases of malignant germ cell tumors of the testis compares in every single case the compositions of the primary tumors with the structures of their metastases, typed separately according to the classifications of the WHO Panel and the British Testicular Tumour Panel. Consequences for these two nomenclatures regarding the tumor categories are outlined.

Materials and Methods

At the Department of Pathology of Zürich University, from 1961 until August 1975, 64 autopsies of patients (aged 18 to 74 years) with malignant tumors of the testis were performed. 3 cases of malignant lymphoma also affecting the testes were not further investigated. 9 of the remaining 61 autopsy cases of malignant germ cell tumors had to be excluded. In 2 of these 9 cases, showing seminomatous in one and choriocarcinomatous metastases in the other, the slides of the primary tumors were lost. 2 cases of primary embryonal carcinoma

and teratoma (malignant teratoma intermediate)[1] also had to be excluded since in one case all secondaries were completely necrotic, and the second patient, dying of postoperative sepsis, showed no metastatic deposits, just as a further patient did 18 years after orchidectomy for primary seminoma. He died of metastatic carcinoma of the esophagus. 4 cases (1 seminoma, 1 embryonal carcinoma and teratoma (malignant teratoma intermediate), 2 choriocarcinomas) with predominantly mediastinal and retroperitoneal distribution of the tumor had to be excluded. In 3 of these 4 cases, the testes revealed no primary lesion. The retroperitoneal choriocarcinoma of the fourth case presumably originated from an ectopic right testicle which had been missed and failed to be found by surgery several years before the manifestation of the germ cell tumor, but final prove of testicular origin could not be given because no testicular tissue was found in the retroperitoneal tumor mass.

Of the remaining 52 cases the primary tumors and the metastases were categorized according to the classifications of the WHO and the British Testicular Tumour Panel, and the diagnoses of the primary lesions and of the metastases compared in every single case.

Since the WHO classification and the significant deviations of the modified British Testicular Tumour Panel classification are not yet published, the two proposed nomenclatures are briefly outlined below.

I. Preliminary Classification of the WHO Panel on Testicular Tumours
(Listed for Germ Cell Tumors Only)

A. Tumors of One Histological Type

1. Seminoma. A tumor composed of quite uniform large cells with clear cytoplasm and well-defined cell borders. Variable amount of lymphocytic infiltration and fibrous stroma reaction is a typical feature. Tumors of similar patterns but considerable nuclear variation and increased mitotic activity are designated anaplastic seminomas.

2. Spermatocytic Seminoma. A particular tumor composed mainly of three types of cells. The bulk of the tumor consists of cells of intermediate size, but lymphocyte-like cells and giant cells are also found in variable amounts. The cells have eosinophilic cytoplasms and round nuclei which may show spireme-like patterns similar to those seen in spermatocyte I. Mitoses may be numerous but metastases are apparently rare.

3. Embryonal Carcinoma. A tumor composed of cells of primitive epithelial appearance with clear cytoplasm, growing in acinar, tubular, papillary, and solid patterns with variable amounts of mesenchymal stroma. Completely solid tumors may be mistaken for anaplastic seminomas.

4. Yolk Sac Tumor (Endodermal Sinus Tumor, Orchioblastoma). A tumor usually confined to children, growing typically in a loose network pattern. Tubular, papillary, and solid growth may also be present. Similar tumors occur in adults, though rarely pure, usually within other germ cell tumors.

5. Polyembryoma. A rare tumor composed predominantly of so-called embryoid bodies.

6. Choriocarcinoma. A highly malignant, usually very hemorrhagic tumor composed of syncytiotrophoblasts and cytotrophoblasts. This tumor category is strictly reserved for pure forms only. True cytotrophoblast is identified only in intimate relationship to syncytiotrophoblast, either alone is insufficient for

1 The corresponding term of the British Testicular Tumour Panel's nomenclature is always indicated in brackets.

the diagnosis of choriocarcinoma. Villous formation, however, is not required.

7. Teratoma. A tumor composed of tissue derived from the different germinal layers. The *mature teratoma* is a tumor composed exclusively of well-differentiated tissue. *Immature teratoma* is separated from the mature form by the presence of immature tissue, e.g. resembling embryonal nervous tissue. *Teratoma with malignant transformation* is a rare tumor showing malignant tissue components other than typical embryonal carcinoma.

B. Tumors of More Than One Histological Type

Any combination of histological types may occur. The relative amount of each component should be estimated and recorded. Regarding frequency and prognosis, two combinations are most significant:

1. Embryonal Carcinoma and Teratoma. This is the most frequent combination.

2. Choriocarcinoma and Any Other Type of Germ Cell Tumor. This combination has a grave prognosis.

II. Classification of the British Testicular Tumour Panel

[Collins and Pugh, 1964; Pugh (Personal Communication) 1974]

1. Seminoma (S). The same features are required for diagnosis as listed in the WHO specifications. The term anaplastic seminoma does not exist.

2. Teratoma Differentiated (T.D.). After reinvestigating their cases of differentiated teratoma, the British authors agree on separation of teratoma into mature and immature forms, the latter were grouped hitherto as malignant teratoma intermediate.

3. Malignant Teratoma Intermediate (M.T.I.). This group corresponds fairly well to the category of embryonal carcinoma and teratoma of the WHO typing. The identification of mature tissue or of organoid tissue differentiation, even in smallest parts, establishes as M.T.I. the tumor which elsewhere contains malignant tissue.

4. Malignant Teratoma Undifferentiated (M.T.U.). A tumor composed entirely of malignant undifferentiated teratomatous tissue. A common appearance is an acinopapillary pattern with variable amount of stroma. The former category of malignant teratoma anaplastic (M.T.A.) is now subsumed under this group. The malignant teratoma undifferentiated coincide completely with the embryonal carcinoma of the WHO classification.

5. Malignant Teratoma Trophoblastic (M.T.T.). The identification of cytotrophoblast and syncytiotrophoblast is handled in the same manner as indicated in the WHO specifications. However, two important differences must be strongly emphasized: First, the British Testicular Tumour Panel requires villous-like formations of syncytio- and cytotrophoblasts, and second, if the histological criteria are fulfilled the diagnosis is M.T.T. regardless of the size of the trophoblastic area and the histological appearance of the remainder of the tumor.

6. Combined Tumors. Reserved category for tumors in which distinct teratomatous and seminomatous components can be identified. The teratomas which contain "seminoma-like" areas are willfully excluded.

Table 1. Distribution of the 53 primary testis tumors according to the classifications of the World Health Organization and the British Testicular Tumour Panel

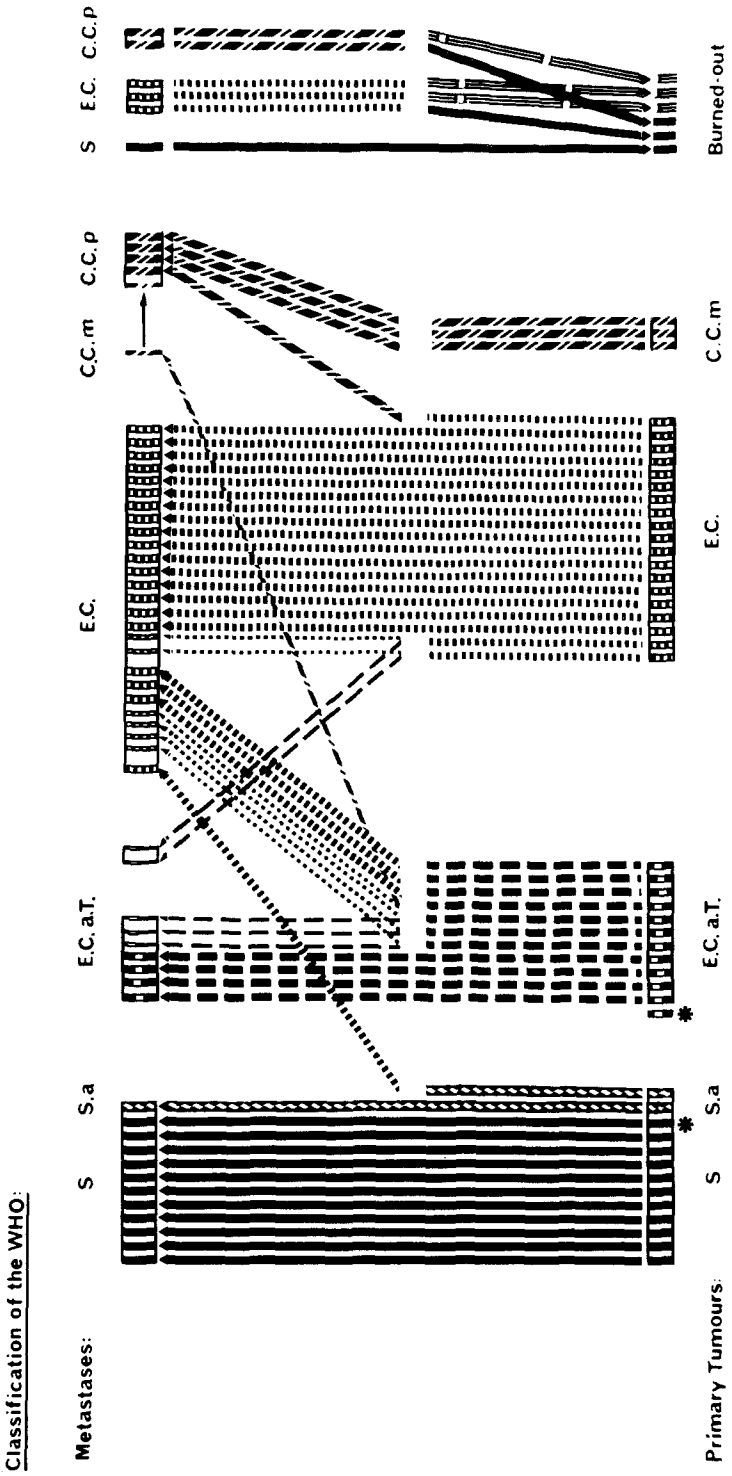
WHO classification	Number of cases	Number of tumors	British classification	Number of cases	Number of tumors
Unilateral Tumors			*Unilateral Tumors*		
Seminoma	10	10	Seminoma	12	12
Seminoma anaplastic	2	2			
Teratoma	—	—	Teratoma differentiated	—	—
Embryonal carcinoma and teratoma	11	11	Malignant teratoma intermediate	11	11
Embryonal carcinoma	19	19	Malignant teratoma undifferentiated	19	19
Choriocarcinoma pure	—	—			
Choriocarcinoma and other types	3	3	Malignant teratoma trophoblastic	3	3
Burned-out tumors	6	6	Burned-out tumors	6	6
Bilateral simultaneous tumors			*Bilateral simultaneous tumors*		
Seminoma, left; embryonal carcinoma and teratoma, right	1	2	Seminoma, left; malignant teratoma intermediate, right	1	2
Total:	52	53	Total:	52	53

Results

The distribution of the 53 primary tumors in 52 cases is shown in Table 1. They are classified according to the nomenclatures of the WHO and of the British Testicular Tumour Panel. In Fig. 1 the structures of the primary tumors and of the corresponding metastases are compared and graphically related to each other in every single case. For greater clearness, the survival time is not considered.

The 10 *typical seminomas* of the 12 patients affected with unilateral primary seminoma metastasize as seminoma. In one of the 2 *anaplastic seminomas* mitotic activity is also increased in the seminomatous metastases. The second case however, reveals embryonal carcinomatous (undifferentiated teratomatous) secondaries, highly altered by therapy and therefore difficult to classify. Some metastases resemble an anaplastic seminoma, but epithelial, sometimes papillary structures usually identifiable at the margin of necrotic tissue show the teratomatous origin. In the patient suffering from bilateral simultaneous tumors of the testes, only seminomatous secondaries are found. Hence the leftsided seminoma metastasized, and the patient was cured by orchidectomy concerning his rightsided embryonal carcinoma and teratoma (malignant teratoma intermediate).

6 of the 52 cases belong to the category of *combined tumors* of the BrTTP. In all 6 cases distinct nodules of seminoma are recognizable, associated in 3 cases with a M.T.U., and in the 3 remaining cases with either a M.T.I., a scarring T.D.,


Classification of the WHO:
Metastases:
S
S.a
E.C. a.T.
E.C.
C.C.m
C.C.p
S
E.C.
C.C.p
Burned-out
C.C.m
E.C.
E.C. a.T.
S
S.a
Primary Tumours:

Classification of the British TTP:

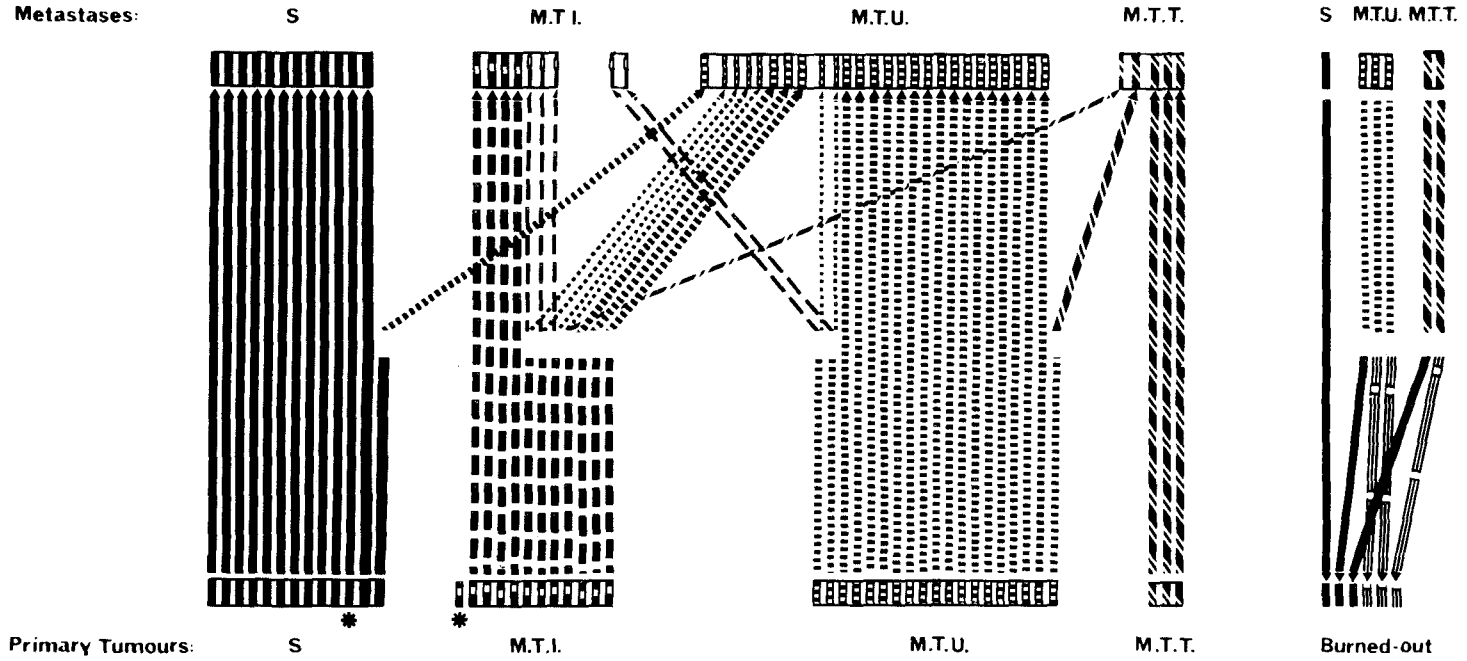


Fig. 1. Schematic diagram of the confrontation of the histologic structures of the primary tumors with their metastases. Survival times are not considered. The cases are represented by stripes that point at the appertaining metastases and split if more than one type of metastases were found. *S* Seminoma, *S. a.* Seminoma anaplastic, *E. C. a. T.* Embryonal Carcinoma and Teratoma, *E. C.* Embryonal Carcinoma, *C. C. m.* Choriocarcinoma combined with other types, *C. C. p.* Choriocarcinoma pure, *M. T. I.* Malignant Teratoma Intermediate, *M. T. U.* Malignant Teratoma Undifferentiated, *M. T. T.* Malignant Teratoma Trophoblastic. *Burned-out.* Retrogressed or so-called burned-out testicular tumors (see p. 49).

* Patient with bilateral simultaneous tumors showing only seminomatous metastases.

or a M.T.T. The metastases in these 6 cases are of teratomatous structure, seminomatous tissue is not identifiable. However, again in some instances necrosis makes critical examination difficult. These 6 combined tumors are subsumed in the corresponding teratomatous tumor groups of Table 1 and Fig. 1.

In our material there are no metastasizing *differentiated teratomas.*

In the 10 cases with primary *embryonal carcinoma and teratoma* (malignant teratoma intermediate), the differentiated tissue elements are composed mainly of cysts lined up by cubical or columnar epithelia sometimes showing ciliation and keratinization. In 5 of the 10 cases, cartilage nodules are found in the surrounding loose connective tissue, thus increasing the resemblance to a bronchus. The amount of differentiated and undifferentiated tissue considerably varies in these primary tumors. In 2 of the 10 patients more than one half of the primary neoplastic tissue consists of mature elements, only in one of these an equal relation is also found in the metastases. The second case shows only embryonal carcinomatous (undifferentiated teratomatous) secondaries, with the exception of one metastasis in the lung, where a single cyst lined up by columnar epithelium is recognizable. In 3 further cases in which the primary tumors contain differentiated and undifferentiated tissue elements in a ratio of about 1:3 to 1:5, only undifferentiated secondaries are identifiable. Finally, in 4 cases the primaries reveal only very small amounts of differentiated teratomatous tissue surrounded by larger embryonal carcinomatous (undifferentiated teratomatous) tumor masses. The same proportion is also maintained in the secondary deposits of two of these four cases. In the third case, only embryonal carcinomatous (undifferentiated teratomatous) metastatic tissue is recognizable. In the fourth case, an embryonal carcinomatous and teratomatous (intermediate teratomatous) metastasis of the liver was surgically removed three months before death. At autopsy, embryonal carcinomatous (undifferentiated teratomatous) metastases are found in the stomach and in an abdominal lymph node. The other metastases in the brain, lungs, kidneys, and the pancreas however, are of pure choriocarcinomatous nature. The thorough reexamination of the better differentiated liver metastasis reveals a small hemorrhagic focus of choriocarcinomatous tissue which is probably responsible for the widespread choriocarcinomatous metastatic lesions found at autopsy.

In 16 of the 19 cases with primary *embryonal carcinoma* (malignant teratoma undifferentiated), the metastases are all of the same undifferentiated type. In 2 of the 19 patients embryonal carcinomatous (undifferentiated teratomatous) and differentiated teratomatous metastases are found. The differentiated metastases are located exclusively in the lymph nodes. Pure choriocarcinoma is observed at all metastatic sites in the last of these 19 patients, however, choriocarcinomatous tissue is not identifiable in the available specimen of the primary tumor. This last patient died of his metastases two months after orchidectomy.

The 3 primary *malignant teratoma trophoblastic* in this series correspond to the group of *choriocarcinoma and any other type* of the WHO classification. We have no pure forms of choriocarcinoma in our material. In 2 of the 3 cases, choriocarcinomatous and embryonal carcinomatous (undifferentiated teratomatous) tissues are identifiable in the primary tumor. In the third case additional differentiated teratomatous tissue is found. It is worth mentioning that all primary

trophoblastic foci are very small compared with the remainder of the tumor, but, without exception, all the metastases are of pure choriocarcinomatous nature. The survival times of these 3 patients are very short. Two patients died 4 and 11 months after orchidectomy, one patient 3 months after showing symptoms of metastases of his primary tumor located in an ectopic intraabdominal left testis.

Lesions referred to as *retrogressed* or *burned-out testicular tumors* are observed in the gonads of 6 patients. In 2 of them the widespread metastases are of pure choriocarcinomatous type, the accompanying testicular lesions consisting of a small scarred teratoma differentiated in the first, and of a small seminoma with an associated distinct fibrous scar in the second case. Rudiments of differentiated teratoma encircled by dense fibrous tissue containing few hemosiderin deposits are observed in 2 further cases in which only embryonal carcinomatous (undifferentiated teratomatous) tissue is identifiable within the metastatic lesions. In one of the remaining 2 cases the metastatic deposits reveal seminoma-like tissue intermingled with papillary and acinar epithelial structures resembling the so-called orchioblastoma. Unfortunately, only sparse histological material of the testicular lesion is available, showing a microscopically small intratubular and extratubular seminoma. In the last case, one testicle is completely replaced by dense homogenous fibrous tissue, and only a few seminiferous tubules are detectable. Identifiable seminomatous deposits in the duodenal submucosa and in abdominal paraaortal lymph nodes show extensive tuberculoid stroma reactions, thus indicating a strong host response to the tumor. The contralateral testis of this patient is completely free of germ cell tumor.

Discussion

Classifications of testicular tumors of well-practicable use were presented by Friedman and Moore (1946), Dixon and Moore (1952, 1953), Collins and Pugh (1964), and Mostofi and Price Jr. (1973). A common feature of their classifications is the attempt to obtain a general view by creating few tumor groups, especially of the heterogenous germ cell tumors which were the decisive factor for the immense and confusing number of nomenclatures elaborated by different authors in the last decades. At present, pathologists usually apply to the nomenclatures of Mostofi and Price Jr. (1973) and of Collins and Pugh (1964). The nomenclature of the WHO Panel on Testicular Tumours to be issued in a short time largely conforms to the classification of Mostofi and Price Jr. In the near future, Pugh and co-workers will also publish a revised and moderately simplified issue of the 1964 classification. Simplifying classifications are, however, only of advantage if the structures of the primary tumors and of their metastases are identical to some extent and vice versa. We therefore carefully examined the histological structures of the primary tumors and of their metastases applying to both the WHO and the modified British nomenclatures separately.

The classification of our primary tumors of germ cell origin and of their metastases turns out to be rather easily practicable with both classifications (Table 1). However, the comparison of the histological structure of the primary tumors

with their metastases evokes a variety of deviations depending on the tumor categories investigated and the nomenclatures applied (Fig. 1).

The *typical seminomas*, thoroughly examined, metastasize as seminoma. This group of tumor is apparently a very homogenous category. Dixon and Moore (1952, 1953) and Mostofi and Price Jr. (1973) however, found considerable deviations of the histologic structure of the metastases associated with primary seminoma. About 65% of the secondaries showed seminoma, the others were embryonal carcinomas in 26%, teratomas in 4%, and choriocarcinomas (only Dixon and Moore, 1952, 1953) in 9%. In contrast to these observations, only one out of our 12 seminomas, an anaplastic type, dissociates from the primary pattern, showing embryonal carcinoma (undifferentiated teratoma) at metastatic sites. Since transition of seminoma into other histological patterns has not yet been found, the nonseminomatous metastases of primary seminoma most likely originate from undetected nonseminomatous areas in the primary tumors (Dixon and Moore, 1952, 1953). A possible origin from misinterpreted primary embryonal carcinoma must also be taken into consideration, since the distinction of seminoma from preponderatly solid growing embryonal carcinoma showing extensive lymphocytic infiltration may be difficult (Hartmann and Peyron, 1919; Friedman and Moore, 1946; Schnyder, 1952; Pugh and Smith, 1964; Mostofi and Price Jr., 1973). In cases with anaplastic seminoma, this distinction can even be impossible. 3 out of 5 patients with primary anaplastic seminoma, reported by Maier *et. al* (1968), dying rapidly of metastatic disease showed embryonal carcinoma in their metastases. Thus correct diagnosis of the primary tumors is doubtful. The term anaplastic seminoma is very delicate; it may even be misleading.

The distinct seminomas within *combined tumors* (Collins and Pugh, 1964) do not seem to metastasize. Equal findings were reported by Pugh and Thackray in 1964. It must be assumed that seminomas in combined tumors, histologically indistinguishable from pure seminomas, are of different biological behavior. Are they tumors derived from atypical germ cells caused by unknown irritation of the primary teratomatous tumor as Wilms (1896), Banzer (1943), and von Albertini (1955) proposed? Or are they differentiated final stages of a neoplastic primordial germ cell that also gives rise to the teratomatous part of the combined tumors, and thus giving support to the theory of germ cell origin of both seminoma and teratoma? (Ewing, 1942; Friedman and Moore, 1946; Dixon and Moore, 1952, 1953; Mostofi and Price Jr., 1973.)

The structures of the metastases of *embryonal carcinomas combined with teratoma* (malignant teratoma intermediate) and of *pure embryonal carcinoma* (malignant teratoma undifferentiated) are mostly similar. Forecasts concerning the quantitative relation of teratomatous (differentiated teratomatous) and of embryonal carcinomatous (undifferentiated teratomatous) components in the metastatic tissues are not yet possible. Differentiated structures however, are more often seen in the secondaries of embryonal carcinomas combined with teratoma (malignant teratoma intermediate) than in pure embryonal carcinomas (malignant teratoma undifferentiated). In the latter, the metastases are usually of the embryonal carcinomatous (undifferentiated teratomatous) type. The comparison of primary with secondary tumor tissues clearly shows that these two

tumor categories (embryonal carcinoma combined with teratoma and pure embryonal carcinoma) are not very distinct entities. Therefore, the conceptual term malignant teratoma of the British Panel for both these tumor categories seems justified, indicating that there are transitional forms between teratoma and embryonal carcinoma and thus reflecting more adequatly the event of unpredictable development of either metastatic teratoid or embryonal carcinomatous tissue. The better prognosis of embryonal carcinoma combined with teratoma however, sufficiently justifies the maintenance of special subgroups which are *embryonal carcinoma and teratoma*, and *pure embryonal carcinoma* (malignant teratoma, intermediate and undifferentiated type). Yet exact definition of these tumor categories should be given.

The remarkable differences of frequencies reported concerning the embryonal carcinoma combined with teratoma and the pure embryonal carcinoma demonstrate the problems in applying the criteria outlined in the A.F.I.P. atlas (3.5% and 36% by Benbanaste, 1965; 17.6% and 20.7% by MacKay and Sellers, 1966; and 23% and 19% by Mostofi and Price Jr., 1973). The rigid yet unusual criteria of the British Panel warrant results easier to compare. Of course the frequencies of these two tumor groups will always depend on the number of specimens investigated from both the primary and the metastatic tumor tissues.

A disputable matter is the classification of *choriocarcinomas*. Mostofi (1973), Mostofi and Price Jr. (1973), and the WHO Panel distinguish between pure choriocarcinoma and combinations of choriocarcinoma with any other type. Collins and Pugh (1964) diagnose a malignant teratoma trophoblastic if the histological criteria are fulfilled, regardless of the size of the trophoblastic area and of the histological structure of the remainder of the tumor. Evidently, the histological structure of metastatic material and the clinical course of these cases only provide more information about the significance of true trophoblastic areas within other germ cell tumors. As our cases clearly show, smallest foci of choriocarcinoma give rise to pure and exclusively choriocarcinomatous metastases, a fact that has already been observed by Dixon and Moore in 1952. The importance of trophoblastic tissue is further strongly supported by our observations in a case in which a small trophoblastic area was found within a differentiated teratomatous metastasis of the liver 18 months after removing an embryonal carcinoma combined with teratoma (malignant teratoma intermediate) of the left testis. The autopsy, only three months later, revealed widespread pure choriocarcinomatous metastases apparently caused by the liver focus. The metastases of the embryonal carcinomatous (undifferentiated teratomatous) type found in a paraaortal lymph node and the stomach were probably of primary tumor origin. None of our cases of choriocarcinoma combined with other germ cell tumor types (malignant teratoma trophoblastic), included is a further case with pure choriocarcinoma at metastatic sites but undetected primary trophoblastic focus, survived more than one year after the diagnosis of either primary or secondary foci of trophoblastic tissue. The findings of Friedman and Moore (1946), some of their cases with focal primary choriocarcinoma were free of metastatic choriocarcinomatous tissue, are not contrary to our results. Friedman and Moore classified cytotrophoblasts, frequently seen in embryonal carcinoma, already as foci of choriocarcinoma.

Our results would suggest that the distinction between pure choriocarcinoma and choriocarcinoma combined with any other type is not of clinical relevance.

The extremely low incidence of pure forms—Collins and Pugh (1964) observed none in about 1,050 testicular tumors, Mostofi and Price Jr. (1973) reported only 18 cases in 6,000 testis tumors—evokes doubt of their existence. Beside of choriocarcinomatous tissue one usually also observes malignant teratomatous tissue in the primary lesions of these cases. The British authors therefore classify the choriocarcinomas as malignant teratomas trophoblastic which are a subgroup of the comprehensive category of malignant teratomas. They consider the different types of malignant teratomas only to represent different stages of tumor differentiation to either somatic (intermediate type) or trophoblastic (trophoblastic type) structures probably derived from the undifferentiated teratomatous type or its precursor. This concept of tumor differentiation is actually very similar to the one outlined by the American authors (Friedman and Moore, 1946; Moore, 1951; Dixon and Moore, 1952, 1953), but the term of malignant teratoma of the British authors seizes these events in a more comprehensive manner. The malignant teratomas intermediate have a better prognosis than the undifferentiated types, whereas the trophoblastic forms have a very grave prognosis, regardless of the presence of pure or combined primary tumors. For practical purposes therefore, a single tumor group comprising the pure and the combined choriocarcinomas is reasonable.

A particular biological phenomenon is the occurrence of *so-called burned-out primary testicular tumors*. Observations of retrogressed primary tumors and of associations of small teratomas with widespread choriocarcinomatous or embryonal carcinomatous (malignant teratomatous) metastases have been reported by several authors (Stärk, 1918; Prym, 1927; Symeonidis, 1943; Rottino and DeBellis, 1944; Roth, 1950; Rather *et al.*, 1954; Azzopardi *et al.*, 1961; Azzopardi and Hoffbrand, 1965; Crook, 1968; Salm, 1972; Meares and Briggs, 1972). Rudiments of differentiated teratomas or distinct scars associated with or without foci of seminoma within testicular tissue are referred to as burned-out tumors in this investigation. Since seminomas quite often show extensive stromal reaction, complete scarring of primary seminoma would not be an unexpected finding. However, the nonseminomatous germ cell tumors too, may scar over and easily be overlooked. Furthermore, the paradoxical appearance of teratomatous metastases in association with a small seminoma of the testis must induce careful search for undetected small teratomas or scars containing so-called hematoxylin bodies in some instances (Azzopardi *et al.*, 1961; Azzopardi and Hoffbrand, 1965). In approximately 10% of our autopsy cases we observe corresponding testicular lesions. Unfortunately, frequencies are not reported in any of the other available investigations. Neither the WHO Panel nor the British Panel take into account the apparently high incidence of burned-out primary testis tumors in their tumor nomenclatures. According to our results the introduction of a category of "burned-out tumors" would be of value. Two thirds of our corresponding cases came to autopsy without any suspicion of a germ cell tumor disease. In one third of the cases, the diagnoses of retroperitoneal embryonal carcinoma (malignant teratoma undifferentiated) had been made. The diagnosis of true extragenital germ cell tumors is only admissible if the thoroughly examined testes are free of germ cell tumor or lesions referred to as burned-out testis tumors.

We wish to express our sincere thanks for providing additional histologic material to Prof. M. Aufdermaur, Luzern, Prof. H. Cottier, Bern, Dr. B. Egloff, Winterthur, Prof. F. Gloor, St. Gallen, Prof. H. A. Hienz, Krefeld, Prof. F. K. Kössling, Bremen, PD Dr. J. P. Mühlethaler, Aarau, Prof. G. Müller, Chur, Prof. P. Riniker, Locarno, Prof. E. Schairer, Ulm, PD Dr. R. Siebenmann, Zürich, and PD Dr. J. Torhorst, Basel.

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