Over metastering van kanker

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SUMMARY

In the Introduction the influence of mechanical factors on metastasis is given. The reasons are mentioned, for which in this thesis attention is paid especially to the routes of metastasis

Section I is devoted to a general survey.

In the introduction to this section the arguments for the embolic theory of metastasis are given and the opinions of investigators like HANDLEY and MÜLLER rejected. The use of the word „permeation" is suggested.

Chapter 1 deals with lymphatic metastasis, which is regarded as a process that takes place step by step in the normal direction of the lymph flow. Paradoxical lymphatic metastasis, distinguished by the skipping of a lymph node group, as well as retrograde lymphatic metastasis, are considered of minor importance. The necessity of distinguishing between direct extension, especially lymphatic permeation, and metastasis is emphasized.

Chapter 2 deals with haemic metastasis, our knowledge of which has been especially augmented by the work of WALTHER. Because of this it is now possible to offer several laws of nearly universal application:

a) haemic metastasis can begin by the infiltration of veins by cancer, or by the discharging of lymph, containing cancer cells, into the superior caval vein.

b) the transportation of cancer cells through the bloodvessels takes place only as far as a network of capillaries, because this latter acts as a „filter" for the tumour emboli. Further dissemination can only take place, when the metastase has infiltrated through the „filter". In this way the process progresses step by step.

c) depending on the location of the primary tumour haemic metastasis can take the form of the „pulmonary-vein-type", „caval-vein-type" or „portal-vein-type". These types are marked by the sequence of three „filters", which are formed by the capillaries of liver, lung and organs of the systemic circulation. The existence of „mixed types" is mentioned. These types enable the physician to consider haemic metastasis in terms of „regional organs" in the same way

as he has been accustomed to think of lymphatic metastases in terms of regional lymph nodes.

d) the comparative frequency of metastasis in the organs of the systemic circulation is determined by a „standard sequence", which is: liver, skeleton, kidney, adrenal gland, etc. This sequence is present in the majority of the various primary tumours.

Chapter 3 deals with transcoelomic metastasis, which can be regarded too as a process, proceeding step by step by the passing over from one cavity to another.

In *Chapter 4* the other routes of metastasis are dealt with, namely those by way of the cerebrospinal fluid, over epithelial surfaces and by way of glandular ducts. Their significance if at all, is small or negligeable.

In *Chapter 5* the problem of paradoxical haemic metastasis is considered. According to this investigation it is at the utmost such a rarety, that „explanations" can be of only minor importance. Most important is a p p a r e n t l y paradoxical metastasis, caused by the existence of small, undiscovered metastases in the lungs. The general opinion that carcinomas of prostate gland, mammary gland and thyroid gland have a preference for metastasis in the skeleton has been found to be true. According to the investigations of WALTHER the distribution of metastases in the skeleton is not influenced by the location of the primary tumour. Towards metastasis by way of the vertebral venous plexus — which is according to BATSON of special importance in carcinoma of the prostate gland — a reserved attitude is pleaded for.

In *Chapter 6* some problems of metastasis are discussed, such as the so-called „antiblastic" function of the spleen, „Virchow's rule", and the surgical curability of „solitary" metastases in organs.

In *Chapter 7* the peculiarities of fetal metastasis are examined, starting from the existing anatomical differences between the fetal circulatory system and the conditions after birth. Important are: *a*) the „short-circuit" of the pulmonary circulation by the way of foramen ovale and ductus Botalli; *b*) the fetal placental circulation, by the way of which tumour emboli are probably transported without being arrested and without giving rise to placental metastases; *c*) the ductus venosus Arantii, by way of which probably only few tumouremboli by-pass the liver, when haemic dissemination of fetal cancer takes place. Because of these factors fetal cancer is distinguished by the frequent occurence of metastasis in the liver. This applies not only to dissemination from the primary tumour, but also

acquired that fetal metastasis could be investigated preferably in neuroblastoma of the adrenal gland. Two types of metastasis are usually distinguished here: the „Pepper-type" and the „Hutchison-type". Arrangement of published cases according to age shows the connection of early death with metastasis in the liver in general, with extensive metastasis in the liver and with the „Pepper-type". These data give considerable support to the supposition that fetal metastasis has its own properties, which are determined by the anatomy of the fetal vascular system, and which are the main reasons for the formation of the „Pepper-type" of metastasis in neuroblastoma. Beside the types of metastasis mentioned in Chapter 2, which are taken from WALTHER, a „fetal vena-cava-type" is described in world and figure.

The chapter is concluded with a short discussion on genetic factors, present in the relation of metastasis between mother and fetus.

Section II deals with the special discussion of metastasies, startng from 1732 autopsy-records of the labaratory of pathology at Groningen. These cases are classified as *a*) certain cases of cancer (*Chapters 1 to 22*), *b*) cancer with uncertain diagnosis (*Chapter 23*) and *c*) tumour-like diseases of malignant character (*Chapter 24*).

In the introduction to this section the relative value of autopsy-findings is emphasized and account is given of the work-method followed.

Generally the chapters of Section II deal with the following subjects: facts not directly related to metastasis (§ 1), a short discussion on the routes of metastasis (§ 2) and the recorded extension (§ 3). Direct extension is mentioned briefly, full attention is paid to indirect extension. Relations of extension to age, sex, location and histology are studied and the figures of WALTHER are comparatively given. Some special facts are discussed: the „preference" of carcinoma bronchiale to metastasize in the brain and problems concerning gelatinous forms of this tumour (Chapter 1); metastasizing in „Virchow's lymph-node" and in the ovaries (Chapter 5); the location of metastases in the liver (Chapter 6); the intrahepatic extension of primary liver-carcinoma (Chapter 7); so-called „implantation-metastases" of the endocardium (Chapter 8); the metastasizing-properties of „typical" and „atypical" Grawitz-tumours (Chapter 10); a type of tumour of the thyroid gland, here designated as „carcinoma solidum alveolare fusocellulare" (Chapter 20); some interesting tumours of the adrenal gland, for instance a „malignant adenoma" in a boy of four months old, showing the „brewers-type" and some cases

of neuroblastoma, showing the „Pepper"- or „Hutchison-type".

In *Chapter 25* consideration is given to multiple primary malignant tumours and a survey of the studied cases.

Chapter 26 deals with the totaling of the collected data. Studied are:

a) the connection between sex and extension (no statistical significance);

b) the greater frequency of metastases in younger patients (significant);

c) the influence of the primary location on the extension (table 85), the frequency of lymph node metastases (table 86) and of metastases in organs (table 87), comparing the accuracy of the collected data with those of WALTHER; the differences between the mentioned types of haemic metastasis; the „standardsequence", according to the autopsy-material of Groningen;

d) the connection between histology and extension. In agreement with WALTHER, data were obtained, according to which lymphatic (44%) and haemie (42%) dissemination are about equally frequent in carcinoma, while in sarcoma lymphatic (30%) dissemination is less and haemic (52%) dissemination more frequent. Coelomic dissemination was recorded in 20% of the cases of carcinoma and in 16% of the cases of sarcoma. In undifferentiated carcinoma, metastasis is more frequent than in differentiated carcinoma (significant).

A list of numbers of the compiled autopsies concludes the thesis.