Online ISSN 2623-2723
Print ISSN: 2338-0373
Jurnal Widya Medika Vol. 8 No. 2 Oktober 2022
https://doi.org/10.33508/jwm.v8i2.3864

PANCOAST TUMOR : A CASE REPORT

Epriyanto T. Darmadi [1) 2)], Ivan Tjokrowinoto [1)]

ABSTRACT

Introduction*: Pancoast tumor, or superior sulcus tumor, is defined as a tumor that grows on the thoracic inlet or grows on a pleuropulmonary peak that is found beyond the initial cost. These tumors may invade upper ribs, muscle, vertebral, subclavian vessels, the inferior portion of the brachial plexus, sympathetic nervous system, and stellate ganglion. Pancoast tumors are mostly caused by non-small cell lung cancer.* ***Case description****: A 59-year-old man came to the emergency room with complaints about a lack of pain in his left chest. Other symptoms reported by the patient include chest discomfort, stiffness, pain rising and subsiding on the left arm that may spread back and forth, and weight loss. Chest CT Scan with contrast shows a heterogeneous mass appears at the left lung's tip, pushing the left lung's upper lobe, bronchiectasis at the lower lobe of the left lung, destruction of the left coastal bones 1, 2, and 3, and tracheobronchial supero-inferior lymphadenopathy. Anatomical pathology results round cell tumors favor adenocarcinoma with poorly differentiated metastasis.* ***Discussion****: Diagnosis of Pancoast tumor is supported by patient symptoms, imaging results, and biopsies. This patient's complaints and symptoms are unusual, leading doctors to believe that the cause is not a Pancoast tumor. Remember that Pancoast Tumors are not the only thing that can cause Pancoast syndrome, though they are the most common. The results of this patient's biopsy rule out other causes of Pancoast tumors and are consistent with the cause of Pancoast tumors, namely adenocarcinoma, a type of non-small cell lung cancer.* ***Conclusion:*** *Chronic and progressive complaints and unintentional weight loss become "red flags" that may indicate the start of the malignancy process. A good clinical approach can help detect these tumors early, improving the patient's prognosis.*

Keywords: *Pancoast tumor, superior sulcus tumor, adenocarcinoma*

ABSTRAK

Pendahuluan: Tumor Pancoast atau *Superior Sulcus Tumors* adalah tumor yang tumbuh pada *thoracic inlet* atau tumbuh di sulkus apeks pleuropulmonal yang berada di atas *costae* pertama. Tumor Pancoast dapat menginvasi *costae* bagian atas, otot, vertebra, pembuluh darah subklavia, pleksus brakialis bagian bawah, sistem saraf simpatis dan ganglion. Tumor Pancoast paling banyak disebabkan oleh *non-small cell lung cancer*. **Deskripsi kasus**: Laki-laki 59

tahun datang ke ruang gawat darurat dengan keluhan nyeri pada dada kiri yang memberat. Keluhan lain yang dirasakan pasien adalah dada terasa tidak nyaman, kaku, nyeri yang hilang timbul dan menjalar ke belakang dan tangan kiri, serta penurunan berat badan. *Computerised Tomography* (CT) Scan toraks dengan kontras menunjukkan massa heterogen di apeks paru kiri, mendorong lobus atas paru kiri, bronkiektasis pada lobus bawah paru kiri, destruksi *costae* 1, 2 dan 3 kiri dan limfadenopati trakeobronkial supero-inferior. Hasil patologi anatomi didapatkan *round cell tumors favor adenocarcinoma with poorly differentiated metastasis*. **Diskusi**: Diagnosis Tumor Pancoast didukung oleh gejala, hasil pencitraan dan biopsi. Keluhan dan gejala pasien tidak mengarah pada Tumor Pancoast. Penyebab terbanyak Sindroma Pancoast adalah Tumor Pancoast, tetapi tumor tersebut hanya salah satu penyebab. Hasil biopsi pasien menyingkirkan penyebab lain dan memastikan bahwa terdapat Tumor Pancoast jenis *adenocarcinoma*, sebuah *non-small cell lung cancer*. **Kesimpulan**: Keluhan yang berlangsung kronik dan progresif serta penurunan berat badan yang tidak disadari menjadi "tanda bahaya" yang mengindikasikan kemungkinan terdapat proses keganasan. Pendekatan klinis yang baik dapat mendeteksi Tumor Pancoast lebih awal sehingga prognosis pasien lebih baik.

Kata kunci : Tumor Pancoast, tumor *sulcus superior*, *adenocarcinoma*

1)Department of Radiology, Faculty of Medicine, Widya Mandala Catholic University of Surabaya, Indonesia.
2) Division of Radiology, Primasatya Husada Citra Hospital Surabaya, Indonesia. Jl. Prapat Kurung Selatan No. 1, Surabaya, Indonesia

INTRODUCTION

Pancoast tumor, or superior sulcus tumor, is defined as a tumor that grows on the thoracic inlet (1,2) or grows on a pleuropulmonary peak that is found beyond the initial cost (3). Pancoast tumors are uncommon and account for 3–5% of lung carcinomas(4). These tumors may invade upper ribs, muscle, vertebral, subclavian vessels, the inferior portion of the brachial plexus, sympathetic nervous system, and stellate ganglion. These tumors are characterized by Horner's syndrome (ptosis, miosis, anhidrosis), ipsilateral shoulder and arm pain, paresis, and atrophy of thenar muscles(5,6). Pancoast tumors are mostly caused by non-small cell lung cancer (NSCLC) (4–6). Non-small cell lung cancer , most commonly adenocarcinoma, is predominantly caused by Pancoast syndrome. Squamous cell carcinoma is the most common cause in developed countries. Diagnosis of Pancoast tumors is often delayed, and it is mistaken for a musculoskeletal disorder affecting the shoulder region. Pancoast tumors should be differentiated from Pancoast syndrome characterized by radiating parascapular

https://doi.org/10.33508/jwm.v8i2.3864

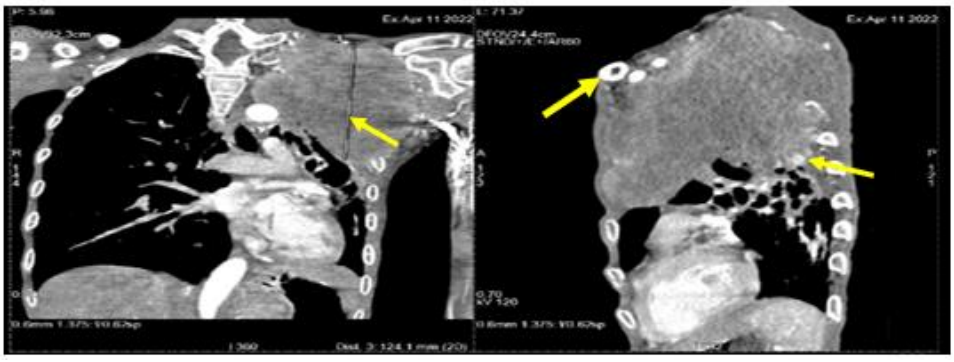
pain, hand intrinsic muscles atrophy, and Horner's syndrome. (2,3,7,10).

Case Description

A 59-year-old man came to the emergency room with complaints about a lack of pain in his left chest from the last one year. Other symptoms reported by the patient include chest discomfort, stiffness, pain rising and subsiding on the left arm that may spread back and forth, symptoms worsened in the last four months, and weight loss has become more pronounced in the last two months. Weakness or decreased sensitivity in the upper left limb is denied. Patients say that in the last two months, there has been a decrease in appetite; although there is no abnormality in the digestive tract, adult coughing has been ruled out.

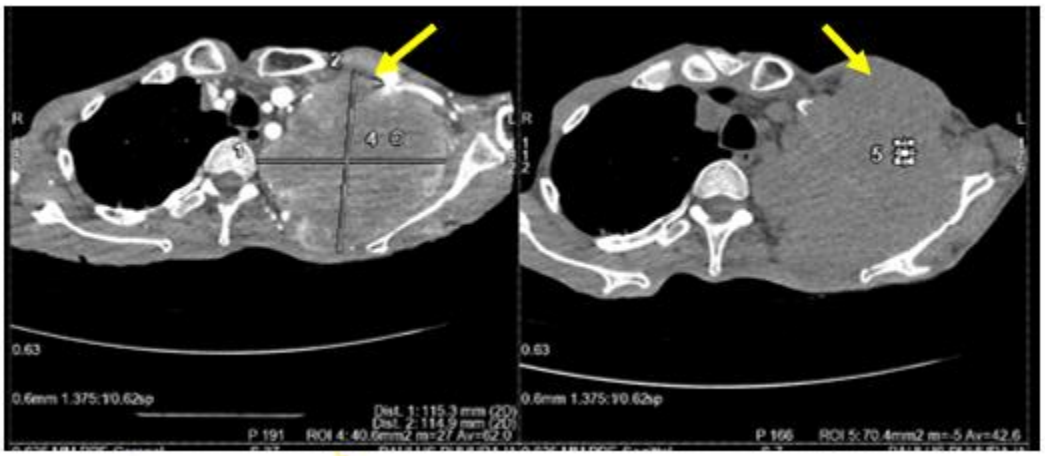
History of smoking from a young age and a day of about 12 cigarettes / one pack. The family history of the tragedy is disputed. Work as an employee. Physical examination revealed significant signs of a 2-centimeter upper left supraclavicular well-defined mass, weak lung percussion, increased upper left vocal fremitus, and decreased left lung auscultates compared to the right lung. Movement of the thoracic vertebrae is not performed, as the patient cannot tolerate pain.

A heterogeneous mass appears at the left lung's tip, pushing the left lung's upper lobe, which measures 11.49 x 11.53 x 12.41 cm and has a contrast enhancement (42 to 62 U) in contrast a subside. The lower lobe of the left lung has a honeycomb appearance. In addition, bronchiectasis in the left lung inferior lobe, destruction of the left coastal bones 1, 2, and 3, and tracheobronchial supero-inferior lymphadenopathy. According to the Union Internationale Contre le Cancer and the American Joint Committee on Cancer, this patient's CT thorax revealed an apical Pancoast tumor with radiological stage T4N3M1b (stage IV). Anatomical pathology results round cell tumors favor adenocarcinoma with poorly differentiated metastasis with negative epidermal growth factor receptor (EGFR).



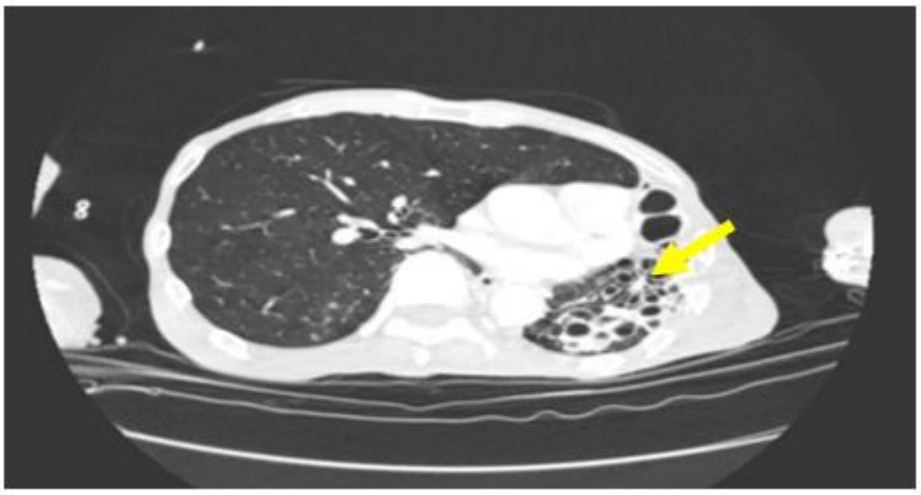
Picture 1. Chest CT Scan with Contrast (coronal and sagittal plane-mediastinu)

Aterogeneous mass (white arrow) appears at the apex of the left lung pushing the Aterogeneous mass (white arrow) appears at the apex of the left lung pushing the upper lobe of the left lung inferiorly. This mass has a height of 12,41 cm. The lower lobe of the left lung has a honeycomb appearance (yellow arrow).



Picture 2. Chest CT Scan with (left) and without (right) Contrast (axial plane-mediastinum)

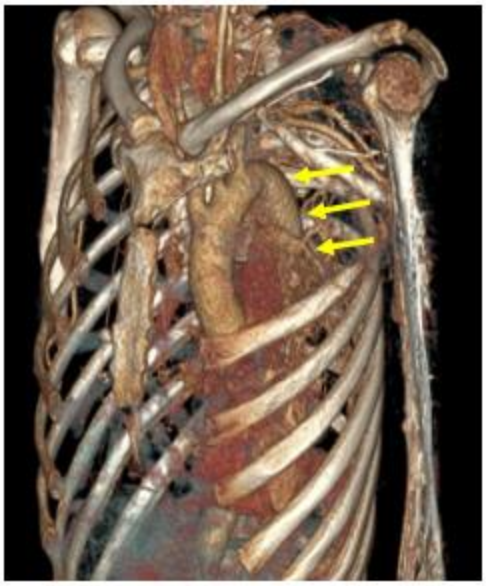
A heterogeneous mass (yellow arrow) appears at the apex of the left lung, which measures 11.49 (length) x 11.53 (wide) cm and has a contrast enhancement (42 to 62 U).



Picture 3. Chest HRCT Scan with Contrast (axial plane-Lung)

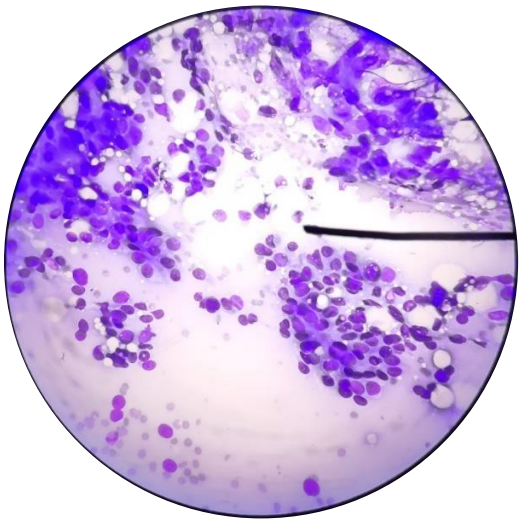
The lower lobe of the left lung has a *honeycomb appearance* (yellow arrow).

Online ISSN 2623-2723
Print ISSN: 2338-0373
Jurnal Widya Medika Vol. 8 No. 2 Oktober 2022
https://doi.org/10.33508/jwm.v8i2.3864



Picture 4. Volume Rendering

Because they were destroyed, the left coastline bones 1, 2 and 3 are not visible in VR view (bold yellow arrow).



Picture 5. Anatomical Pathology

According to microscope directions, round cell tumors was found to diagnose adenocarcinoma with poorly differentiated metastasis

T (Primary Tumor)		Label
T0	No primary tumor	
Tis	Carcinoma in situ	Tis
T1	Tumor ≤ 3 cm,	
T1a (mi)	Minimally invasive adenocarcinoma	T1a (mi)
	Superficial spreading tumor in central airways	T1a SS
T1a	Tumor ≤ 1 cm	T1a ≤ 1
T1a	Tumor > 1 but ≤ 2 cm	T1b > 1-2
T1b	Tumor > 2 but ≤ 3 cm	T1c > 2-3
T1c		
T2	Tumor > 3 cm but ≤ 5 cm or tumor involving :	T2 visc pl
	Visceral pleura , main bronchus , atelectasis to hilum	T2 centr
T2a	Tumor > 3 but ≤ 4 cm	T2a > 3-4
T2b	Tumor > 4 but ≤ 5 cm	T2b > 4-5
T3	Tumor > 5 but ≤ 7 cm or	T3 >5-7
	Invading chest wall, pericardium, phrenic nerve	T3 inv
	Or separate tumor nodule(s) in the same lobe	T3 satell
T4	Tumor > 7 cm or	T4 > 7
	Tumor invading: mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, esophagus, spine; or	T4 inv
	Tumor nodule(s) in a different ipsilateral lobe	T4 ipsi nod
N (Regional Lymph Nodes)		
N0	No regional node metastasis	
N1	Metastasis in ipsilateral pulmonary or hilar nodes	
N2	Metastasis in ipsilateral mediastinal/subcarinal nodes	
N3	Metastasis in contralateral mediastinal/hilar, or supraclavicular	
M (Distant Metastasis)		
M0	No distant metastasis	
M1a	Malignant pleural/pericardial effusion or nodules	M1a pl dissem
	Or separate tumor nodule (s) in a contralateral lobe	M1a contr nod
M1b	Single extrathoracic metastasis	M1b single
M1C	Multiple extrathoracic metastatsis (1 or >1 organ)	M1c multi

Picture 6. Staging Classification

(The Eighth Edition Lung Cancer Stage Classification (sogapar.info)

DISCUSSION

Pancoast tumors are benign tumors that grow in the apex region of the brain and affect the surrounding structure. The patient who has been affected by this

tumor is 60 years old or older, while this patient is 59 years old (11). This patient's complaints and symptoms are unusual, leading doctors to believe that the cause is not a Pancoast tumor. The pain is not very specific, and the lack of weakness in the left side's upper extremity does not suggest any nervous system involvement in the area, such as the brachialis plexus. The ulna nerve is more commonly affected by these tumors (1), but they can also affect the vagus nerve, phrenic nerve, and laryngeal recurrent nerve (12). Honer's syndrome is only found in 15-50 percent of these tumors, not in these patients (13). Smoking, shortness of breath, progressively worsening symptoms, and unintentional weight loss can lead to suspicion of a malignancy in the respiratory tract. The results of the patient's physical examination also indicate a process occurring in the lungs, which supports the presence of a malignancy.

Diagnosis of Pancoast tumors is supported by patient symptoms, imaging results, and biopsies. Remember that Pancoast Tumors aren't the only thing that can cause Pancoast syndrome, though they are the most common. Schwannoma, mesothelioma, hemangioma, fungal abscess, tuberculosis, hydatid cysts, and bacterial infections are some examples of cases that can provide an overview of Pancoast syndrome. Immunosuppressed patients, such as those undergoing chemotherapy, HIV treatment, or diabetes treatment, are more likely to contract serious infections than those who are not (14-16). The results of this patient's biopsy rule out other causes of Pancoast tumors, such as other primary tumors, and are consistent with the cause of Pancoast tumors, namely adenocarcinoma, a type of non-small cell lung cancer (1,2).

CONCLUSION

Chronic and progressive complaints and unintentional weight loss become "red flags" that may indicate the start of the malignancy process. In these patients, anamnesis, physical examination, and radiodiagnostics were all inconclusive in confirming the diagnosis of Pancoast Tumor. The most important examination is a biopsy so that the entire differential diagnosis can be eliminated, and appropriate procedure

REFERENCES

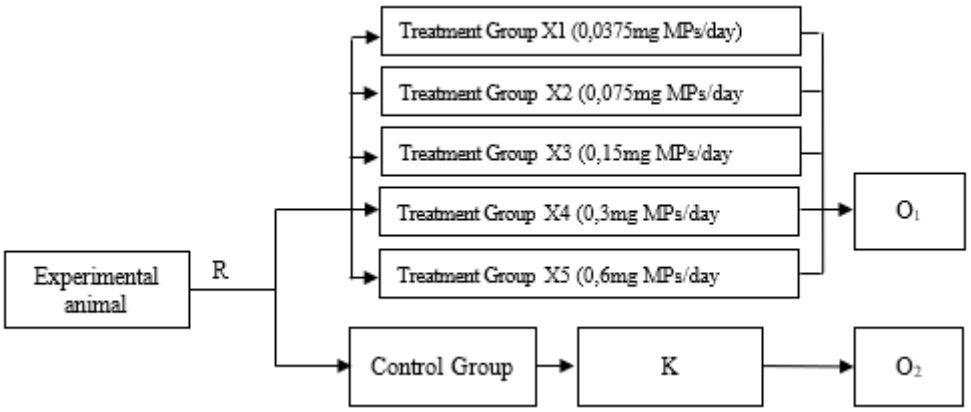
1. Vipin D. Villgran; Rebanta K. Chakraborty; Sujith V. Cherian. Pancoast Syndrome. NIH. 2022 Feb;
2. Panagopolous N, Leivaditis V, Koletsis E, Prokakis C, Alexopoulos P, Baltayiannis Ni, et al. Pancoast Tumors: Characteristics and Preoperative Assessment. Journal of Thoracic Disease. 2014;6.
3. Harold Simon and Alfred C. Moon. Pitfalls in the Diagnosis of Pancoast Tumor. Radiology. 1964;82(2).
4. Mohamoud S, Oyawusi M, Weir RL, Halbert EO, Millis RM, Gebremedhin T, et al. Pancoast Tumor Presenting With Multiple Joint Pains : A Case Report. Journal of Medical Case Reports. 2022 Mar;
5. al Shammari M, Hassan A, al Jawad M, Farea A, Almansour A, al Yousif G, et al. Pancoast Tumor : The Overlooked Etiology of Shoulder Pain in Smokers. American Journal of Case Reports. 2020 Sep;
6. Ronan L, Souza SD', Ronan LA. Pancoast's tumor presenting as shoulder pain in an orthopaedic clinic.
7. Cunha A, Quintela M, Costa C, Quispe-Cornejo AA, Freitas-Silva M. Pancoast Tumor as the Initial Presentation of a Metastatic Colon Adenocarcinoma. PubMed. 2021;13(2).
8. Panagopolous N, Leivaditis V, Koletsis E, Prokakis C, Alexopoulos P, Baltayiannis Ni, et al. Pancoast Tumors: Characteristics and Preoperative Assessment. Journal of Thoracic Disease. 2014;6.
9. Harold Simon and Alfred C. Moon. Pitfalls in the Diagnosis of Pancoast Tumor. Radiology. 1964;82(2).
10. Almanzar C, Maxwell S, Gomez M, Ansari O, Silva L. Pancoast Syndrome Due to High Grade Anaplastic Tumor. HCA Healthcare Journal of Medicine. 2021 Feb 26;2(1).
11. Gundepalli SG, Tadi P. Lung Pancoast Tumor. National Library of Medicine. 2021;
12. Mohamoud S, Oyawusi M, Weir RL, Halbert EO, Millis RM, Gebremedhin T, et al. Pancoast Tumor Presenting With Multiple Joint Pains : A Case Report. Journal of Medical Case Reports. 2022 Mar;
13. Marulli G, Battistella L, Mammana M, Calabrese F, Rea F. Superior sulcus tumors (pancoast tumors). Annals of

Translational Medicine. 2016 Jun 1;4(12):1–13.

14. Das A, Choudhury S, Basuthakur S, Das SK, Mukhopadhyay A. Pancoast's Syndrome due to Fungal Abscess in the Apex of Lung in an Immunocompetent Individual: A Case Report and Review of the Literature. Case Reports in Pulmonology. 2014;2014:1–4.
15. Foroulis CN, Zarogoulidis P, Darwiche K, Katsikogiannis N, Machairiotis N, Karapantzos I, et al. Superior sulcus (Pancoast) tumors: Current evidence on diagnosis and radical treatment. Vol. 5, Journal of Thoracic Disease. Pioneer Bioscience Publishing; 2013.
16. Glassman LR, Hyman K. Pancoast tumor: A modern perspective on an old problem. Vol. 19, Current Opinion in Pulmonary Medicine. 2013. p. 340–3.

MATERIALS AND METHODS

This sort of quantitative analytic study employs an experimental methodology using animal subjects. This purely experimental study used a control group design with just post-test measures. This design began by dividing the experimental animals into six groups, namely the control group, the treatment group X1, X2, X3, X4, and X5, and then making microscopic observations after administering the treatment to the treatment group for a predetermined amount of time. This design model is depicted in the figure below.



Note:

R : Random
X : Microplastic exposure dose distribution (MPs)
K : No exposure to microplastics (MPs)
O_1 : Observations and measurements in the treatment group
O_2 : Observations and measurements in the control group

In this work, the experimental unit was male white rat wistar strain (Rattus norvegicus strain wistar). The experimental unit selected for this study must meet the inclusion criteria but not the exclusion criteria; otherwise, it will be dropped from the study. The study's inclusion criteria were: Two months old (±1 week) white male rats and weighed between 150 (± 20 grams). While the exclusion criteria were sick white rats as determined by a veterinarian's checkup, the inclusion criteria were healthy white rats. White rats are characterized by their lethargic movement, thick white hair, wounds, and hazy eyes. This study's dropout criteria

were rats that died during the research which was determined by the absence of rat vital signs. Thirty white rats (Rattus norvegicus strain wistar) and their reserves were divided into five treatment groups (each with five rats) and one control group (5 rats). Using a random allocation technique, rats were randomly divided into six groups. To guarantee internal validity and prevent bias in this study, the researcher did not know to which group the rats were assigned, so all groups were considered equal.

The independent variable in this study was microplastics concentration (MPs). The dependent variables were intestinal and pancreatic function. The connecting variable was cell damage in the pancreas and intestines. While the control variables determined in this study were the method of administering microplastics orally using a probe, the microplastic diameter of ≤20 µm, the solvent in the form of aquabides, and the post-exposure evaluation time of 90 days, the experimental variables were the method of administering microplastics orally using a probe, the microplastic diameter of ≤20 µm, and the and post-exposure evaluation time of 90 days.

The following table provides operational definitions of study variables, measurement methods, measuring scales, and measurement outcomes:

No	Variable / Sub-variable	Variable Operational Definition	Measurement Results (Indicators) Variable	How to Measure Variables	Measuring instrument	Measuring Scale
1	Microplastic Dosage (MPs)	The number of plastic particles measuring 20 µm was administered to Rattus norvegicus strain wistar via an oral probe.	The number of plastic particles with a diameter of ≤20 m in milligram units is divided into five experimental doses, namely X1, X2, X3, X4, and X5.	Examined under a microscope and recorded on the laboratory result form.	Scanning electron microscope and milligram scale	Ordinal
2	Changes in the morphology of pancreatic tissue	The degree of morphological changes of pancreatic tissue in histopathological preparations with HE staining, which indicates the occurrence of injury, consists	The total score for the four assessment components is as follows: 1. Necrosis: no necrosis (score 0), <10% necrosis (score 1), 10%-40% necrosis (score 2), >40% necrosis (score 3).	Observed under a binocular light microscope and recorded the resulting form	Binocular light microscope.	Ordinal

		of 4 components of a semiquantitative assessment, namely necrosis, formation of vacuoles in acinar cells, degree of inflammation, and acinar edema.(13).	2. Formation of vacuoles in acinar cells: none (score 0), <20% acinar cells containing vacuoles (score 1), 20%-50% acinar cells containing vacuoles (score 2), >50% acinar cells containing vacuole (score 3) 3. Inflammation degree: none (score 0), inflammation in the interlobular area (score 1), inflammation in the intralobular area (score 2), inflammation in the inter-acinar area (score 3) . 4. Acinar edema: none (score 0), interlobular edema (score 1), intralobular edema (score 2), interacinar edema (score 3).			
3	Changes in the morphology of the small intestine tissue	The degree of changes in the morphology of the small intestine tissue on histopathological preparations with HE staining indicating the occurrence of injury was categorized into a score of 1-5 according to the scoring system used in	The assessment uses a scoring system, as follows: 1. Score 1: mild inflammatory cell counts in the mucosa. 2. Score 2: mild inflammatory cell counts in the mucosa and submucosa. 3. Score 3: moderate inflammatory cell count in the mucosa and submucosa,	Observed under a binocular light microscope and recorded on the results form.	Binocular light microscope	Ordinal

		previous studies.(14).	accompanied by slight shortening of the villi. 4. Score 4: dense inflammatory cell infiltration and submucosal lymphoid aggregation, accompanied by moderate shortening of the villi. . 5. Score 5: dense to transmural inflammatory cell invasion, accompanied by villous atrophy and crypt damage			
4	Changes in the morphology of the colon tissue	The degree of changes in the morphology of the colon tissue on histopathological preparations with HE staining, which indicates the occurrence of an injury process, is categorized into a score of 1-4 according to the scoring system used in previous studies.(14).	The assessment uses a scoring system, as follows: 1. Score 1: mild inflammatory cell counts in the mucosa. 2. Score 2: mild inflammation of the inflammatory cells in the mucosa and submucosa, accompanied by a minimal decrease in the number of goblet cells. 3. Score 3: moderate inflammatory cell counts in the mucosa and submucosa, accompanied by a decrease in the number of goblet cells and crypt abscesses and/or ulcerations.	Observed under a binocular light microscope and recorded on the resulting form.	Binocular light microscope.	Ordinal

	. 4. Score 4: dense inflammatory cell invasion, may be transmural, accompanied by multiple crypt abscesses and extensive ulceration.	

Data gathered from histopathological preparations of Rattus norvegicus strain Wistar will be evaluated for completeness and appropriateness. The data was then displayed and analyzed using version 25 of the statistical program for the social sciences. The presentation of univariate data as distribution tables, mean values, and microscopic images. In the meanwhile, bivariate data is displayed via cross-tabulation. Due to the ordinal nature of the examination findings, the statistical analysis was conducted with the SPSS program, specifically the logistic regression test.

RESULTS AND DISCUSSION

Microplastic Exposure Material

This research employs polyethylene plastic. A polymer of low-density polyethylene extracted from food packaging bags. The FCT Z100 miller machine is used to process food packaging bags into a powder of the desired fineness. The resulting plastic powder was then filtered via an 800-mesh sieve. The filtered powder was then inspected using a microscope with a magnification of 400 and a scale of 10 meter.

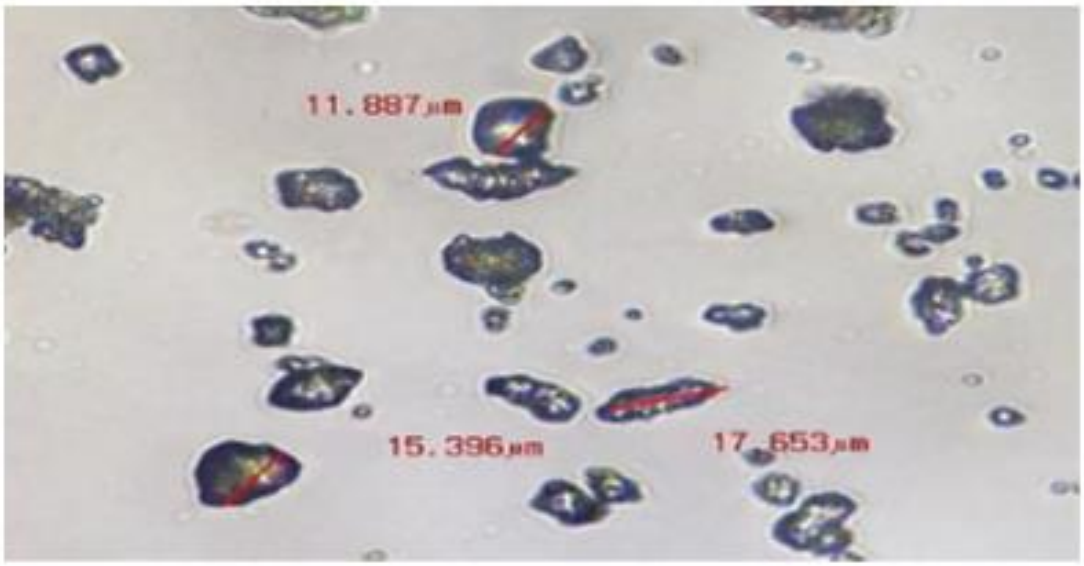


Figure 1. Microscopic picture of polyethylene particles that have been filtered to a size less than 20 μm using the FCT Z100 miller machine.

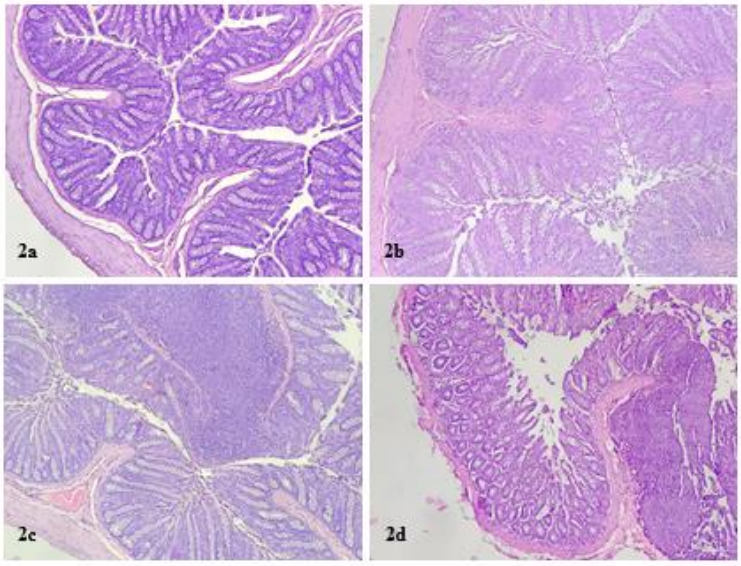


Figure 2. Microscopic view at 400 magnification of the small intestine; a) minimal inflammatory cell infiltration in the mucosa (score 1), b) minimal inflammatory cell infiltration in the mucosa and submucosa (score 2), c) and d) dense inflammatory cell infiltration and submosaic lymphoid aggregation, accompanied by shortening of the villi (score 4)

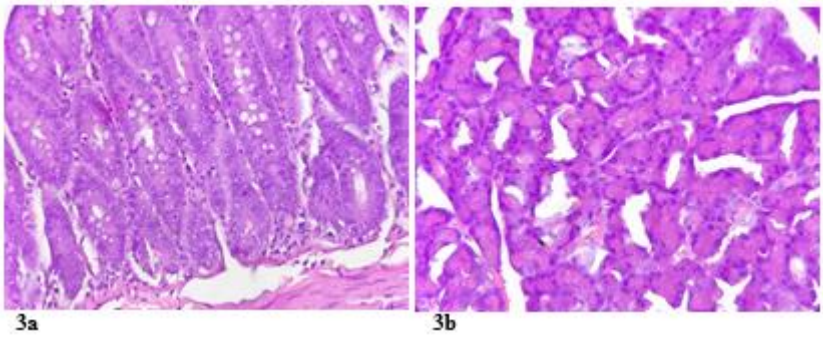


Figure 3. a) Microscopic structure of the large intestine, light infiltration of inflammatory cells in the mucosa, no decrease in the number of goblet cells; b) The microscopic structure of the pancreas, exocrine gland acini did not show significant histologic changes.

Figure 2 and 3 are pictures of the changes found through a microscopic examination with HE staining, then an analysis of the injury process is carried out according to the scoring system. Based on the preceding image, it can be concluded that the microplastics utilized as research exposure materials have a size range of ≤18 µm. Visible microplastic particles are not permeable to light, leading to the conclusion that they are solid particles.

Sharp edges can also be noticed on the microplastic particle

Table 1. Correlation Test and Small Intestine Different Test

No	Comparison Group	Sig Non-Parametric Correlations (2-tailed)	Sig Mann-Whitney (2-tailed)
1.	K-X1	0.173	0.164
2.	K-X2	0.030	0.036
3.	K-X3	0.049	0.054
4.	K-X4	0.019	0.027
5.	K-X5	0.059	0.063

The comparison between the control group and exposure groups X2, X3, and X4 produced significant results (P<0.05), whereas the comparison between the control group and exposure groups X1 and X5 showed nonsignificant results (P<0.05). The findings of the correlation test between the control group and the X2 and X4 exposure groups were statistically significant (P<0.05), indicating that a significant relationship existed. As the correlation test between the control group and the exposure groups X1, X3, and X5 showed insignificant findings (P<0.05), it was determined that there was no meaningful association between the two groups.

Table 2. Frequency and Percentage of Tissue Damage Assessment Grades

Grade	**Control Group n (%)**	**Treatment Group n (%)**
1	3 (42.8)	2 (5.7)
2	3 (42.8)	15 (42.9)
3	1 (14.4)	7 (20)
4	0 (0)	10 (28.6)
5	0 (0)	1 (2.9)

In the control group sample, 42.8% of the sample belongs to grade 1, 42.8% belongs to grade 2, and 14.4% belongs to grade 3, where there are five levels. These results indicate that the control group had varying degrees of damage, with the highest grade being 3. In the exposure group, 28.6% of the samples were from the fourth grade, and 2.9% were from the fifth grade. These data indicate that the damage in the exposure group samples was variable and increasingly

severe until it reached grade 5, but the damage in the control group samples only reached grade 3

Table 3. Correlation Test and Large Intestine Difference Test

No	Comparison Group	Sig Non-Parametric Correlations (2-tailed)	Sig Mann-Whitney (2-tailed)
1.	K-X1	0.109	0.107
2.	K-X2	0.063	0.066
3.	K-X3	0.109	0.107
4.	K-X4	0.552	0.530
5.	K-X5	0.059	0.063

According to table 3, the comparison between the control group and each exposure group did not yield statistically significant findings (P <0.05). Correlation test results were also inconclusive between the control group and the full exposure group (X1-X5).

Table 4. Frequency and Percentage of Grade Assessment of Colon Tissue Damage

Grade	**Control Group n (%)**	**Treatment Group n (%)**
1	0 (0)	0 (0)
2	6 (85.7)	16 (45.7)
3	1 (14.3)	19 (54.3)
4	0 (0)	0 (0)

Based on the information in table 4, it is known that 85.7% of the samples are included in grade 2, and 14.3% of the samples are included in grade 3, which is separated into four assessment components. These results imply that the control group has experienced mild to moderate damage. In this semiquantitative assessment, 45.7% of the samples from the exposure group were in sample grade 2, and 54.3% were in sample grade 3.

Table 5. Correlation Test and Pancreatic Difference Test

No	Comparison Group	Sig Non-Parametric Correlations (2-tailed)	Sig Mann-Whitney (2-tailed)
1.	K-X1	0.179	0.170
2.	K-X2	0.013	0.060
3.	K-X3	0.147	0.141
4.	K-X4	1.000	1.000
5.	K-X5	0.337	0.317

6.	K and X1-X5	0.179	-

According to table 5, the comparison between the control group and each exposure group did not yield statistically significant findings (P <0.05). Correlation test results were also inconclusive between the control group and the full exposure group (X1-X5).

Table 6. Frequency and Percentage of Tissue Damage Assessment Grades

Grade	Control Group n (%)	Exposure Group n (%)
0	0 (100)	1 (2.7)
1	7 (100)	26 (70.3)
2	0 (0)	0 (0)
3	0 (0)	10 (27)
4	0 (0)	0 (0)

In table 6, 100% of the samples are included in grade 1, which consists of four assessment components. These results indicate that the control group has suffered minimal damage. In this semi-quantitative assessment, 27% of grade 3 samples were included in the exposure group.

The part of an organism directly exposed to microplastics is the digestive system, and it is believed that the small intestine is one of the most impacted organs. Several research has demonstrated that one of the harmful effects of a substance is an increase in inflammatory responses in tissues, but other studies have found the opposite[15–17]. Here, histological observations of the small intestine revealed a substantial difference in the degree of inflammatory cell infiltration between the control group and the X-2, X-3, and X-4 exposure groups, and an average tissue damage score was determined. Compared to the control group, the total exposure group experienced more severe symptoms which may be caused by the accumulation of microplastics. This condition has the potential to cause changes at the biomolecular level, such as increased expression of proteins and pro-inflammatory mediators and impaired intestinal cell permeability, which, in the early stages, have not altered the tissue structure to the point where they are recognizable in histology preparations.

The review article by Hirt and Body-Malapel indicated that a decrease in mucus secretion and the transcription factor of the primary gene linked with mucin

expression was one of the toxic effects of microplastic accumulation in the colon (Muc-1) [16]. The colon histology in this study showed a slight but non-statistically significant difference in the degree of tissue damage (including a decrease in the number of goblet cells) between the control and exposure groups because HE staining does not allow for a detailed assessment of mucus secretion, requiring a further study on mucus secretion in the large intestine utilizing PAS staining or immunohistochemistry against Muc-1 antibodies.

There is so little research on the effects of microplastics on the pancreas, particularly in vertebrates, that data on the effects of microplastics on pancreatic tissue are nearly nonexistent. This study found no significant differences in the appearance of exocrine pancreatic tissue between the control and exposure groups. Additional observations of the pancreatic endocrine area can be used as material for further research.

CONCLUSIONS

From the findings about the effect of microplastic feeding on intestinal and pancreatic cell damage, the following conclusions can be drawn:

1. Comparing the control group and each exposure group to the small intestine, the Pearson correlation test in groups K with X2, X3, and X4 and the Mann-Whitney difference test in groups K with X2 produced significant results. In the control group, there was no evidence of damage or light damage; in the exposure group, 42.9% of the samples were grade 2, 20% were grade 3, 28.6% were grade 4, and 2.9% included grade 5.
2. Neither the Pearson correlation test nor the Mann-Whitney difference test revealed any significant differences between the control group and each group exposed to the large intestine. Furthermore, demonstrated that there was moderate to mild damage in the control group. In contrast, 45.7% of the samples in the exposure group were from grade 2, and 54.3% were from grade 3.
3. Comparing the control group to each group exposed to the pancreas, the Pearson correlation test for groups K with X2 and X4 and the Mann-Whitney difference test for groups K and X4 yielded significant results. Furthermore, showed no damage/light damage occurred in the control group, whereas 27% of grade 3 samples were found in the exposure group.

4. The correlation test results between the control group and the entire exposure group (X1-X5) showed significant results in the small intestine but not in the large intestine and pancreas tissue.
5. The results above show the effect of microplastic administration on damage to small intestinal cells.

ACKNOWLEDGMENTS

The authors would like to express their gratitude to LPPM UKWMS for providing funding for this study. To the UKWMS Faculty of Pharmacy's Biomedical Laboratory and the UNAIR anatomical pathology laboratory. Finally, for our students who participated in the research.

.

REFERENCES

1. Garside M. Global plastic production from 1950 to 2020 (in million metric tons)*. Statista. 2019;
2. Agustina Hidayat Y, Kiranamahsa S, Arya Zamal M. A study of plastic waste management effectiveness in Indonesia industries. AIMS Energy [Internet]. 2019;7(3):350–70. Available from: http://www.aimspress.com/article/10.3934/energy.2019.3.350
3. Prokić MD, Radovanović TB, Gavrić JP, Faggio C. Ecotoxicological effects of microplastics: Examination of biomarkers, current state, and future perspectives. TrAC Trends Anal Chem [Internet]. 2019 Feb;111:37–46. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0165993618304710
4. Frias JPGL, Nash R. Microplastics: Finding a consensus on the definition. Mar Pollut Bull [Internet]. 2019 Jan;138:145–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0025326X18307999
5. GESAMP, 2016. Sources, fate and effects of microplastics in the marine environment (part 2). Available: http://www.gesamp.org/publications/microplastics-in-the-marineenvironment- part-2.
6. Huang J-S, Koongolla JB, Li H-X, Lin L, Pan Y-F, Liu S, et al. Microplastic accumulation in fish from Zhanjiang mangrove wetland, South China. Sci Total Environ [Internet]. 2020 Mar;708:134839. Available from: https://doi.org/10.1016/j.scitotenv.2019.134839
7. Wang Y-L, Lee Y-H, Chiu I-J, Lin Y-F, Chiu H-W. Potent Impact of Plastic Nanomaterials and Micromaterials on the Food Chain and Human Health. Int J Mol Sci [Internet]. 2020 Mar

3;21(5):1727. Available from: https://www.mdpi.com/1422-0067/21/5/1727

8. Campanale, Massarelli, Savino, Locaputo, Uricchio. A Detailed Review Study on Potential Effects of Microplastics and Additives of Concern on Human Health. Int J Environ Res Public Health [Internet]. 2020 Feb 13;17(4):1212. Available from: https://www.mdpi.com/1660-4601/17/4/1212
9. Karbalaei S, Hanachi P, Walker TR, Cole M. Occurrence, sources, human health impacts and mitigation of microplastic pollution. Environ Sci Pollut Res [Internet]. 2018 Dec 31;25(36):36046–63. Available from: http://link.springer.com/10.1007/s11356-018-3508-7
10. Wright SL, Kelly FJ. Plastic and Human Health: A Micro Issue? Environ Sci Technol [Internet]. 2017 Jun 20;51(12):6634–47. Available from: https://pubs.acs.org/doi/10.1021/acs.est.7b00423
11. Deng Y, Zhang Y, Lemos B, Ren H. Tissue accumulation of microplastics in mice and biomarker responses suggest widespread health risks of exposure. Sci Rep [Internet]. 2017 May 24;7(1):46687. Available from: http://www.nature.com/articles/srep46687
12. Poma A, Vecchiotti G, Colafarina S, Zarivi O, Aloisi M, Arrizza L, et al. In Vitro Genotoxicity of Polystyrene Nanoparticles on the Human Fibroblast Hs27 Cell Line. Nanomaterials [Internet]. 2019 Sep 11;9(9):1299. Available from: https://www.mdpi.com/2079-4991/9/9/1299
13. Zhang H, Li Y, Li L, Liu H, Hu L, Dai Y, et al. Propylene glycol alginate sodium sulfate alleviates cerulein-induced acute pancreatitis by modulating the MEK/ERK Pathway in mice. Mar Drugs. 2017;15(2):1–14.
14. Ulrike Erben, Christoph Loddenkemper KD, , Simone Spieckermann DH, Markus, Heimesaat M, Zeitz1 M, , Britta Siegmund AAK. A guide to histomorphological evaluation of intestinal inflammation in mouse models. Int J Clin Exp Pathol. 2014;7(8):4557–76.
15. Hirt N, Body-malapel M. Immunotoxicity and intestinal effects of nano- and microplastics : a review of the literature. 2020;7:1–22.
16. Yee MS-L, Hii L-W, Looi CK, Lim W-M, Wong S-F, Kok Y-Y, et al. Impact of Microplastics and Nanoplastics on Human Health. Nanomater (Basel, Switzerland) [Internet]. 2021 Feb

16;11(2):496. Available from: https://pubmed.ncbi.nlm.nih.gov/33669327

17. Sun H, Chen N, Yang X, Xia Y, Wu D. Effects induced by polyethylene microplastics oral exposure on colon mucin release, inflammation, gut microflora composition and metabolism in mice. Ecotoxicol Environ Saf [Internet]. 2021;220:112340. Available from: https://www.sciencedirect.com/science/article/pii/S0147651321004516