Symptoms in Cancer of the Pancreas

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The differential diagnosis of patients suffering from cancer of the pancreas covers a large part of abdominal medicine. A patient with obstructive jaundice is a potential candidate for cancer of the head of the pancreas, while many patients with unexplained upper abdominal symptoms might have cancer of the body or tail. Textbooks are seldom able to indicate at what stage of a disease symptoms become manifest. It is not surprising that symptoms such as loss of weight, pain, and vomiting in patients with pancreatic cancer are found just before their death. Furthermore, most lists of clinical symptoms are compiled by surgeons who, unfortunately, are not the first doctors to see the patients (Warren et al., 1967; Webster, 1975; Collure et al., 1974; Diamond and Fischer, 1975). What are the early symptoms of pancreatic cancer? Their recognition may make earlier diagnosis possible and may decrease the delay between first symptoms and diagnosis in a disease that has been described as one of the unsolved problems of clinical medicine (Khankanion et al., 1977). Despite some advanced diagnostic techniques (Dimagno et al., 1977; Fitzgerald et al., 1978) there is still no improvement in the five year survival figure.

Definitions

According to the Dutch dictionary, a symptom is ‘every phenomenon that has any significance for the recognition of a disease’. Thus, no distinction is made between a subjective sensation and an objective sign. A sign is just one of the symptoms. But a glossary is needed for the understanding of different kinds of sensation that signal to the patient that something is wrong. Thus, we distinguish first, presenting and admission symptoms. We proposed the following definitions—

First symptoms: Those symptoms that are retrospectively interpreted as the first manifestations of the disease.

Presenting symptoms: Those symptoms that bring the patient to his GP.

Admission symptoms: Those symptoms that bring the patient to the hospital.

First symptoms are of importance because better interpretation could lead to earlier diagnoses. Though studies have been published on the prognostic significance of first symptoms in colorectal cancer (Khankanion et al., 1977), melanoma (Einhorn et al., 1974) and non-Hodgkin lymphoma (Cabanillas et al., 1978), no such investigation was found for pancreatic carcinoma.

Material and Methods

In our hospital we have surveyed retrospectively the case histories from 1976 back to 1970 of 60 consecutive medical or surgical patients with histologically proved pancreatic carcinoma. Sex incidence was equal. The average age was 70, though some patients were under 50 years old. The location of the tumour was in the head of the pancreas in 78 per cent (47 patients) and in the body/tail in 20 per cent (12 patients) of the cases. One patient had cancer of the ampulla of Vater and is included with those who had cancer of the head of the pancreas.

Results

First Symptoms

Table 1 gives the most striking first symptoms in these 60 patients. Pain is predominant. In the beginning the patient reports a vague dull sensation in the right or left hypochondrium or in the mid-epigastrium. It bears no relation to meals or the kind of food eaten, and is most intense during the night. Lying down intensifies the pain, which causes the patient to adopt bizarre postures in order to obtain relief. It may radiate to the back, like the pain of patients with cancer of the stomach, other retroperitoneal malignancies or an aortic aneurysm. It might resemble the kind of pain in benign diseases of the pancreas, though a relationship to meals is more

| Symptom                        | Tumour of the head (48 patients) | Tumour of the body/tail (12 patients) |
|--------------------------------|----------------------------------|--------------------------------------|
| Loss of weight                 | 33  70                           | 10  85                                |
| Pain in abdomen                | 37  79                           | 10  85                                |
| Jaundice                       | 8   17                            | 0   0                                 |
| Nausea and vomiting            | 21  45                           | 4   33                                |
| Constipation                   | 13  28                           | 7   58                                |
| Bad taste                      | 4   9                            | 1   8                                 |
| Mental changes                 | 12  26                           | 2   17                                |

Table 1. First Symptoms.
probable in these cases. Chauffard (1908) described the pain as violent, with 'constriction in a corset'. We have the impression that this violent pain is a relatively late symptom. The change from dull to severe pain may be caused by an extension of the tumour into the posterior parietes around the coeliac axis, with invasion of its associated neural plexus (Warren et al., 1968). Like this pain, jaundice occurs relatively late, even in cases of cancer of the head of the pancreas. Only 17 per cent of the patients had jaundice as a first symptom, which equalises the symptomatology of first symptoms in head and body/tail cancer. Similarly, loss of weight is equally frequent in both groups. For practical purposes, we describe loss of weight as the loss of one stone (6.35 kg) in two months without intentional dieting. Nausea also scores heavily, with 40 per cent. The mental alterations show, remarkably enough, a higher percentage in the head group. We know of some psychiatric studies of these so-called functional complaints (Savage et al., 1952; Fras et al., 1967) which we often dismiss as hysterical (Hulst, 1940). To our surprise, a relatively frequent symptom of body/tail cancer turns out to be constipation (58 per cent in our study). We once observed a case of constipation leading to sub-ileus. A bad taste in the mouth was often a first symptom. The possibility that the bad taste was caused by metastases in the liver could not be ruled out. Rare symptoms are watery diarrhoea with hypokalaemia and achlorhydria (Schmitt et al. 1975), which are probably signs of hormonal activity, and steatorrhoea, night sweating and flatulence. In our series, thrombosis of venous or arterial vessels was not observed as a first symptom; it has been given much more attention as a symptom of pancreatic cancer than it seems to deserve (Gore, 1953; Sproul, 1938; Lieberman et al., 1961).

At the end of this enumeration of first symptoms, we want to emphasise the point of cell kinetics. How long should a tumour grow to reach a volume of one cubic centimetre? Do these 10 milliard cells, as in breast cancer, need 30 multiplications and does one multiplication take 100 days? Is their presentation caused by influence on systemic metabolism, on hormonal activity, or on local invasion?

Presenting Symptoms

In this study we were not able to distinguish the presenting symptoms from the first and admission symptoms.

Admission Symptoms

The delay between first symptoms and admission is extremely long and probably one of the main reasons for the inoperability of the pancreatic tumour. Our figures (Table 2) are identical with other publications, but certainly too optimistic, probably because of the retrospective character of all these studies. The symptoms that led to admission of the patient to hospital are summarised in Table 3. Jaundice has become the commonest symptom in cancer of the head. This form of obstructive jaundice may in some cases be intermittent. Fever is a frequent symptom, in rare cases caused by inflammation of the gallbladder.

Table 2. The delay between first symptoms and admission.

| Delay (weeks) | Tumour of the head (48 patients) | Tumour of the body/tail (12 patients) |
|--------------|----------------------------------|-------------------------------------|
| 0 — 2 weeks  | 2 cases (4.4%)                   | 0 cases (0%)                        |
| 2 — 4 weeks  | 6 cases (12.8%)                  | 1 cases (8.3%)                      |
| 4 — 8 weeks  | 11 cases (23.5%)                 | 5 cases (25%)                       |
| 8 — 16 weeks | 18 cases (37.9%)                 | 9 cases (58%)                       |
| 16 — 32 weeks| 7 cases (14.9%)                  | 4 cases (33.3%)                     |
| 32 — 64 weeks| 3 cases (6.5%)                   | 1 cases (8.3%)                      |

Table 3. Admission Symptoms.

| Admission symptoms | Tumour of the head (48 patients) | Tumour of the body/tail (12 patients) |
|--------------------|----------------------------------|-------------------------------------|
| Jaundice           | 39 cases (83%)                   | 0 cases (0%)                        |
| Pain in abdomen    | 16 cases (34%)                   | 8 cases (67%)                       |
| and/or back        |                                  |                                     |
| Nausea             | 13 cases (28%)                   | 4 cases (33%)                       |
| and vomiting       | 4 cases (9%)                     | 5 cases (42%)                       |
| Loss of weight     | 5 cases (11%)                    | 2 cases (17%)                       |
| Fever              |                                  |                                     |

Table 4. Physical Signs.

| Physical signs     | Tumour of the head (48 patients) | Tumour of the body/tail (12 patients) |
|--------------------|----------------------------------|-------------------------------------|
| Jaundice           | 39 cases (83%)                   | 1 cases (8%)                        |
| Hepatomegaly       | 32 cases (68%)                   | 9 cases (75%)                       |
| Palpable           |                                  |                                     |
| gallbladder        | 21 cases (45%)                   | 0 cases (0%)                        |
| Palpable mass      | 2 cases (4%)                     | 6 cases (50%)                       |
| Thrombophlebitis   | 1 case (2%)                      | 1 case (8%)                         |
| Ascites            | 3 cases (6%)                     | 1 cases (8%)                        |

The clinical picture (Table 4) shows a liver enlarged either by metastases or by biliary compression and enlargement of the gallbladder. A mass was palpable—in 50 per cent of body/tail tumours, sometimes accompanied by a short systolic murmur in the left hypochondrium (Serebro, 1965), as in cases of renal artery stenosis, aortic sclerosis and gross splenomegaly. This bruit is caused by compression of the splenic artery, while narrowing of the splenic vein is responsible for enlargement of the spleen. Neither vascular sign was encountered in our series but we realise that these features are found more frequently when they are specifically looked for. Furthermore, our series had no controls; we do not know what differential value some of the symptoms have in relation to other abdominal diseases.
Discussion

As first symptoms we found the triad: loss of weight, vague abdominal pain, sometimes radiating to the back, and nausea. There was no significant difference in the symptomatology of early cancer of the head and of the body/tail of the pancreas. A patient with this triad should be considered as a potential candidate for carcinoma of the pancreas, especially when there are risk-factors like smoking, biliary reflux, chronic and/or hereditary or calcifying pancreatitis and, perhaps, diabetes mellitus (Wynder et al., 1973; Mainz and Webster, 1974). The patient should have the benefit of all sophisticated modern diagnostic methods.

Aware of our ignorance of many simple points in clinical medicine, of the importance of the study of first symptoms in promoting an early diagnosis, and aware of the line of thinking called 'decision making in medicine' (Lindley, 1975), we hope that a prospective investigation, in which more attention is paid to first symptoms than was done in the past, will shed some light on the problem of the relationship between first symptoms, early diagnosis and prognosis.

References

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Chauffard, M. A. (1908) Bulletin de l'Académie de Médecine (Paris), 60, 242.

The Empire's Lepers

A mid-Victorian interest in leprosy seems strange for a College founded by physicians living within seven miles of Charing Cross. But the College's leprosy committee came to realise that the disease was as far-flung as the British Empire. The Governor of the Windward Islands approached the Colonial Secretary, the Duke of Newcastle, in 1862, to suggest an inquiry into the prevalence of leprosy in Her Majesty's colonies, as he thought that the number of cases was increasing. The Under-Secretary of State wrote to the College in May of that year. 'His Grace is disposed to think that advantage would result from the adoption of Governor Walker's suggestion . . . and should be obliged for any assistance which they may be enabled to afford him in order to the subject being put in train.' Accordingly the College formed a leprosy committee with Dr Milroy as secretary. They framed a long interrogatory with 17 main questions that was sent by the Colonial Office to all parts of the empire, from Bermuda to the Cape of Good Hope, from New Brunswick to Cairo and on to Hong Kong with a mass of reports to come from India. The key question was whether or not leprosy was contagious. No, said the College from its first replies, it was probably an hereditary disease. If that is so, said the Duke of Newcastle, what about the 'questions respecting laws and regulations for the restraint or seclusion of lepers founded on the popular notion of the disease being contagious?' The College was willing to support His Grace's intention to repeal laws affecting the personal liberty of lepers. A report of over 300 pages was published by the College in 1867, collating all information received, in elegant style and great detail. In 1875 the Colonial Office, but not the College, was impressed by Hansen's account of the bacterial nature of leprosy and asked if the College had changed its opinion that leprosy was not contagious. The College committee held to their expressed opinion and continued to do so, with decreasing certainty, until 1897 when they accepted that leprosy was a communicable disease.