Chronic pancreatitis in India: the changing spectrum

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The spectrum of chronic pancreatitis in India is changing, with increased occurrence in older patients, incidence of milder disease including milder diabetes, increasing longevity, and increasing association with alcoholism and smoking

A 58-year-old man was admitted to our hospital with abdominal pain. He had a history of alcohol intake of >80 g a day for more than 30 years. His blood sugar was within normal limits, while his serum amylase and lipase were elevated. There was no history of steatorrhoea and the faecal fat excretion was within normal limits. Computerised tomography of the abdomen revealed the presence of small ill-defined calculi in the pancreatic ducts with speckled margins. Endoscopic retrograde cholangio-pancreatography showed mild ductal dilatation. With this clinical presentation and imaging characteristics, a diagnosis of alcoholic chronic pancreatitis (ACP) was made.

This is the spectrum of chronic pancreatitis patients I and my colleagues in gastroenterology are now seeing in India, which is in stark contrast to the chronic pancreatitis patients I saw as a trainee 25 years ago. Has the spectrum of chronic pancreatitis in India changed?

CHARACTERISTICS OF CHRONIC PANCREATITIS

Chronic pancreatitis is a condition characterised by irreversible destruction and fibrosis of the exocrine parenchyma, leading to exocrine pancreatic insufficiency and progressive endocrine failure resulting in diabetes. ACP is the most common type of chronic pancreatitis seen in the western world, while in tropical countries like India, tropical chronic pancreatitis (TCP) was once far more common.

TCP, a juvenile form of chronic calcific non-alcoholic pancreatitis and seen almost exclusively in the developing countries of the tropical world, has a characteristic presentation. Some of its unique features are younger age at onset, presence of large intraductal calculi (hallmark for the diagnosis of TCP), an accelerated course of the disease leading to diabetes and/or steatorrhoea, and a high susceptibility to pancreatic cancer.¹⁻⁴

Over the years, chronic pancreatitis in India has shown a change, with an increased occurrence in older patients, incidence of milder disease including milder diabetes, increasing longevity, and increasing association with alcoholism and smoking.

CHANGING DISEASE SPECTRUM

Are we seeing a change in the spectrum of the disease? A recent article by Balakrishnan *et al*, comparing the cohort of chronic pancreatitis patients two decades before and now, brought out some very interesting observations. The disease now occurs in older people, with both the age at onset and age at presentation being nearly a decade later now than in the previous cohort.⁵ The presentation of the disease has become more heterogeneous, with only about 10–15% of patients presenting with the classical picture of TCP. Currently, around 33% of patients presenting with chronic pancreatitis have ACP. Quite interestingly, TCP has recently been reported from regions that fall outside the “tropics”.⁶ While the frequency of classical TCP is decreasing, pancreatitis due to alcohol, smoking and probably other environmental toxins is on the rise.

In fact, the recent consensus report on the prevalence of chronic pancreatitis in the Asia-Pacific region highlighted the high prevalence of chronic pancreatitis in South India, where our centre is situated, to the tune of 114–200/100 000 population in contrast to 4.2/100 000 population in Japan.⁶

With recent reports of autoimmune pancreatitis (AIP) occurring in India—a condition which usually occurs in older patients (according to studies in the Japanese literature)—it would appear that the spectrum of chronic pancreatitis has definitely changed in our country.⁷ There had been no reports of AIP from India before this study, which could be due more to failure to recognise it as a clinical entity rather than the rarity of the

disease. However, now that AIP has been identified as a distinct clinical entity, and with increasing awareness of the condition, more and more reports of AIP can be expected in the future.

WHY HAS THE DISEASE SPECTRUM CHANGED?

What could be the reason for this change in the spectrum of chronic pancreatitis in India? The genetic make up could not have changed over two decades. It is more likely that changes in environmental factors and dietary and lifestyle patterns have played a role. The fact that many developing countries are facing a silent epidemic of non-communicable diseases, a facet of the health transition associated with industrialisation, could be a contributing factor. In fact, in developing countries such as India, non-communicable diseases (for example, coronary artery disease, chronic kidney disease) are the major cause of mortality compared with communicable diseases, in stark contrast to the previous decade when communicable diseases were responsible for the bulk of mortality. This change in the spectrum of disease pattern highlights the change in the lifestyle and dietary factors in India over the past decade.⁸

Rice replacing cassava—one of the factors implicated in TCP—as the staple diet,⁹ and an increase in the alcohol consumption and smoking habits, may have contributed to the changing spectrum. In the study by Balakrishnan *et al*, 33% had alcoholic pancreatitis defined by a daily alcohol intake of ≥80 g for at least 5 years, which was almost three times higher than their previous cohort of patients two decades before.⁵ Also, the burden of industrialisation, exposure to xenobiotics and excess production of free radicals, which are known to damage cellular membranes¹⁰ and result in pancreatic injury, have contributed to this change.¹¹

ACP and TCP seem to be two ends of the spectrum of chronic pancreatitis, and we seem to be seeing a mix of patients who present with features overlapping both ends of this spectrum. Due to differences in aetiological factors, the clinical presentation of these two conditions shows some differences. However, between these extremes lie patients with diverse intermediate presentations, including the so-called idiopathic pancreatitis and AIP. ACP is often caused not by alcohol alone, but also by co-factors such as smoking, diet and genetic influences. Similarly, in TCP, secondary co-factors such as alcohol, even in small quantities, smoking and other environmental toxins may play a role. Because of the interaction of so many factors, in a

particular patient more than one aetiological factor may operate in tandem and dominate, and their contributions may determine the final clinical presentation. Adding to this presentation are those patients with AIP who present with no or only mild symptoms and obstructive jaundice similar to patients with pancreatic carcinoma, thus contributing further to the diversity of clinical presentation of chronic pancreatitis in India.

VARIABILITY IN PRESENTATION

The variability in presentation cannot be explained by genetic factors alone. In a recent study SPINK1 mutations were observed in 47% of TCP patients.¹² Mutations in SPINK 1 were observed in a majority of ACP patients too.¹³

There are also some reports of the existence of a "subclinical pancreatopathy" in persons living in developing countries¹⁴; the pancreatic juice in healthy Indian subjects has low enzyme levels and high calcium and lactoferrin levels, making them more susceptible to inflammation. Balakrishnan *et al* highlighted that the pancreas, which is already conditioned by subclinical pancreatopathy with underlying genetic influences in the form of SPINK mutations, might succumb to a second "hit" when exposed to dietary or environmental toxins, alcohol or smoking, that cause injury to the gland directly and through oxidant stress.⁵

Whereas the classical TCP seems to be on the decline, we can expect to see, in the coming years, a rapid rise in so called idiopathic chronic pancreatitis due to the interaction of many factors, with clinical presentation overlapping both TCP and ACP. Chronic pancreatitis is now associated with, or secondary to, a variety of toxic insults to the pancreas, including alcohol, smoking, environmental and dietary toxins, and infections, and further reports on the occurrence of AIP in India can be expected in the future.

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