The Distribution of Metastases in the Liver

A Quantitative Postmortem Study

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Summary. Seventy-five livers with metastases were cut sagitally into 1 cm thick slices. A total number of 11,581 metastases sections was exactly mapped. There was an average of 154 metastases sections per liver. The average diameter of the metastases was 1 cm. 40% of the metastases reached to the hepatic surface, and 60% were invisible due to their deposition in the internal parenchyma. In 8% of the livers there were only superficial metastases (average 3.2 metastases), and in 12% were only deep metastases detected (average 2.6). The total number of superficial metastases increased with increasing diameter of the secondary tumors.

An approximately homogeneous distribution of hepatic metastases within the liver parenchyma has been demonstrated.

Key words: Carcinoma metastases – Liver neoplasms – Distribution of metastases

Introduction

The pathways of metastatic spread and the frequency of metastases in different organs are well known. According to Schwartz (1964), hepatic metastases may be expected in at least half of the patients in whom an organ drained by the portal vein is the seat of cancer. However, we have been unable to find any systematic analysis of the distribution of hepatic metastases. We do not know whether hepatic metastases are homogeneously distributed in the liver parenchyma, or whether the hepatic surface is favored as is suggested by autopsy findings (Pack and Brasfield (1955)). Knowledge of the distribution of hepatic secondary tumors is of practical importance at laparoscopy, since it would be very useful to infer the likely features of the whole liver from inspection of a part of hepatic surface. It could be very useful for the surgeon intending to resect a solitary or a very few visible hepatic metastases to know something about the distribution of hepatic metastases.

There is at least a theoretical interest in knowing the distribution of metastases not only in the liver, but also in other organs.

Materials and Methods

A series of 127 liver autopsies performed at the Institute of Pathology, University of Düsseldorf was studied in patients with carcinoma. Hepatic metastases were present in 75 livers. Cirrhotic livers with metastases were excluded because we do not know whether hepatic cirrhosis influences the distribution of metastases in the liver.

The livers were frozen (to $-6°$ C), and cut sagitally into slices of 1 cm thickness. The slices were covered with a sheet of glass. The outlines of the slices and the contours of each metastasis were outlined exactly upon the pane of glass, from which they were transferred to parchment paper. We thus obtained an exact documentation of all metastases in the sections (Fig. 1). In addition, all metastases which were visible at the surface were separately registered and the diameter of all metastases was evaluated.

To extend our knowledge of the distribution of hepatic metastases in the liver parenchyma sections of liver slices of 30 livers with more than 50 metastases were investigated. We took an approximately rectangular area from three slices in the center reaching from the upper to the lower surface of the liver. The areas were subdivided into five approximately identical parts (Fig. 2). We determined the number of metastases in each area. The metastases were always assigned on the basis of the site of the center of metastases.

Next we wanted to get an idea about the weight relation of liver tissue mantles of various thicknesses to the remaining internal parenchyma. We cut 12 livers of different shapes and sizes into 1 cm thick slices, and separated 1 cm thick tissue mantles from 6 livers and $^1/_2$ cm thick mantles from the other 6 livers. We determined the average weight of the 1 cm and of the $^1/_2$ cm thick superficial hepatic mantle and related it to the remaining internal parts of livers.
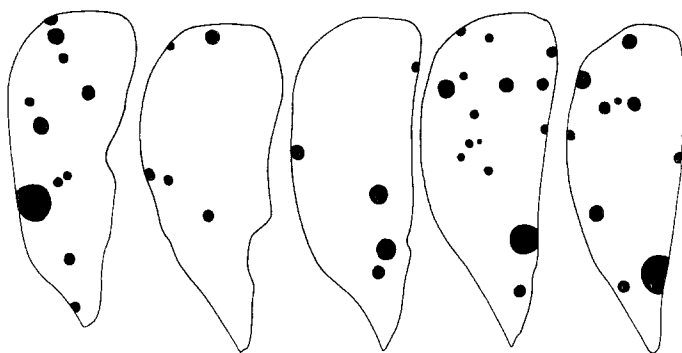

Fig. 1. Documentation of sectioned metastases in liver slices (S.Nr. 1015/79)
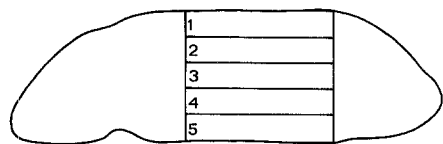

Fig. 2. Representative section of a liver slice, subdivided into five approximately identical zones

Results

1. Total Number of Cut Metastases in the Slices of the Individual Livers

Altogether we found 11,581 sectioned metastases in the 75 livers, 154 per organ in the average. Nearly half of the examined livers (35) had 1–50 sectioned metastases, 21 less than 10, 15 less than 5. In 7 cases we found only one metastasis. Three livers showed much more than 1,000 sectioned metastases.
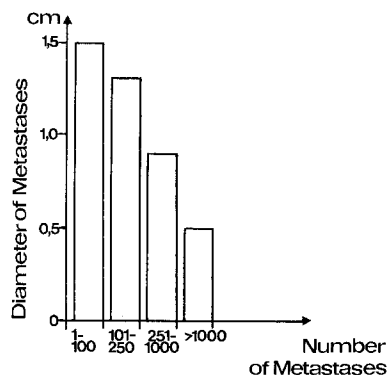
Fig. 3. Diameter of metastases in relation to the total number of metastases

The method used in this study enabled us to find the total number of metastases visible macroscopically in each 1 cm thick liver slice, but not the precise number of metastases, because big metastases are sometimes cut more than once and small metastases sometimes do not appear in the surface of the slice. The total number can be roughly estimated when the average diameter is known.

2. Average Diameter of Metastases

Most of the metastases were approximately round, except for confluent metastases. Superficial metastases often appeared to be hemispherical.

The mean diameter of all 11,581 metastases sections was exactly 1.0 cm. In 47 livers (62%), the average diameter was between 0.4–2.0 cm. In 10 livers, it was more than 2 cm.

3. Diameter of Metastases and Number of Metastases

Four groups were formed (Fig. 3) in order to check the relation between diameter and number of metastases. We found a continuous diminution of average diameter with increasing number of metastases.

4. Number of Metastases Visible at the Surface

Forty percent of the 11,581 cut metastases reached the hepatic surface and 60% were invisible due to their position in the internal parenchyma. Taking the average percentage in each individual liver as a basis for the calculation we arrived at 45% superficial cut metastases. Figure 4 shows the percentage of superficially cut metastases. The somewhat skewed distribution curve reaches a maximum at values between 40–49%. This histogram contains only livers with both superficial and deep metastases. In 6 livers (8%) we found only superficial metastases. One of these livers had 9 sectioned metastases (of a squamous epithelial carcinoma of the lung), one had 4, two had 2, and two showed only 1 metastasis. The average was 3.1 metastases per liver. The average diameter was 0.9 cm.
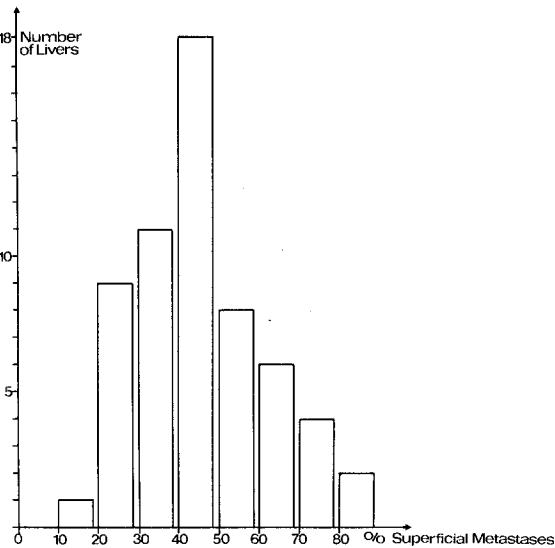
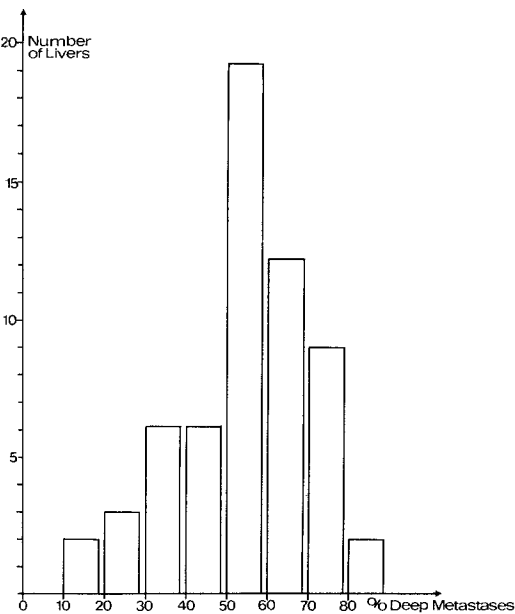**Fig. 4.** Percentage of superficial metastases in the individual livers

Fig. 5. Percentage of deep metastases in the individual livers

5. Number of Deep Metastases

Figure 5 shows the distribution for each liver. We also found a skewed distribution curve, the maximum was at 50–59%. 9 livers showed exclusive deep metastases (one liver with 9 metastases of a carcinoma of the bladder), the average was 2.6 cut metastases, the average diameter was 0.7 cm.
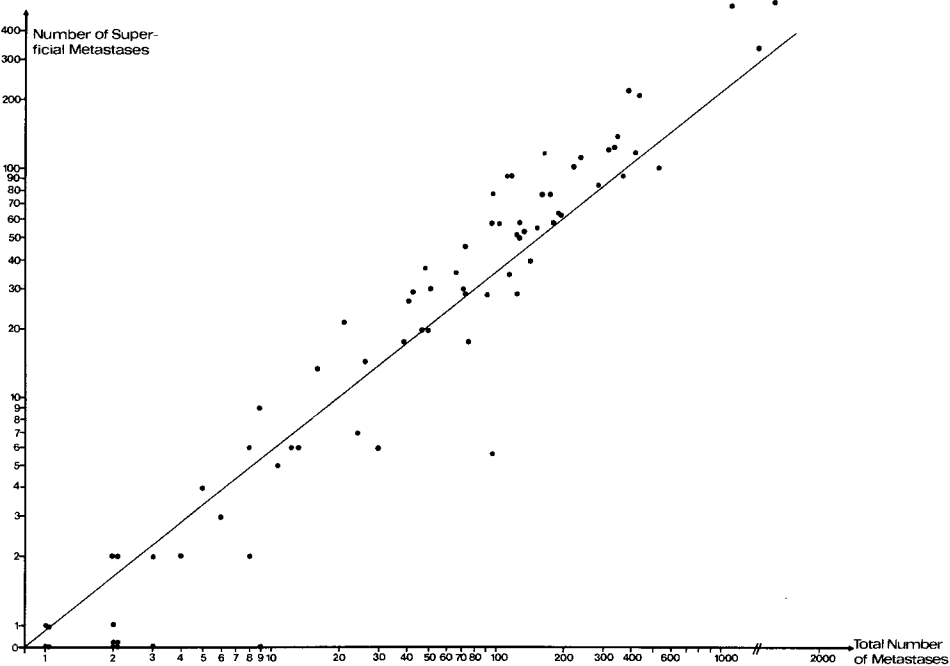
Fig. 6. Superficial metastases in relation to the total number of metastases in the individual livers (1 point = 1 liver)
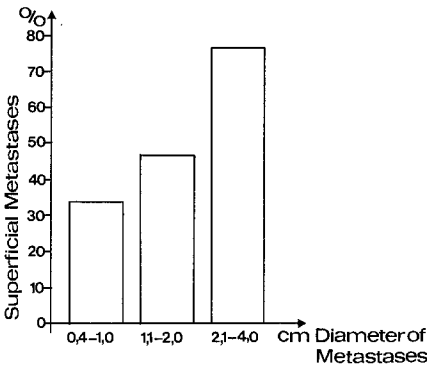

Fig. 7. Percentage of superficial metastases in relation to the mean diameter of metastases

6. Superficial Visible Metastases in Relation to Total Number

Figure 6 shows the results. We found an approximately linear increase in superficial metastases dependent on the total number. The rise of regression curves was about 38°.

7. Superficial Metastases in Relation to Diameter of Metastases

Not only the total number influences the quantity of superficial metastases but also their size. This is demonstrated in Fig. 7, in which the percentage
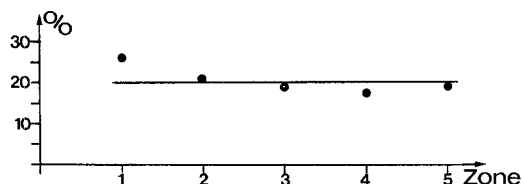
Fig. 8. Distribution of metastases in the 5 zones of the representative liver sections, see Fig. 2

of superficial metastases is registered in relation to the diameter. The increase in superficial metastases with increasing diameter is evident. 33.7% of superficial metastases were small (diameters between 0.4–1.0 cm), and 76% of superficial metastases were large (diameters between 2.1–4 cm) which is statistically a highly significant difference ($P < 0.001$).

8. Topographic Distribution of Metastases Within the Liver Parenchyma

Up to now we have considered only superficial and deep metastases. We shall now examine the topographic distribution of metastases in the different zones from the upper to the lower surface in the selected segments of the liver (Fig. 2). This evaluation is based on 780 sectioned metastases in 30 livers, each with more than 50 sectioned metastases. Figure 8 shows their distribution in the 5 equal sized zones. The mean values of zone 2–5 show good agreement between 18.2–19.5%. We found 25.8% secondary lesions in the superficial zone (zone 1). This difference was not statistically significant. Thus there was an approximately homogeneous distribution of metastases in the different zones of the liver.

9. Weight of Liver Mantle and of Internal Parenchyma

The average percentage weight of a 1 cm thick superficial liver mantle, taken from 6 livers between 1,000–2,500 g, was 46%. We found an average of 31.1% for an $^1/_2$ cm thick superficial tissue mantle.

Discussion

Systematic analyses of the distribution of hepatic metastases are still lacking. Pack and Brasfield (1955) and some other authors suspected preferential colonization of the hepatic surface by metastases, but they did not document it. In the present study we found an approximately homogeneous distribution of the hepatic metastases. There was no significant predilection for any part of the liver. We found an average of 40% superficial metastases. At first sight, this value seems to be very high, but these superficial metastases are not only to be found directly under the hepatic capsule, which they rarely infiltrate (Josephson and Wallace (1978)). They extend into deeper parts of the liver mantle too. With an average metastasis diameter of 1 cm, as found in our material, all metastases with a center 0.5 cm or less away from the hepatic surface had to reach the surface.

An 0.5 cm thick superficial liver mantle is about 31.1% of the total liver mass. With a completely homogeneous distribution of metastases, this liver mantle should contain 31.1% of all hepatic metastases. On average, these secondary lesions should reach to the hepatic surface. This value (31.1%) is not far from the 40% superficial metastases we found. With regard to metastases, very near to the surface and perceived by the naked eye as superficial, the difference is even smaller. (The 1 cm thick superficial liver mantle amounts to about 46% of total liver mass). These findings show a very slight preference for superficial liver parenchyma by hepatic metastases. However, there is no significant difference from a homogeneous distribution.

A nearly homogeneous distribution of metastases over the whole hepatic parenchyma would correspond well with the concept of a homogeneous blood supply to all parts of the liver.

The average diameter of metastases in our material was 1.0 cm. This corresponds well with the observation that most metastases in the liver are smaller than 2 cm, as many authors found at autopsy (Hugh (1958); Ozarda and Pickren (1962); Sabitzer et al. (1974)).

Our finding of decreasing average of metastases with increasing total number of metastases is easily to be understood, because the volume of the liver is limited. The increasing number of superficial metastases with increasing diameter of metastases is also easily explained, namely, each metastasis which has unimpeded growth must finally reach the surface of the liver.

It is very difficult for the clinician to detect hepatic metastases smaller than 1.0 cm preoperatively. The limit of scintigraphic detection of metastases is a diameter of more than 3 cm. The best method for detecting hepatic metastases of about 1 cm diameter is liver scanning with computer tomography.

At laparoscopy, about 40% of the hepatic surface is visible (Mc Bride (1979). This area is sufficient if many nodules are present. However, if there are only a few metastases, the possibility of false negative results from laparoscopy increases. Inspection during surgery can also bring false negative results. In 12% of our liver collection, metastases were located only in the internal parenchyma (average value: 2.6 sectioned metastases). If only a few superficial metastases are to be seen, it should be expected that there are more in the invisible depth of the organ. In 8% of our cases, we found only superficial metastases, with an average of 3.2 metastases. The chance of resecting the total number of hepatic metastases by resecting all visible superficial liver metastases is very small, since we found ratio of 2:3 between superficial and deep metastases. We observed this in our material with solitary superficial metastases. Occasional solitary metastases, at most 4 single metastases restricted to one lobe of the liver, may be removed surgically in colon carcinoma (Brunschwig (1963); Flanagan and Foster (1967); Bengmark and Hafström (1969); Foster (1970); Nielsen et al. (1971); Wanger (1974); Hegemann and Mühe (1974)).

Unfortunately it is not possible to say anything definite about the presence of metastases in the internal parenchyma of the liver when a very few superficial metastases are detected. Altogether, our collection includes 21 livers with less than ten metastases. In 6 livers (28.5%) there were exclusively superficial metas-

tases, in 9 livers (43%) metastases were located only in the inner parenchyma, and both surface and the inner parenchyma were affected in 6 cases (28.5%).

Livers in which there were also deep metastases predominated in our material even when there were only 2 superficial metastases (in 5 livers altogether). In three livers which apparently showed only 1 superficial metastasis, 2 livers had a solitary metastasis, and in the third a deep metastasis was detected.

Up to now only Ozarda and Pickren (1962) have presented data on superficial and deep hepatic metastases in a small-scale study. They found only deep metastases in 10.6% and only superficial metastases in 18.0%. No information on methods or the distribution of hepatic metastases was presented.

It has been shown by the present study that a simple method allows an insight to be obtained into the distribution of carcinoma metastases in an organ. This method should be applicable to corresponding studies of different organs, for instance the lungs or the kidney.

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