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FOURTEEN PERSONAL CASES OF PNEUMOCYSTIS CARINII PNEUMONIA*

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IN A RECENT PAPER[64] we reported a personal series of 13 Canadian cases of *Pneumocystis carinii* pneumonia. However, as the cases in this paper were discussed strictly from the viewpoint of pathological anatomy, we consider it worth while to give a description of the clinical side of the picture and to correlate it with our pathological findings. We have been able to add a fourteenth case to our series since then (Case 14 in Table I).

As is now widely known, the disease has been frequently observed in Europe (over 2000 cases reported) but until recently was thought to be nonexistent in Canada. However, after a detailed review of the autopsy material from Ste. Justine Hospital, Montreal, from the year 1927 on (5102 files were restudied and 3186 lungs were re-examined histologically for this purpose), we have found two cases dating as far back as 1930. Other cases were seen later in the reviewed material, and four were personally autopsied by the author (Cases 8, 9, 12 and 13, Table I). In addition to the cases encountered at Ste. Justine Hospital one case was found in the old autopsy material of the Montreal Children's Hospital (Dr. F. W. Wiglesworth) and this goes back to the year 1934. Another quite recent case was observed at Notre-Dame Hospital, Montreal (Drs. L. C. Simard and S. Lauzé). A third typical case was very recently diagnosed by Dr. J. P. Thériault at Maisonneuve Hospital, Montreal. The last three cases are added to our series by kind permission of the respective pathologists. Thus our series consists of the 14 cases shown in Table I.

TABLE I.—OUR SERIES OF 14 CANADIAN CASES OF PNEUMOCYSTIS CARINII PNEUMONIA.

Case number	*Sex*	*Prematurity*	*Date of death*	*Age at death*	*Autopsied at*
1.	F	Yes	26/ 5/1930	2½ months	Ste. Justine Hospital
2.	F	No	26/10/1930	2½ "	" "
3.	M	?	29/ 8/1935	2½ "	" "
4.	M	No	1/11/1936	4 "	" "
5.	M	Yes	27/ 7/1941	3½ "	" "
6.	M	Yes	30/ 1/1947	2½ "	" "
7.	M	Yes	13/ 4/1947	3 "	" "
8.	M	No	28/ 7/1955	2 "	" "
9.	F	No	22/ 8/1955	3 "	" "
10.	F	?	4/ 8/1934	3 "	Montreal Children's Hospital
11.	F	?	28/ 1/1958	2 "	Notre-Dame Hospital
12.	F	No	20/ 1/1958	3 "	Ste. Justine Hospital
13.	F	?	12/ 2/1958	2 "	" "
14.	M	?	8/ 4/1958	2½ "	Maisonneuve Hospital

Nine of these cases were lent to Dr. J. W. Gerrard for statistical purposes, and have been mentioned in his recent article.[25] Since our last communication with him, we have been able to add another five cases to our list (Cases 10, 11, 12, 13 and 14). Other Canadian cases have been reported by Gagné and Hould (three cases), Gerrard and Moore (two cases), Donohue (two cases), Hoogstraten and McLandress (one case) and McMillan and Hamperl (one case). The total number of all known Canadian cases, including ours, is now thought to be 23.

In the present paper we shall summarize the case reports of our three most recent cases (Cases 12, 13 and 14), compare their clinical picture with that of the older ones in our series, and try to correlate our findings with the pathological aspects of the disease.

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CASE REPORTS

CASE 12 (Table I).—The patient, a girl aged 2 months, was admitted to Ste. Justine Hospital on December 18, 1957, for gastro-enteritis. A considerable degree of dehydration was noted at the time of admission. On December 23, 1957, the child developed an abscess on the left thigh. The abscess was opened on December 26 by two surgical incisions, and pus and blood were evacuated. On January 1, 1958, however, another abscess formed on the right thigh. On January 15, cough appeared suddenly, followed by slight dyspnœa; however, the chest was completely clear on auscultation. Gradually dyspnœa became more and more intense so that on January 19, the child showed very marked respiratory distress and cyanosis, still however with total absence of abnormal auscultatory signs. On January 20, the child was in fairly satisfactory condition while in an oxygen tent, but cyanosis reappeared instantly when she was taken out of the tent. Temperature remained fairly constantly between 99° and 100° F., except once when 102° F. was noted. The child died in cyanosis and respiratory distress on January 20.

The following laboratory tests were performed during life: Stool (December 19, 1957): presence of *E. coli* 0127 B 8; numerous Candida; Salmonella and Shigella negative. Electrolytes (December 19, 1957): chlorides 107.3; sodium 132; potassium 2.41; calcium 5.23 mEq./l. Urine (December 20, 1957): slightly opaque; density 1010; reaction alkaline; bacteria ++++; leukocytes ++; epithelial cells ++; mucus +.

Blood counts	*Dec. 19, 1957*	*Dec. 27, 1957*	*Jan. 1, 1958*
R.B.C.	2,820,000	2,550,000	4,500,000
W.B.C.	3450	9300	9000
Hb	67.2%	46%	90.6%
Colour index	1.2	0.9	1.0
Neutrophils	34%	43%	48%
Monocytes	1%	4%	8%
Lymphocytes	63%	46%	42%
Eosinophils	2%	7%	2%
Thrombocytes	197,400	not counted	not counted
Reticulocytes	——	1.1%	——

X-ray examination of the lungs revealed a finely mottled appearance with peripheral emphysema (Fig. 1).

Autopsy report.—The body was that of a female child, 52 cm. in length and 3 kg. in weight. The skin was very pale. There was no pneumothorax, and a small quantity of serous liquid was found in the pleural spaces. Very marked bullous emphysema was present on the lung surfaces. The lung itself was congested, and of whitish-pink colour, showing here and there a bluish hue. It was firm on palpation, and on section the tissue was quite homogeneous and whitish-pink, not without a certain resemblance to hepatic parenchyma. On the left superior lobe, a small brownish elevated spot was found which, on subsequent histological examination, proved to be a capillary angioma.

On opening of the trachea and of the great bronchi a considerable quantity of thick yellowish material was found, causing a partial obstruction of the airways. The mucous surface of the bronchi was somewhat roughened and here and there even granular.

The histological picture of the rest of the lung was that of a typical *Pneumocystis carinii* pneumonia (Fig. 2). In some regions of the lungs there were typical hyaline pseudomembranes.

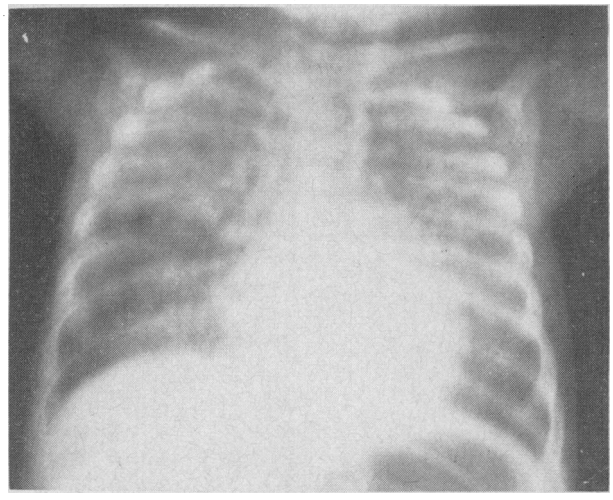

Fig. 1.—Chest radiograph of Case 12, showing finely mottled appearance of the lung parenchyma and presence of peripheral emphysema.

As regards the other organs, it is sufficient to note that there was a marked steatosis of the liver. No parasites were found in other organs.

CASE 13 (Table I).—The patient was an adopted child of female sex weighing 7 lb. 7 oz. (3.4 kg.) at birth. She was admitted to Ste. Justine Hospital on February 11, 1958, at the age of two months, for a dry, non-productive cough which had started about a week earlier. The cough was first paroxysmal in character and occurred several times a day, during which time the child seemed to suffocate. A symptom-free period of several days then followed, after which the cough reappeared and became so frequent that the child was in a constant state of suffocation and unable to take food by mouth. Temperature was normal all the time. On admission there were fairly severe cyanosis, an intense dyspnœa, some rhonchi over the left lung, and hypersonority over the right lung. Thoraco-synthesis to relieve possible intrapleural hypertension was attempted. This was followed by a subcutaneous emphysema. The radiograph taken at this time is reproduced in Fig. 3.

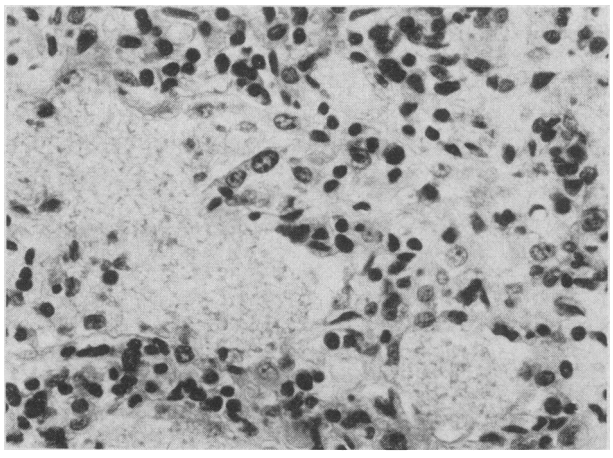

Fig. 2.—Histological preparation of the lung in Case 12, showing typical interstitial *Pneumocystis carinii* pneumonia with parasite-filled alveoli. Hæmalum-phloxin-saffron. × 500.

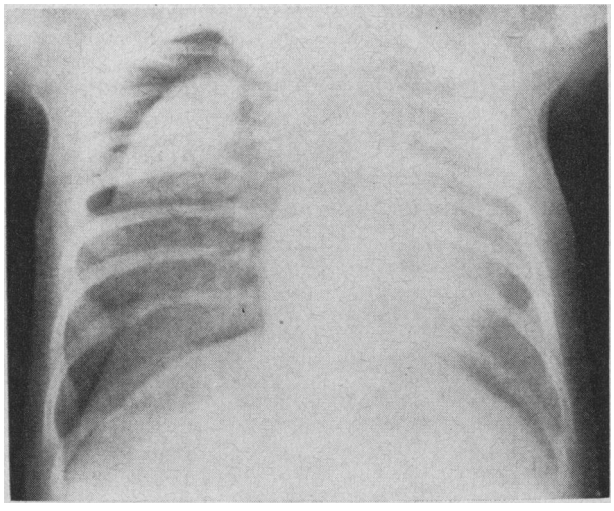

Fig. 3.—Chest radiograph in Case 13, showing a pneumothorax on the right side with marked consolidation of the right upper lobe. The right lower lobes and the left lung show the characteristic mottled appearance with peripheral emphysema.

The child died on the next day in deep cyanosis. Use of the oxygen tent did not seem to have any great effect on the course of the disease.

Autopsy report.—The body was that of a girl measuring 56 cm. in length and weighing 3.75 kg. On opening the thoracic cavity, a pneumothorax was noted on the right side. The surface of the right lung was covered by emphysematous bullæ, extending to the mediastinum and the pericardium. There was also bullous emphysema on the surface of the left lung. Both lungs, larger in size than normal, were very firm on palpation (especially the right superior lobe) and did not float on water. The surface of the lung parenchyma was pale pink and showed here and there bluish spots. Visceral pleura was smooth, and many small white-yellowish nodules, measuring from one to a few mm. in diameter, could be seen by transparency. On section, the gross appearance was the same except that in the consolidated portions there was marked "hepatization". Microscopically, the lungs presented a typical picture of *Pneumocystis carinii* pneumonia (Fig. 4).

No parasites were found outside the lung, and the pathological examination of other organs did not reveal any particular abnormalities. Their description is therefore omitted.

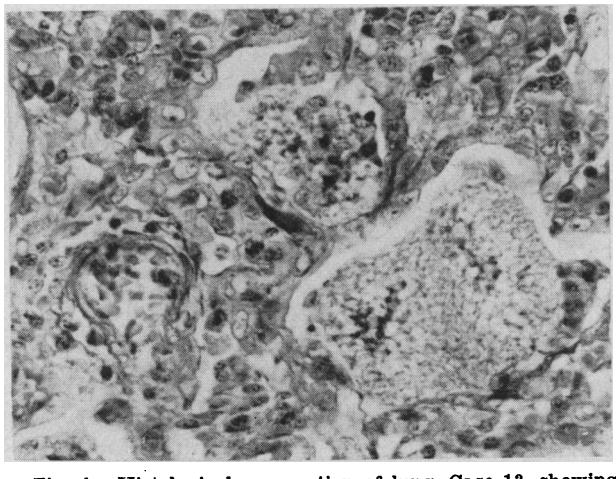

Fig. 4.—Histological preparation of lung, Case 13, showing typical *Pneumocystis carinii* pneumonia. Magenta after fixation in osmic acid (Marchi). × 500.

CASE 14 (Table I).—The patient was a boy, aged 2½ months, admitted to Maisonneuve Hospital for furunculosis, diarrhœa and athrepsia. Before admission, he developed a dry, non-productive cough, accompanied by anorexia and a certain degree of somnolence. Physical examination on admission revealed marked dyspnœa which was attributed to a left pneumothorax. Thoracosynthesis was performed and was followed by a marked remission of symptoms. However, two days later, the child died in cyanosis and respiratory distress.

At autopsy, typical Pneumocystis pneumonia was found. The histological picture of the lung is represented in Fig. 5. No *Pneumocystis carinii* was detected in other organs.

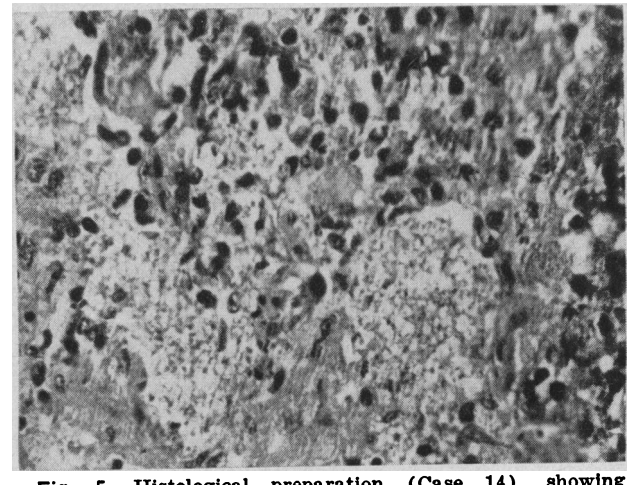

Fig. 5.—Histological preparation (Case 14), showing typical *Pneumocystis carinii* pneumonia. Masson's trichrome. × 500.

COMMENT

The three case histories presented reflect rather faithfully the clinical picture prevailing in the whole of our histologically proven series of 14 cases; from these the general features of the disease may be outlined as follows:

Both sexes are equally affected (7 males and 7 females in our series). Age incidence in our series lies between 2 and 4 months. Exceptionally, however, even adults may be affected (for example, the case of McMillan and Hamperl). The incidence of prematurity in our series approaches the 40% reported in the literature (Cases 1, 5, 6 and 7 were known to be prematures).

The role of debility (whether due to prematurity or to other causes) seems to be of major importance. In one of our cases (Case 5) this coexisted with a diffuse ulcero-purulent bronchitis, the *Pneumocystis carinii* pullulating among the purulent foci without even causing a characteristic plasma-cellular reaction (the only atypical case in our series). In another case (Case 4) *Pneumocystis carinii* pneumonia was associated with cytomegalic inclusion disease (Figs. 6 and 7). We will not speculate here on whether in this particular case the cytomegalic inclusion disease was responsible

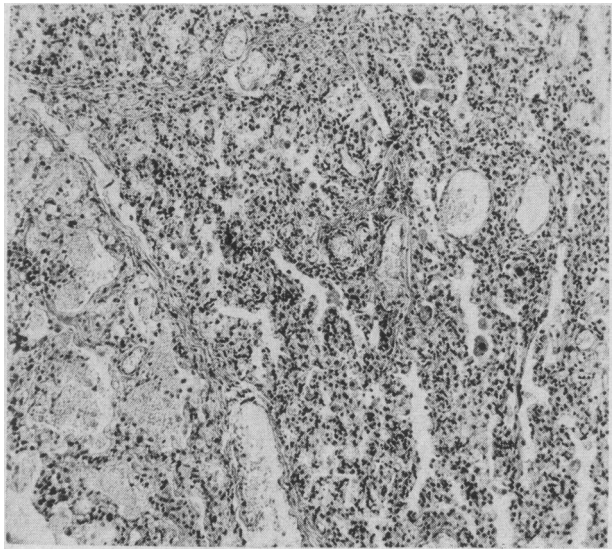

Fig. 6.—Histological preparation of lung (Case 4), showing coexistence of typical *Pneumocystis carinii* pneumonia (on left) and of typical cytomegalic inclusion disease (on right). Hæmalum-phloxin-saffron. × 125.

for the conditions necessary to the growth of the Pneumocystis, or whether the particular state of debility is equally necessary for the development of both diseases. To give a third example, in Case 12, the child may have been weakened by recurrent abscess formation and also by a pathogenic *E. coli* infection. One infant (Case 9) was debilitated by a central nervous system condition accompanied by spasmodic rigidity of all four extremities. One infant (Case 10) was suffering from pronounced thyroid deficiency, and another had diarrhœa and was suffering from furunculosis (Case 14).

The clinical picture is rather suggestive although by no means pathognomonic. The illness starts by a sudden onset of periods of dry, unproductive cough accompanied by signs of suffocation. Cyanosis and polypnœa are rather pronounced and there is marked sternal retraction. Oxygen usually brings relief, but symptoms recur as soon as it is discontinued. At no time is there a febrile state,

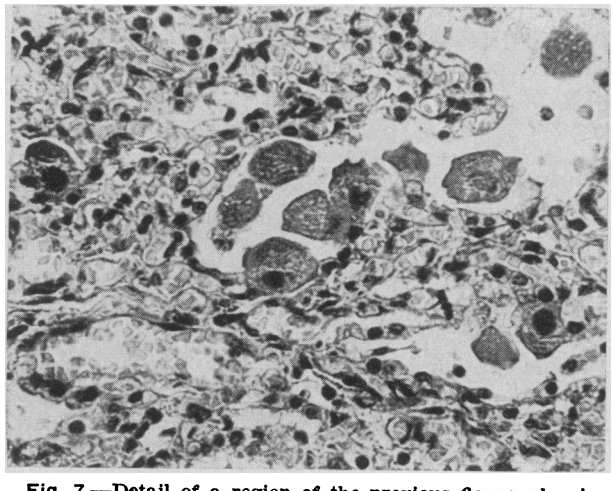

Fig. 7.—Detail of a region of the previous figure, showing typical cytomegalic inclusions. Hæmalum-phloxin-saffron. × 500.

except when the disease is complicated by another infection.

Often there seems to be a symptom-free period of a few days' duration after the initial onset of the disease, which in our opinion merits special consideration. Such a symptom-free period was definitely present in seven of our cases (Cases 2, 3, 4, 6, 7, 8 and 12 in Table I). It may also be detected by studying certain case histories in the literature (Ammich, Gerrard and Moore, Gagné and Hould), although its significance did not attract the attention of the respective authors. Should the symptom-free period prove to be a common feature in the course of the disease, it would become a valuable tool for its clinical diagnosis.

In explanation of this phenomenon, the following hypothesis might be suggested. The initial period of suffocation may be caused by œdema and formation of hyaline pseudomembranes (especially well represented in certain regions of the lung of our Case 12), perhaps due to some sort of hypergic reaction. The disappearance of the exudate associated with pseudomembranes might then explain the remission of symptoms for a few days. This would be followed by new periods of suffocation which now, however, are due to the direct obstruction of bronchi and alveoli by masses of the pullulating Pneumocystis. In both periods of the clinical course of the disease, there would thus be a purely mechanical obstacle to adequate oxygenation. Further observations are necessary in order to evaluate the exact incidence of the "symptom-free period".

Spontaneous pneumothorax is not rare, our Cases 13 and 14 being good examples.

In uncomplicated cases, the auscultatory signs over the lungs are absent or nearly so.

White blood cell counts are variable and for this reason cannot be depended upon; often they may be quite high (18,850 in Case 7; 23,000 in Case 9; 28,000 in Case 11) but sometimes they may be surprisingly low (8900 in Case 8).

The x-ray picture of the lung does not permit differentiation from other conditions such as milk-aspiration pneumonia. All we can say in a typical case is that there is absence of air in certain (usually peri-mediastinal) regions of the lung parenchyma, accompanied by emphysema in other (usually peripheral) regions.

The question of epidemiology is still unanswered, and our series was of no help in this respect, as we were unable to trace any definite relations between our cases.

The disease is said to end fatally in about 40% of cases. This, it seems to us, is impossible to establish, for there is no way of making an absolutely positive diagnosis during life (except in cases where a needle biopsy of the lung is

performed*). The complement fixation test (Barta) has still to be perfected to give absolutely reliable results. Non-fatal cases certainly do exist, and it is left to the ability of clinicians to seek them out, to learn to make a positive diagnosis during life, and then of course to find a specific treatment.

SUMMARY

Clinical histories of our three most recent cases of *Pneumocystis carinii* pneumonia are commented on and compared with findings in the whole series of our 14 Canadian cases.

Correlation of clinical features and pathology of some aspects of the disease is attempted; the possible diagnostic importance of a commonly occurring symptom-free period of a few days after the initial onset of the disease is stressed.

I wish to thank Professor J. L. Riopelle for his kind interest in this paper and for his valuable advice in its preparation.

I am indebted to Drs. F. W. Wiglesworth, L. C. Simard, S. Lauzé and J. P. Thériault for offering me their cases to be added to this series.

ADDENDUM

Since this paper was submitted for publication, we have autopsied still another typical case at Ste. Justine Hospital, that of a boy who died on June 24, 1958, at the age of 2½ months. This brings the number of cases in our personal series to 15 and that of all officially known Canadian cases to 24.

It appears then that the disease is much more common in this country than has been thought, and we have only to open our eyes to see it.

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RÉSUMÉ

Les histoires cliniques de nos trois derniers cas de pneumonie à Pneumocystis sont commentées en comparaison avec celles de notre série entière de 14 cas canadiens.

Une corrélation anatomo-clinique de certains aspects de la maladie est tentée, en soulignant l'importance diagnostique possible de la fréquence d'une période asymptomatique de quelques jours qui suit le déclenchement initial de la maladie. G.B.

*Needle biopsy of the lung appears at present to be the only possible way of establishing a positive diagnosis of the disease during life. However, this method is not yet universally accepted and is not performed at Ste. Justine Hospital.

OPERATION FOR CARCINOMA OF THE PANCREATIC BODY AND TAIL

Kibler and Bernatz (*Proc. Staff Meet. Mayo Clin.*, 33: 247, 1958) have recently studied 175 cases of primary carcinoma of the body and tail of the pancreas, operated on at the Mayo Clinic, 1920-1956. Of these 158 were cases of adenocarcinoma, six cases of papillary cystadenocarcinoma, and 11 cases of malignant islet cell lesions. This represents 18% of all malignant lesions of the pancreas coming to operation.

Men were afflicted twice as commonly as women. Pain was the most common symptom, and 82% mentioned pain as an initial symptom. The pain was usually epigastric but in over half the cases extended to the back; it was characteristically aggravated by lying down, and it tended to become constant. Anorexia, dyspepsia and nausea were common; jaundice and phlebitis were late findings. Physical examination was of limited value, except for the ominous cachexia, and a palpable mass in about 40% of cases. No laboratory test was of consistent diagnostic value, and positive x-ray evidence was rare. In fact, the preoperative diagnosis was seldom made with certainty, and in many cases the early impression was of functional disorder only.

Prognosis was very poor, for only an occasional lesion was resectable (7 out of 158 cases), and the average survival for the whole series was three and a half months after operation. Nobody was cured.

Early abdominal exploration when the clinical picture is at all suggestive of carcinoma of the pancreatic body or tail is essential.