Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/5zhhh176

SPECTRUM OF GRANULOMATOUS LESIONS IN A TERTIARY CARE HOSPITAL OF JAMMU - A 03 YEAR RETROSPECTIVE STUDY.

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Abstract-
Background: Granulomas are the commonest lesions that the pathologist come across in routine practice. Granulomatous inflammation is a special type of chronic inflammation that is a manifestation of many infective, toxic, allergic, autoimmune, and neoplastic disease and conditions of unknown etiology.
Materials and methods: This retrospective study included a total of 110 granulomatous lesions received over a period of 3 years from 31st August 2024 to 1st September 2021 in the Department of pathology, GMC Jammu. Diagnosis was confirmed by studying haematoxylin and eosin slides along with the special stains wherever required. The relevant clinical details and laboratory investigations were collected from the hospital case sheets and histopathological requisition forms.
Results: out of 110 cases, the most common type of granulomatous inflammation observed was tuberculosis accounting for (30%) of the cases, followed by leprosy (20%), foreign body granuloma (18.1%) and other causes including sarcoidosis and fungal infections. Lymph node were the most frequently involved sites followed by skin and lungs.
Conclusion: This 3-year retrospective study highlights the predominance of infectious causes especially tuberculosis, in granulomatous disease in our region. Histopathological examination remains a critical tool in diagnosing and differentiating various types of granulomatous inflammation. Awareness of diverse histopathological presentation is essential for accurate diagnosis and appropriate management of the conditions.

Keywords- Histomorphology, Granuloma, caseating necrosis, tuberculosis.

INTRODUCTION

Granulomatous lesions comprise a large family of disorders sharing a common histological feature of formation of granulomas. Granulomas may be confluent or discrete and the degree of necrosis is variable, the cell components may differ, and the presence or absence of features like schaumann bodies and calcification are distinctive.[1]

The granulomatous inflammatory response is the manifestation of many infective, toxic, allergic, autoimmune, neoplasm and conditions of unknown etiology. Granulomatous inflammation can affect every organ of the body, frequently encountered sites are the skin, subcutaneous tissue, lymph nodes and lungs.[2]

Granulomatous inflammation is considered as response to pathogens and persistent irritants of exogenous and endogenous origin. Granulomas are discrete collections of histiocytes with admixture of multinucleated giant cells and inflammatory cells. The granulomas are formed as a result of series of events that involves the interplay of antigen (persistent endogenous /exogenous) resulting in activation of cell mediated type 4 hypersensitivity reaction, activation of macrophages, T&B cell responses with release of chemical mediators of inflammation mainly cytokines.[3]

Granulomatous inflammation is commonly characterised by the formation of distinct granulomas composed of aggregates of epithelioid histiocytes with the peripheral cuff of lymphocytes and plasma cells and occasionally a necrotic centre. The origin of the epithelioid histiocytes begin within the bone marrow as myeloid precursors mature into monocytes which enlarge and enter peripheral circulation when recruited into tissues mature monocytes are renamed as histiocytes. The activation of histiocytes via the innate immune response gives the cells their characteristics epithelioid appearance.[4]

Histopathologically, granulomatous inflammatory lesions present with distinct pattern which include foreign body granuloma, epithelioid granuloma, palisading granuloma, necrotizing granulomas, non-necrotizing granulomas, suppurative granuloma and histiocytic granuloma. Common causes of granulomatous lesions include infectious (mycobacterium tuberculosis, fungal), non-infectious (foreign body, drugs), autoimmune (sarcoidosis, rheumatoid arthritis) neoplastic (Hodgkin disease) and inherited disease (chronic granulomatous disease). [5]

Granulomatous inflammations are common and intriguing problem. The arrival at proper diagnosis is mandatory so that the appropriate treatment can be meted out. Good clinical history, a close histological examination and a clinicopathological correlation is essential in making a final diagnosis. Ancillary studies like (ziehl-Neelsen, Grocott methamine silver), real time PCR, in situ hybridization can be performed to find out the cause of granuloma. However, some granulomas remain unexplained even with ancillary studies and in these instances, good clinical history and clinicopathological correlation are essential in making the final diagnosis.[5]

Aims and objectives.

1. To study morphology and etiology of granulomatous lesions.
2. To differentiate between tuberculous and non-tuberculous granulomatous lesions.
3. To study Acid fast bacilli (AFB) positivity.

Material and methods

This is a retrospective observational study of the cases reported as granulomatous lesions in the Department of Pathology, GMC Jammu over a period of 3 years from 31st August 2024 to 1st September 2021 are taken from the archives of histopathology section of the department and analysed. A total of 110 histopathology cases included in the study. Along with routine haematoxylin and eosin stain, special stains like 5% and 20% ziehl-neelsen stain and PAS stain were done wherever required.

All the granulomatous lesions on tissue biopsy sent for histopathological examination were included in the study. Relevant clinical details and laboratory investigations were collected from the hospital case records and correlated with histological findings. Detailed clinical data was obtained and noted in a structured proforma. This was to obtain information on age, sex, site and distribution of lesion, duration of disease.

Result:
A total of 110 cases of Granulomatous lesions were studied which showed a male predominance with 66 cases while 44 cases were seen in females with M:F ratio of 1.5:1. Most affected age group was from 21 to 30 years with 38 cases (34.5 %).

Majority of granulomatous lesions were seen in lymph nodes 46 cases (41.8%), followed by skin and subcutaneous 26 cases (23.6%), soft tissue 10 cases (9.09%), female genital tract 08 cases (7.2%), respiratory tract 06 cases (5.4%), male genital tract 04 cases (3.6%), breast 02 cases (1.8%), salivary gland 02 cases (1.8%), ENT 02 cases (1.8%), gastrointestinal tract 02 cases (1.8%), urinary tract 01 case (0.9%), bone and joint 01 case (0.9%).

we employed special stains like 5% ZN for (leprae bacilli) and 20% ZN for (tubercle bacilli) wherever required.
Majority of granulomatous lesions were seen in lymph node 46 cases (41.8%), the most common cause of granulomatous lesions was tuberculosis seen in 33 cases (30%) and the most common granuloma found is epithelioid granuloma seen in 54 cases (49.1%)

Foreign body granulomatous lesions identified in 20 cases (18.1%). Most common foreign body identified was suture material followed by ruptured epidermal cyst with keratin material.

The fungal infections were observed in 09 cases (8.1%) of granulomatous lesions. Aspergillus was commonest observed fungal infection, 06 cases (5.4%) followed by histoplasmosis 03 cases (2.7%). PAS stain was used for confirmation of all suspected fungal infection. The histiocytic granuloma was the most common pattern seen in 08 cases of fungal infection.

Sarcoidosis, total 08 (7.2%) cases identified in lung biopsies out of which 06 cases (75%) showed epithelioid granuloma.

The bacterial infections were observed in 04 cases (4.54%) of granulomatous lesion. Histiocytic granuloma was seen in 02 cases (100%) of rhinoscleroma with absence of epithelioid and giant cells and 02 cases (66.6%) of actinomycosis.

Among Hodgkin lymphoma 06 cases (5.4%) were found in lymph node. The granulomatous response to tumour seen in 06 cases (100%) of Hodgkin lymphoma.

The most common cause of granulomatous lesions was tuberculosis seen in 33 cases (30%) and most common histological pattern of granuloma was epithelioid type seen in 30 cases. Zn stain was performed in all cases of TB out of which 22 cases (66.7%) were positive for acid fast bacilli and 11 cases (33.3%) were negative.

Leprosy categorised as tuberculoid, lepromatous and indeterminate as per clinical and pathological criteria in Ridley and Jopling's classification. Out of 22 cases (20.0%) of leprosy, tuberculoid leprosy was seen in 12 cases (54.5%), followed by lepromatous leprosy in 08 cases (36.3%), for indeterminate leprosy seen in 02 cases (9.09%). The 04 cases (18.1%) of epithelioid granuloma and 18 cases (81.8%) of histiocytic granuloma were seen in leprosy.
The cases which are microscopic examination were showing multiple well-formed epithelioid cell granulomas with rim of lymphocytes and distribution through papillary and reticular dermis with the absence of Grenz zone were reported as tubercular leprosy. The cases which on microscopic examination were showing diffuse sheets of foamy histiocytes with presence of Grenz zone reported as lepromatous leprosy and cases with mild inflammation in the dermis with the few lymphocytes and macrophages around dermal nerves and blood vessels classified as indeterminate leprosy.

Histiocytic granuloma was predominant histological pattern in leprosy. Out of 22 cases of leprosy 18 cases (81.8%) were positive for ZN staining and 04 cases (18.1%) were negative.

Total 02 cases (1.8%) of leishmaniasis showing epithelioid granuloma were seen. Cutaneous leishmaniasis can be confirmed as a cause of granulomatous dermatitis with the help of Giemsa stain to demonstrate LD bodies.

Total 02 cases (1.8%) of granuloma annulare showing palisading granuloma in 02 cases were seen.

In 03 cases (2.7%), granulomas were seen of unknown etiology as positive causative factor could not be determined.

Tuberculous lesions affecting the gastrointestinal tract found in appendix 02 cases (1.8%).

Granulomatous lesions of female genital tract constitute tuberculosis of fallopian tube 03 cases (2.7%), tuberculosis of cervix 02 cases (1.8%) and male genital tract constitute tuberculosis of testis 04 cases (3.6%). Urinary tracts comprise 01 case (0.9%) of tuberculosis.

DISCUSSION

In present study, maximum number of granulomatous lesions was found in the age group of 21 to 30 years of age 38 cases (34.5%) followed by 31 to 40 years of age 24 cases (21.8%), similar results were found in other studies[2,6,7,8]while in study done by chandler et al[1] the most common age group involved was 51 to 60 years. Male preponderance was seen with M:F ratio of 1.5:1. This is in concordance with studies by Gulia SP et al[3] and Permi HS et al[6] showed M:F ratio of 1.27:1 and 1.09:1 respectively.

The commonest site involved was lymph node (41.8%), followed by skin and subcutis (23.6%), soft tissue (9.09%), female genital tract (7.2%), respiratory tract (5.4%), male genital tract (3.6%), breast (1.8%), salivary gland (1.8%), Ent (1.8%), GIT (1.8%), urinary tract (0.9%) and bone and joint (0.9%). This is in concordance with study by Kushwah A et al[7] where common site of involvement is lymph node 70 cases (32%) followed by skin and subcutis 64 cases (29%) whereas Permi HS et al[6] reported majority of the granulomas in skin and subcutaneous with 68 cases (24.72%) followed by lymph nodes 59 cases (21.46%).

In our study the most common cause of granuloma was tuberculosis (30%) followed by leprosy (20.0%). Permi HS et al[6] reported tuberculosis (47.26%) and leprosy (12.72%) in their study.

Tuberculosis is much more common in our population despite the active immunization programme through BCG vaccination. TB is common in pulmonary and extrapulmonary sites of infection commonly include lymph nodes, pleura and osteoarticular areas, although any organ can be involved. Tuberculosis is considered firstly in the differential diagnosis of granulomatous disease especially in the countries with a high incidence of tuberculosis, but it is always required to confirm by detailed analysis of clinical and ancillary studies to rule out other granulomatous disease. Tuberculosis must always be excluded despite cases not showing AFB positivity as exact diagnosis is important for the treatment purpose.

In our study, the most common pattern of granuloma seen was epithelioid granuloma seen in majority in tuberculosis 30 cases (90.9%), apart from tuberculosis epithelioid granulomas also seen in leprosy (18.1%), Hodgkin disease (100%), sarcoidosis (75%), leishmaniasis (100%) and in cases of unknown etiology (66.6%). Adhikari RC et al[8] and Permi HS et al[6] also reported epithelioid granuloma as the commonest type in their studies. Whereas in a study by Gulia SP et al[3] most common granuloma reported was necrotising epithelioid type.

ZN stain demonstrated tubercle bacilli in 22 cases (66.6%) out of 33 cases and negative in 11 cases (33.3%) whereas it was 91 (71%) out of 84 cases in a study by Krishnaswamy H et al[9] and 20.74% in a study by Permi HS et al[6]. Acid fast bacilli seen were fragmented or beaded rods present inside the cells or outside near the cell. Considering the limitations in sensitivity and specificity of ziehl Neelsen staining for mycobacterial detection, mycobacterial culture, molecular and serological techniques, histomorphological analysis appears to be the only important and feasible technique for the diagnosis of tuberculosis in some patients.

Leprosy is major cause of granulomatous dermatitis in our study accounting 22 cases (20%) showing tuberculoid leprosy in 12 cases (54.5%), lepromatous leprosy in 08 cases (36.3%) and indeterminate leprosy 02 cases (9.09%) similar scenario seen in a study by Jyotsna Suri et al[14] where leprosy comprise the major reported etiology of the cases of granulomatous dermatitis.

ZN stain demonstrate Leprae bacilli in 18 cases (81.8%) out of 22 cases and negative in 04 cases (18.1%).

The commonest fungal infection was aspergillus 06 cases (5.4%) followed by histoplasmosis 03 cases (2.7%). All cases suspicious of fungal etiology were subjected to PAS stain for confirmation and identification of fungal types. PAS stain showed positivity in 09 cases (100%). Histioytic granuloma demonstrated in 08 cases (88.8%) of fungal infections represent of chronic inflammatory response aimed at containing and isolating the fungal organism that the body is unable to eliminate through regular immune mechanism.

Our result were comparable to other studies by Permi HS et al[6] and Adhikari RC et al[8] who also found aspergillus as the most common fungal infection in their studies 06 cases (25%) and 03 cases (23%) respectively.

Neoplasm is known to be associated with the granulomatous response in the parenchyma mainly seen in Hodgkin disease. In present study 06 cases of Hodgkin lymphoma (5.4%) diagnosed, all of them showing epithelioid granuloma. The presence of granulomas in tumour parenchyma has largely been attributed to the cytokine of either the main tumour or other cells composing the tumour background. In other cases, the granulomatous inflammation may be found in the lymph nodes draining the primary tumour either with or without metastatic cancer. Wherever granuloma is seen in the draining lymph node in a case of cancer it should be carefully scrutinized for the presence of malignant cells. In a study by Permi HS et al[6] granulomatous response was seen at the periphery of tumour area and also in the draining metastatic lymph nodes with total of 16 tumour cases with Hodgkin lymphoma in 02 cases (12.5%).

In our study total 20 cases of foreign body seen in which 18 cases forming foreign body granuloma and 02 epithelioid granuloma, histopathologically foreign body granulomas shows foreign body material surrounded by histiocytes, foreign body giant cells, lymphocytes and plasma cells. In a study by Rajeshwari K et al[13] maximum number cases was foreign body type of granuloma accounting 43.3% of the cases.

Sarcoidosis is a granulomatous disease involving multiple organ systems including the lungs, lymph nodes, skin, joints. In our study total 08 cases (7.2%) of Sarcoidosis identified, epithelioid granulomas were observed in 06 cases (75%). Similar results were seen in study by Adhikari RC et al[8] showing sarcoidosis in 02 (5%) cases both showed epithelioid granuloma (100%).

We had 02 cases of rhinosclerosis which forming histiocytic granuloma consisting of plasma cells, mikulicz cell and inflammatory cell in the nasal cavity.

Etiology for granulomatous lesions could not be identified in 03 (2.7%) cases and categorised as idiopathic etiology. The most common pattern of granuloma observed was epithelioid type 02 (66.6%) cases followed by histiocytic granuloma observed in 01 case (33.3%).

CONCLUSION

In our study Granulomatous lesions are more commonly seen in 3rd decade of life with male predominance.

The most common cause of Granulomatous lesion in our study was tuberculosis with lymph node being the most common site. Majority of granulomas had infectious etiology. According to morphology epithelioid was the predominant granuloma followed by histiocytic granuloma. AFB was positive in total 40 cases (36.3%) out of which 22 cases (66.7%) positive for tuberculosis and 18 cases (81.8%) positive for leprosy.

Even after doing the special stains in some cases, it is not possible to find out the etiology of the granulomatous lesion, hence ancillary studies of culture, serology, PCR may be required for confirmation.

Funding -no funding sources.

Conflict of interest- None

References

1. Chander RV, Jayaganesh P, Reddy TP, Srinivasan C. Spectrum of granulomatous lesions in a tertiary care hospital. Indian J Pathol Oncol. 2016 Oct;3(4):611-.
2. Khatib WM, Bisht TV, Shukla DB, Chandrashekhar V. Granulomatous Lesions: An Experience in a Tertiary Care Hospital. Subscription Form. 2016;5(2):87.
3. Gulia SP, Lavanya M, Archana V, Kumar PA, Selvi K. Histomorphological analysis of granulomatous lesions in a teaching hospital, Puducherry. International Journal of Current Research and Review. 2015 May 1;7(9):78.
4. Shah KK, Pritt BS, Alexander MP. Histopathologic review of granulomatous inflammation. Journal of clinical tuberculosis and other Mycobacterial Diseases. 2017 May 1;7:1-2.
5. B, Shaikh & Y, Sonawane & B, Mune & S, Dantkale. (2023). Spectrum of granulomatous lesions in a tertiary care hospital. International journal of scientific research. 49-52. 10.36106/ijsr/0901729.
6. Permi HS, Padma SK, Teerthanath S, Mathias M, Kumar S, HL KP. A histopathological study of granulomatous inflammation. Journal of Health and Allied Sciences NU. 2012 Mar;2(01):15-9
7. Kushwah A, Bhattarai N, Koirala A. A histopathological study of granulomatous lesions. Journal of Pathology of Nepal. 2018 Sep 6;8(2):1341-5.
8. Adhikari RC, Shrestha KB, Sayami G. Granulomatous inflammation: a histopathological study. Journal of Pathology of Nepal. 2013 Oct 24;3(6):464-8.
9. Krishnaswamy H, Job CK. The role of Ziehl Neelsen and Fluorescent stains in tissue sections in the diagnosis of tuberculosis. Indian Journal of Tuberculosis. 1974 Jan;21(1):18-21.
10. 10.George V, Srinivasan S. Histopathological spectrum of granulomatous skin lesions: A review. SBV J Basic Clin Appl Health Sci. 2019;2(3):95-104.
11. Lee M, Lee MS, Lee JS, Ko SY, Jeong SY. Spectrum of imaging findings of chronic granulomatous disease: a single center experience. Diagnostic and Interventional Radiology. 2017 Nov;23(6):472.
12. Hirsh BC, Johnson WC. Pathology of granulomatous diseases: histiocytic granulomas. International journal of dermatology. 1984 Jul;23(6):383-9.

13. Rajeshwari K, Abhishek MG. Histomorphological Profile of Non-Infectious Granulomatous Dermatitis: An Appraisal. JK Science: Journal of Medical Education & Research. 2023 Jan 10;25(1):24-9.
14. Suri J, Bhardwaj S, Kumari R, Kotwal S. A clinicopathological analysis of granulomatous dermatitis: 4 Year retrospective study. JK Science. 2017;19(1):22-5.

Table no 1 Site wise distribution of granulomatous lesions

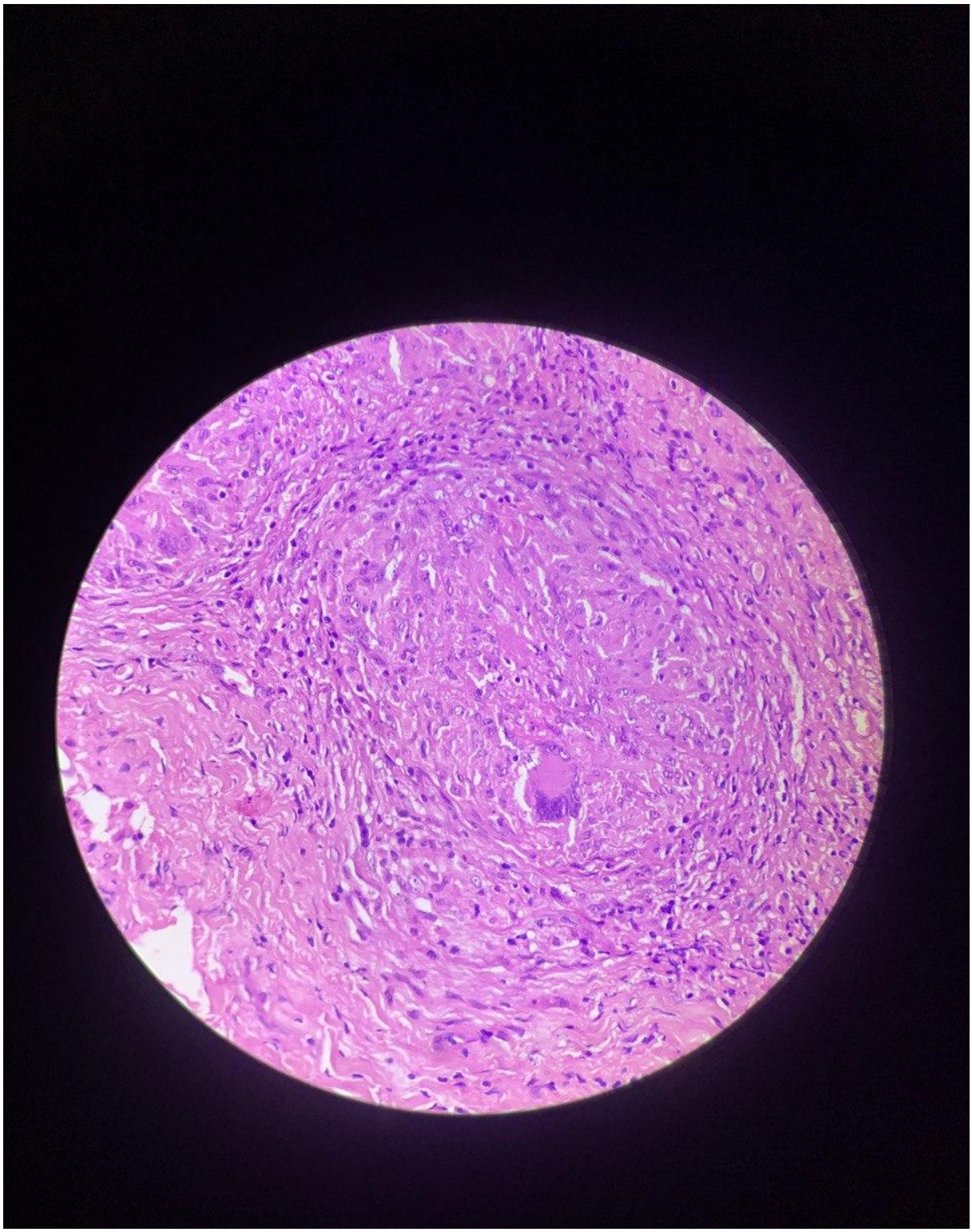
S.NO.	SITE	Number of cases	Percentage
1	Lymph node	46	41.8%
2	skin and subcutaneous tissue	26	23.6%
3	Soft tissue	10	9.09%
4	Female genital tract	08	7.2%
5	Respiratory tract	06	5.4%
6	Male genital tract	04	3.6%
7	Gastrointestinal tract	02	1.8%
8	Ear, nose, throat	02	1.8%
9	Breast	02	1.8%
10	Salivary gland	02	1.8%
11	Bone and joint	01	0.9%
12	Urinary tract	01	0.9%
	TOTAL	110	100%

Table no 2 Distribution of granulomatous lesions according to etiology

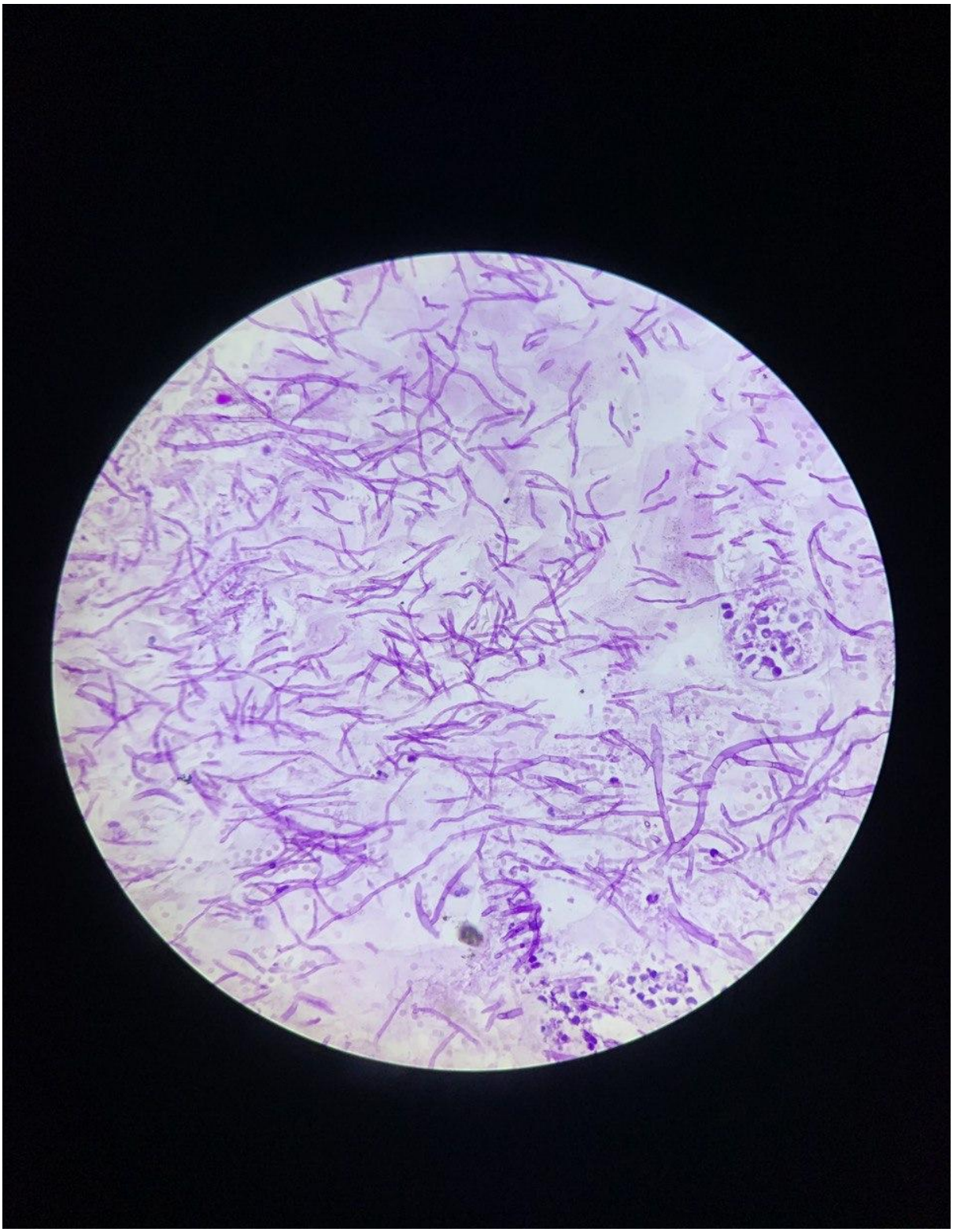
s.no	CAUSES	NO. OF CASES (n)	PERCENTAGE (%)
1	Tuberculosis	33	30%
2	Leprosy	22	20.0%
3	Foreign body	20	18.1%
4	Sarcoidosis	08	7.2%
5	Hodgkin lymphoma	06	5.4%
6	Aspergillus (fungal)	06	5.4%
7	Histoplasmosis (fungal)	03	2.7%
8	Actinomycosis(bacterial)	03	2.7%
9	Rhinosclerosis (bacterial)	02	1.8%
10	Granuloma annulare	02	1.8%
11	Leishmaniasis	02	1.8%
12	Unknown etiology	03	2.7%
TOTAL		110	100%

Table no.3 Site wise distribution of various granulomatous lesion				
s.no	site	Diagnosis	No of cases	percentage
1	Lymph node	TB (20), sarcoidosis (06), Hodgkin lymphoma (06), fungal (06),foreign body (05), unknown (03)	46	41.8%
2	skin	Leprosy (22), granuloma annulare (02), leishmaniasis (02)	26	23.6%
3	Fallopian tube	TB (03), actinomycosis (03)	06	5.4%
4	Cervix	TB (02)	02	1.8%
5	Testis	TB (04)	04	3.6%
6	Urinary bladder	TB (01)	01	0.9%
7	Breast	TB (02)	02	1.8%
8	Salivary gland	Foreign body (02)	02	1.8%
9	Bone	TB (01)	01	0.9%
10	Lungs	Sarcoidosis (02), foreign body (02), fungal (02)	06	5.4%
11	Appendix	TB (02)	02	1.8%
12	Soft tissue	Foreign body granuloma (10)	10	9.09%
13	Ent	Rhinosclerosis(02)	02	1.8%

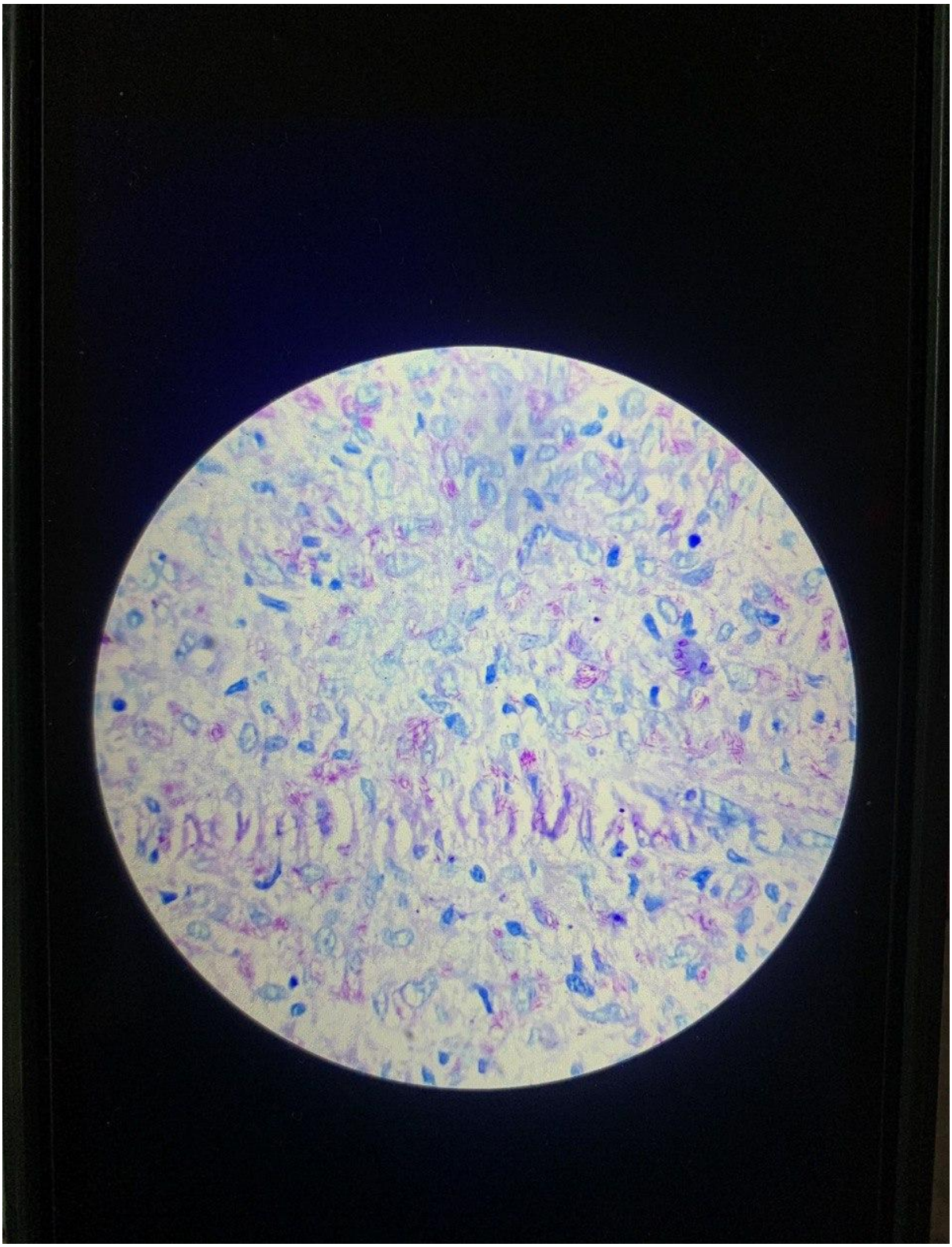
Table no.4 Histopathological pattern of various granulomatous lesions						
s.n	Etiology	Epithelioid	Histiocytic	Foreign body	Palisading	Total (no. of cases & %)
1	Tuberculosis	30(90.9%)	03(9.1%)	0	0	33(100)
2	Leprosy	04(18.1%)	18(81.8%)	0	0	22(100)
3	Foreign body	02(10%)	0	18(90%)	0	20(100)
4	Fungal	01(11.1%)	08(88.8%)	0	0	09(100)
5	Rhinosclerosis	0	02(100%)	0	0	02(100)
6	Actinomycosis	01(33.3%)	02(66.6%)	0	0	03(100)
7	Hodgkin lymphoma	06(100%)	0	0	0	06(100)
8	Sarcoidosis	06(75%)	02(25%)	0	0	08(100)
9	Granuloma annulare	0	0	0	02(100%)	02(100)
10	Leishmaniasis	02(100%)	0	0	0	02(100)
11	Unknown	02(66.6%)	01(33.3%)	0	0	03(100)
	Total	54(49%)	36(32%)	18(16.3%)	02(1.8%)	110(100)



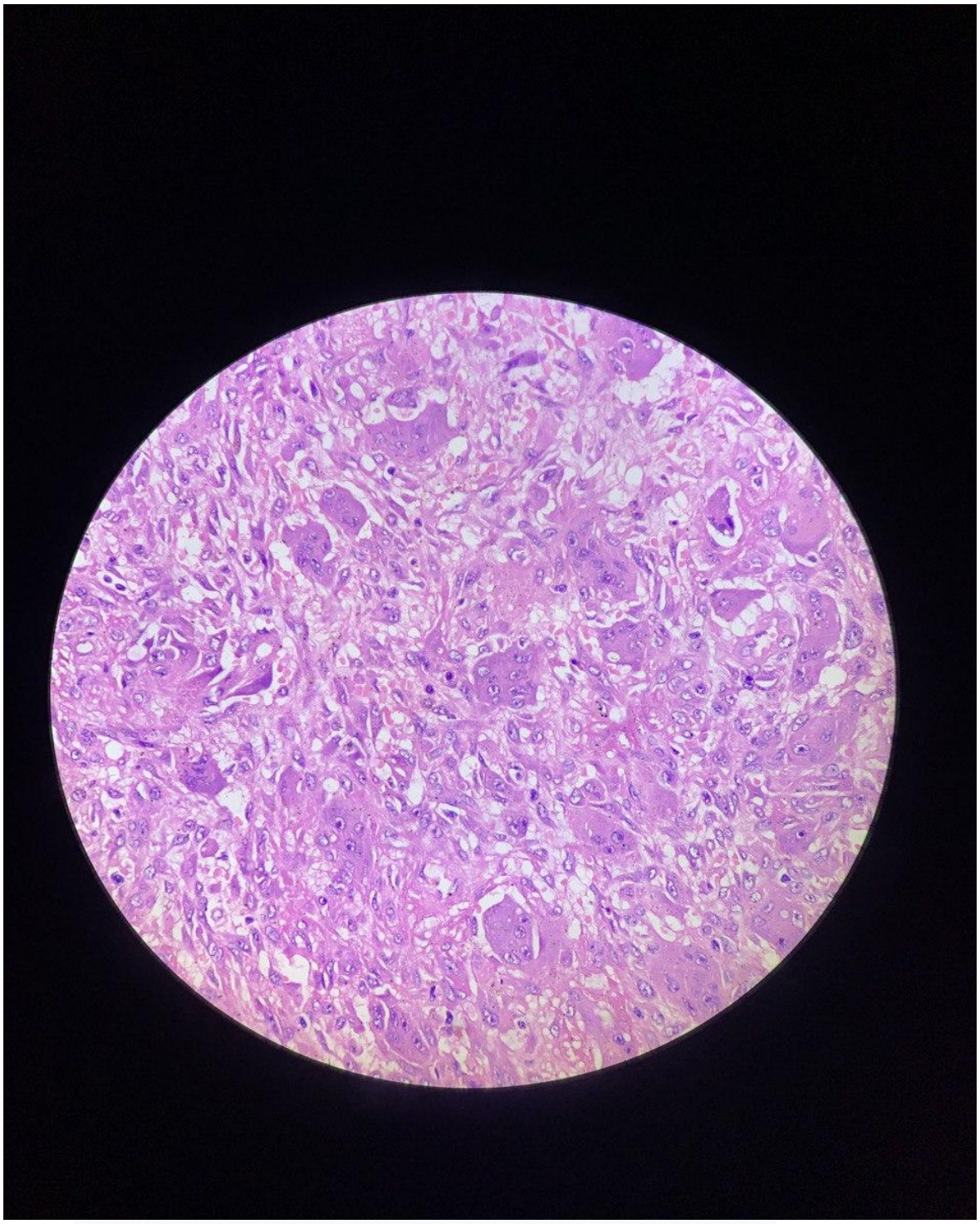
Photograph 1. Shows Granuloma formation with Langhans type Giant cell. (H&E 400)



Photograph 2. Shows numerous septate hyphae (fungal) surrounded by inflammatory infiltrate. (H&E 400)



Photograph no.3 shows numerous acid-fast bacilli positive with ziehl neelsen stain. (H&E 400)



Photograph no 4. Shows multiple Giant cells without necrosis. (H&E 400)