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Determining the stages of kaposi sarcoma through histopathological analysis: identifying the most effective findings

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Abstract:

Objective: Kaposi sarcoma (KS) is a locally malignant angio-proliferative tumor that manifests itself in a variety of histological ways at different stages. Depending on the stage, frequency, and findings they are associated with, histopathological results might have diagnostic relevance. The goal of the research was to establish a finding or set of results, that is significant at distinct phases of KS and can be used to accurately pinpoint that stage.

Methods: The diagnosis of KS patients was examined retrospectively. Investigations were done on the connections between morphological factors and illness phases. The method of multivariate regression and the Chi-Square test were employed in the comparison analysis. The acceptable statistical significance threshold was a p-value less than 0.05.

Results: In this study, different phases of a given condition were analyzed, and it was discovered that there were statistically significant variations in the presence of specific parameters at various stages. With a 25.7 times higher odds ratio, the research showed that the presence of hemosiderin was substantially more common in the plaque stage compared to the patch stage. Similar to this, the odds ratio for the occurrence of mitosis was 3.7 times greater in the nodule stage compared to the plaque stage.

Conclusions: The most reliable and definitive histopathological outcomes for the relevant stage should be used to determine the KS diagnosis.

Keywords: histopathology, kaposi sarcoma, findings

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Introduction:

The gamma-herpesvirus subclass constituent, human herpesvirus 8 (HHV-8), which is a kind of tumor, is crucial in the development of Kaposi sarcoma (KS). Moritz Kaposi, a dermatologist from Hungary, first referred to it as an "idiopathic multi-coloured carcinoma of the skin" in 1872 [1]. In its normal growth, KS exhibits patch, plaque, and nodular phases and is a regionally invasive tumour with little carcinogenic probability [2]. Each stage has distinctive histological characteristics, which makes it more difficult to make a histopathological diagnosis and make a differential diagnosis at each level. Similar arterial sarcoma or epidermal spindle cell tumours in the nodular stage or benign or reactive lesions in the patch stage are among the problematic differential diagnoses [3,4]. For each stage of KS, it is crucial to identify meaningful and trustworthy histopathological diagnostic characteristics.

In our case series, the histological characteristics that were utilized to diagnose KS were assessed. The goal of the research was to establish a finding or set of results, that is distinctive to each phase of KS and may be used to pinpoint a particular stage of KS.

Methods:

Study Design: To review the histological data of 121 instances of Kaposi sarcoma, a retrospective investigation was carried out at Mayo Hospital, Lahore, Pakistan from January 2023 to April 2023. Two pathologists independently analyzed the histological sections to ascertain the frequency, absence, and presence of different characteristics. Stage, acanthosis, cleft-like space, ulceration, fascicle creation, horizontally arranged bundles of vascular tissue, large peripheral vessels, spindle tissues, promontory indication, nodule creation, hemosiderin-laden macrophages, hyaline globules, nuclear atypia, mitotic action, necrosis, extravasated erythrocytes, and cells of inflammation and their form were among these characteristics.

Statistical Analysis: The purpose of the research was to look into the connection between these physical traits and the illness stage. While quantitative assessments were provided as numbers and percentages, qualitative evaluations were done using min, max, and median values. For comparison studies, the Pearson Chi-square test and multivariate regression analysis were used. A p-value of less than 0.05 was considered statistically significant.

Results:

The 121 patients in the current research had a median age of 68.14 years (with a range of 26-93 years) at the time of diagnosis. Males were more likely to have KS (62%) than females, and feet were the most prevalent site (53%). The lower limb (66% of all le sions) had the highest prevalence, followed by the upper limb (16.5%). One tumour was discovered in the scrotum, while head and neck lesions were seen in nine instances, which is unusual (Table 1).

Table 1: Location-wise KS distribution

Location	n(%)
Ear	3(2.5)
Arm	5(4.1)
Buttock	3(2.5)
Hand	10(8.3)
Leg	35(28.9)
Foot	53(43.8)
Others	12(9.9)
Total	121(100)

The following were the occurrences of the examined parameters according to the stages:

90% of patients had horizontally oriented bundles of vascular tissue, inflammatory cells, and extravasated erythrocytes in the patch stage. In the plaque stage, 96.6% of cases showed the "promontory" sign, hyaline globules, or hemosiderin, and 100% of cases had extravasated erythrocytes. Erythrocyte extravasation was seen in 98.8% of patients at the nodular stage, while globules were present in 97.6% of instances. Figure 1 and Table 2 both provide the aforementioned data.

Table 2: Features that are present in more than 80% of people with Karposi's sarcoma in three phases

Patch	Promontory indication of erythrocyte extravasation
	Horizontally arranged bundles of vascular tissue
Plaque	Extravased erythrocytes
	Hemosiderin
	Inflammation
	Globules
	Promontory sign
Nodular	Hyperkeratosis
	Hemosiderin, extravasated erythrocytes
	Globules
	Nodular creation
	Large arteries surround the tumor's edge
	Clefts
	Fascicles
	Spindle cells

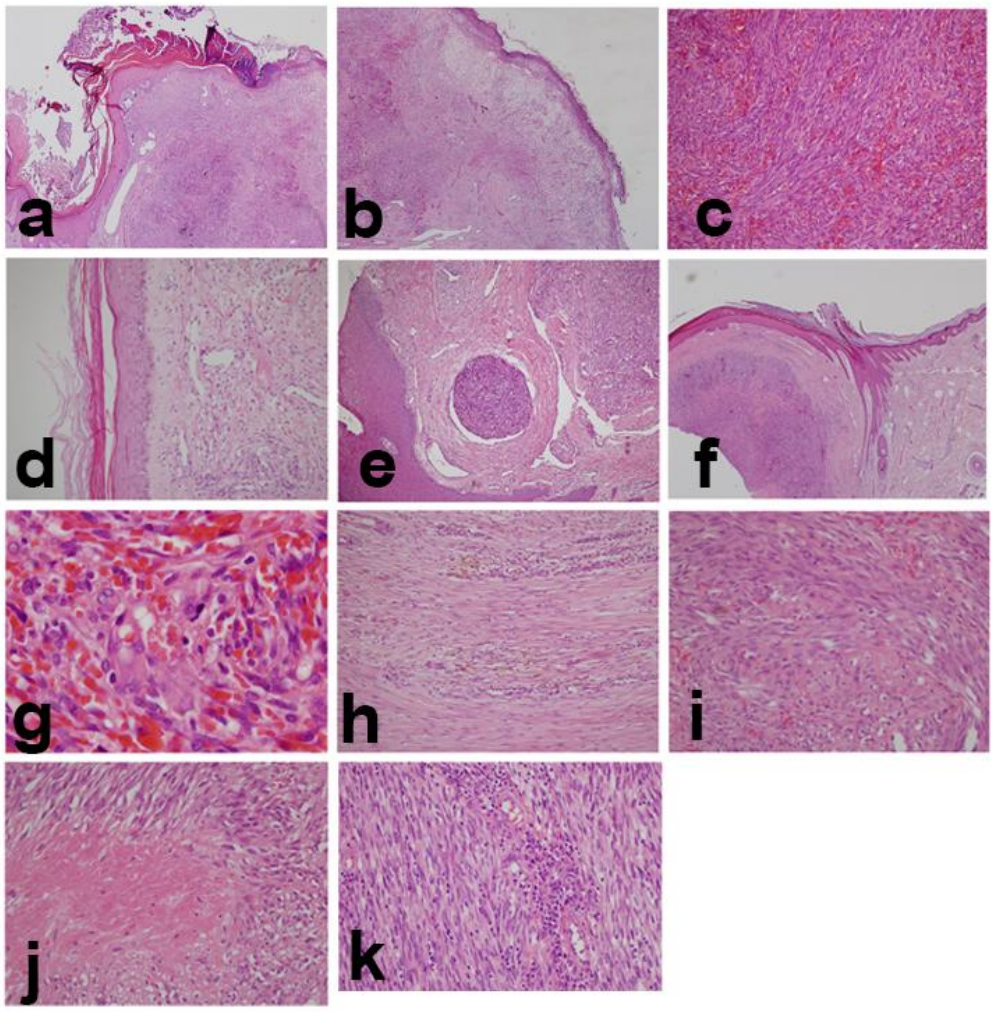

Figure 1: (a) Hyperkeratosis, (b) Ulceration, (c) Spindle cells, (d) Horizontally arranged bundles of vascular tissue, (e) Promontory sign, (f) nodule creation, (g) Extravasated erythrocytes, hyaline globules, (h) Hemosiderin-laden macrophages, (i) Nuclear atypia, (j) Necrosis, (k) Cells of inflammation and their form

Two of the important parameters that the multivariate regression analysis indicated were determined to be statistically significant. With a p-value of 0.02 and a confidence interval spanning from 1.6 to 398.2, it was discovered that the probabilities of harbouring hemosiderin were 25.7 times greater in the plaque stage compared to the patch stage. Similar to the plaque stage, the nodule stage had 3.7 times the chance of having mitosis, with a p-value of 0.002 and a confidence range spanning from 3.8 to 489.7 (Table 3).

Table 3: Examination of the frequency of histological characteristics in each of the three phases of Karposi's sarcoma using multivariate analysis

			Odd Ratio	Standard Error	CI (Range)	p-value
Patch and plaque stages	Globule	p	13,1	1,5	0,6 - 266,3	
		a	1	--	--	0,09
	Hemosiderin	p	25.7	1.3	1.6 - 398.2	
		p	1	--	--	**0,02**
Nodular and plaque stages	Necrosis	p	19,5	6325,0	0,0	
		a	1	--	--	0,9
	Mitosis	p	3,7	1,2	3,8 - 489,7	
		a	1	--	--	**0,002**
	Atypia	p	-0,8	1,3	0,03-6,3	
		a	1	--	--	0.5
	Nodule	p	-0,7	0,9	0,05 - 4,4	
		a	1	--	--	0,5
	Horizontally arranged bundles of vascular tissue	p	-0,2	1,1	0,08 - 6,7	
		a	1			0.7
	Cleft	p	1,1	0,9-101,3		
		a	1	--	--	0,051
	Fasicle	p	1,2	0,4- 57,3		
		a	1			0,1
	Spindle cell	p	-0,8	1,0	0,05 - 3,1	
		a	1	--	--	0,3
	Ulcer	p	0,6	1,4	0,1-32,7	
		a	1	--	--	0,6
	Acanthosis	p	0,2	0,7	0,2 - 5,9	
		a	1	--	--	0,7
	Hyperkeratosis	p	2,4	1,1	1,2 - 96,5	
		a	1	--	--	**0,02**
Nodular and patch stages	Hemosiderin	p	6,8	1,3	0,4 - 103,6	
		a	1	--	--	0,1
	Mitosis	p	3,7	1,1	0,3 - 37,6	
		a	1	--	--	0,2

	Globule	p	0,7	1,8	0,02 - 28,6	
		a	1	--	--	0,8
	Nodule	p	9,5	2,08	0,1 - 562,05	
		a	1	--	--	0,2
	Cleft	p	2,3	1,5	0,1 - 50,2	
		a	1	--	--	0,5
	Fasicle	p	1,6	2,1	0,02 - 113,3	
		a	1	--	--	0,8
	Spindle cell	p	1,2	1,6	0,04 - 33,2	
		a	1	--	--	0,8
	Acanthosis	p	2,7	1,1	0,2 - 27,1	
		a	1	--	--	0,3
	Hyperkeratosis	p	1,3	1,3	0,1 - 19,6	
		a	1	--	--	0,8

Discussions:

The multicentric angio-proliferative spindle cell tumour known as Kaposi sarcoma, which develops from endothelial cells, is heterogeneous in terms of both histopathology and clinical presentation. Men between the ages of 6 and 7 often have numerous lesions on their lower limbs [5-9]. The available literature was found to be consistent with the social background of our case sample.

An incidence of the nodular stage of 36–87.5% has been recorded in earlier investigations [5–9]. The nodular stage (67,8%) accounted for the majority of occurrences in our investigation. On the other hand, according to some research [10], the plaque stage is the one that is most often seen in KS patients who are HIV positive. In our HIV-positive individuals, the nodular stage was typical, although it was impossible to collect serological information on every patient.

Hyaline globules, which are erythrocytic degradation products' repositories and are thought to have diagnostic value in Kaposi sarcoma [11,12,13], despite their lack of specificity. In this investigation, erythrocyte extravasation (98.3%) and hyaline globules (95%) in the cytoplasm of cells were the two most frequent histological features. Significant variations were found in the occurrences of the nodule, globule, atypia, mitosis, necrosis, spindle cell presence, fascicles, cleft-like space, horizontally arranged bundles of vascular tissue, hemosiderin, large peripheral vessels of the tumour, acanthosis, hyperkeratosis, ulceration, and mitosis among the stages.

Small, thin-walled, protruding, endothelium-lined vessels with massive ectatic vessels and skin appendages around them define the early or patch stage of KS. A defining feature of KS is the 'promontory sign,' which is the opening of the smaller artery walls to the lumens of the larger ectatic

neoplastic channels. Around the lesion, there is a small amount of inflammation that is characterized by lymphocytes, plasma cells, extravasated erythrocytes, and macrophages that have hemosiderin on their surface. During the patch stage, the papillary dermis is often intact [14-19]. In our investigation, the most frequent histological changes in this stage were horizontally arranged bundles of vascular tissue, erythrocyte extravasation, and inflammation. However, there was no evidence of necrosis.

Among all the characteristics we employed to accurately pinpoint the plaque stage, the existence of the promontory sign, erythrocyte extravasation, hemosiderin buildup, and inflammation have all been mentioned as beneficial results in the literature [20-24]. According to our research, the promontory observations, erythrocyte extravasation, and horizontal positioning of vascular structures are commonly seen in the patch stage and are statistically significant. Therefore, looking for their comorbidity may aid in confirming the diagnosis of the patch stage. When a tumour is at the plaque stage, proliferating vascular structures invade the dermis and sometimes even the subcutis.

Around the arterial channels that are multiplying, spindle cells start to gather and form bundles. There are additional instances of eosinophilic and hyaline globules [25-28]. The most often seen plaque stage characteristics in this investigation were the promontory sign, hyaline globules, and hemosiderin. Nobody saw any necrosis. Plaque stage samples most commonly showed the promontory sign, which is a hallmark of the patch stage. The most noteworthy histomorphological result in the plaque stage was the presence of hemosiderin as compared to the patch stage." Erythrocyte-containing clefts that divide vascular systems and intersecting, bundled spindle cells are seen in the traditional nodular stage of KS. When cut into transverse sections, the spindle cells resemble a sieve or a honeycomb. Around certain tumours, dilated blood vessels that resemble cavernous hemangiomas may be seen. The tumour may display cellular pleomorphism, necrosis, and mitotic figures at this stage [29,30], and the big cutaneous nodules may ulcerate. In our investigation, subjects identified in the nodular stage most often included histological signs of inflammation, globules, erythrocyte extravasation, and spindle cells. The presence of mitosis in the nodular stage was the most important distinguishing factor from the plaque stage. We think it's helpful to identify between the nodular stage and the other phases by looking for ulceration, necrosis, atypia, and mitosis all at once.

Conclusions:

The demographic information and distribution of histopathological characteristics by stage were comparable to those reported in the literature in this retrospective analysis of KS. When the histological finding that is most conspicuous at a particular stage and best represents that stage is examined, the diagnosis of KS—which has varied histopathological findings at different stages—can be established more conclusively. Additionally, the creation of a scoring system on its own with case studies with a larger number of cases would make it easier to diagnose KS at various stages.

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