

Apparently Primitive Caecal Malignant Melanoma: A Diagnostic and Histogenetic Challenge: A Case Report and Literature Review

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Abstract

Extracutaneous melanomas are in the majority of cases reported in the literature as secondary lesions of a primary skin tumor. Far more rarely do they present themselves as primitive. Extracutaneous melanomas can be grouped into three categories: Ocular; Mucosal, Metastatic. Obviously, the greatest number of lesions is represented by metastatic forms. The Mucosal Melanomas preferably arise in peripheral districts of the gastrointestinal tract (mouth, pharynx, esophagus, anorectal mucosa), respiratory (nose, larynx) and urogenital (Vulva, vagina, cervix).

Keywords: Extracutaneous melanomas • Melanoma • Colectomy

Introduction

All of these lesions are characteristically associated with mucous membranes covered with squamous epithelium. An even smaller percentage is represented by apparently primitive lesions in more deeply visceral districts, such as the lung and gastrointestinal tract. The finding of a Melanoma, apparently primitive at the cecal level, has been considered worthy of mention.

Case Report

A 70-year-old man has been experiencing progressive weight loss, associated with intestinal canalization disorders. These disorders have undergone a progressive aggravation until they assume an occlusive character. The patient is hospitalized. The instrumental examinations highlight an obstructive process at the ileocecal level. The patient undergoes a right colectomy. In the caecal tract there is a nodular formation of 4 cm in diameter, with a soft consistency and a greyish color. In correspondence of the neoformation the mucosal lining appears widely ulcerated and necrotic. In the meso there are some hyperplastic lymph nodes. They are taken numerous fragments of the neoformation. The material is fixed in formalin and embedded in paraffin. The sections are stained with Hematoxylin-Eosin. Sections are also subjected to immunohistochemical investigation with a panel of the following antibodies (Table 1).

Histology

The morphological picture is that of a disordered proliferation of atypical elements of medium-large size, with a globose or spindle shape, provided with a voluminous nucleus with a prominent nucleolus and sometimes large amphophilic cytoplasm. A lively and atypical mitotic activity is noted. Focal areas of recent hemorrhagic infiltration and coagulative necrosis. No structures related to the intestinal mucosa are recognized (Figure 1). An accurate scan

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Table 1. Immunohistochemical investigation with a panel of the following antibodies.

CK MNF116	Monoclonal 1:50 DAKO Agilent
CK AE1/AE3	Monoclonal 1:50 DAKO Agilent
Vimentin	Monoclonal 1:50 DAKO Agilent
Sm. Muscl Act.	Monoclonal 1:50 DAKO Agilent
Desmin	Monoclonal 1:50 DAKO Agilent
CD68	Monoclonal 1:50 DAKO Agilent
C-Kit	Polyclonal 1:400 DAKO Agilent
Dog1	Monoclonal 1:100 /200 BioCare
CD34	Monoclonal 1:20 DAKO Agilent
NSE	Monoclonal 1:50 DAKO Agilent
Cromogr.	Monoclonal 1:50 DAKO Agilent
EMA	Monoclonal 1:50 DAKO Agilent
S-100	Monoclonal 1:400 DAKO Agilent

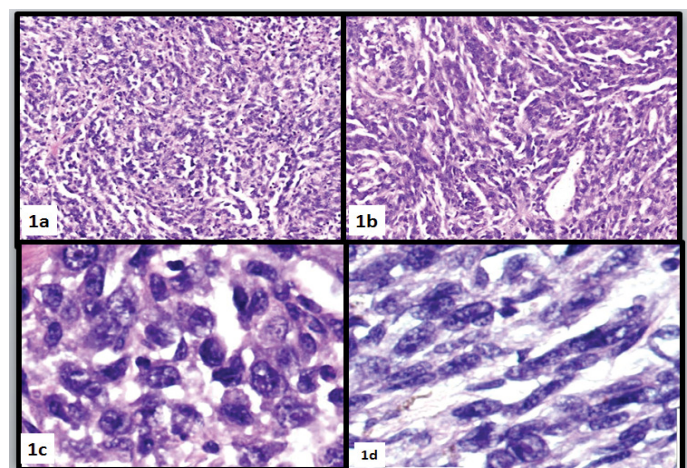


Figure 1 (a-d). Various aspects of neoplastic proliferation. Atypical elements with epithelioid, globose morphology alternate with spindle-shaped cells. HE 120-150x.

of the preparation highlights very rare, scattered elements in whose cytoplasm there are granules of brown pigmentary material (Figure 2).

Immunohistochemistry

The expression of S100 and Vimentin, with the complete negativity of other markers and in relation to the detection of intracellular pigmentary material, has recommended adding the melanocyte markers HMB45 and MELA to

the initial panel. Both of these markers presented intense and widespread reactivity (Figure 3). On the base of the morphological findings and the results of immunohistochemical investigations, the diagnosis of Malignant Melanoma of the cecum is formulated. A subsequent anamnestic investigation and an accurate dermatological review did not reveal the existence of previous or current melanocytic lesions (Table 2).

Discussion

Only 4% to 5% of all primary melanomas do not arise from the skin. Most of the extra cutaneous primary melanomas originate in areas in which the presence of melanocytes is normally documented: eye, nose, throat, larynx, esophagus, ano-rectum, vulva-vagina, uretra. The other visceral sites: small and large intestine, gallbladder, lung, kidney, uterus, spleen are very rare occurrences [1,2]. Melanoma is the most common tumor to metastasize to the Gastro-Intestinal (GI) tract. These tumors are commonly metastases from a cutaneous or less frequently, an ocular primary lesion. Rarely Malignant Melanomas (MM) of the GI tract can be primary tumour. A primary cutaneous lesion was identified in 24 cases (80.0%) with the remaining 6 patients (20.0%) presenting with GI tract involvement as the first site of disease [3]. The existence of primitiveness in these sites is highly controversial, also in relation to the demonstrated possibility of regression of cutaneous melanoma that occurs, according to the Authors from 4% to 10% of cases [4,5].

So much so that the acronym MUP (Melanoma with Unknown Primary) was created for these lesions. Various hypotheses have been advanced about the possibility that truly primary lesions may arise in these sites. An origin from Scwannian neuroblasts [6], from the neural crest [7] and from APUD cells [8-12] has been proposed. Scrolling through the literature it emerges that the

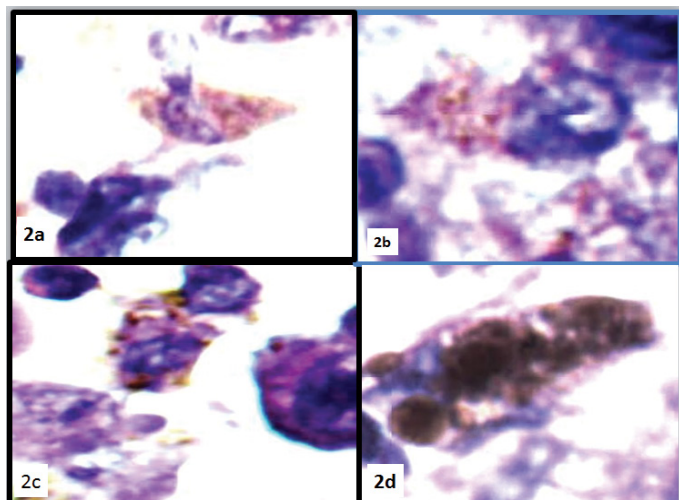


Figure 2 (a-d). Some rare cells in whose cytoplasm there is pigmentary granular material. HE-500x.

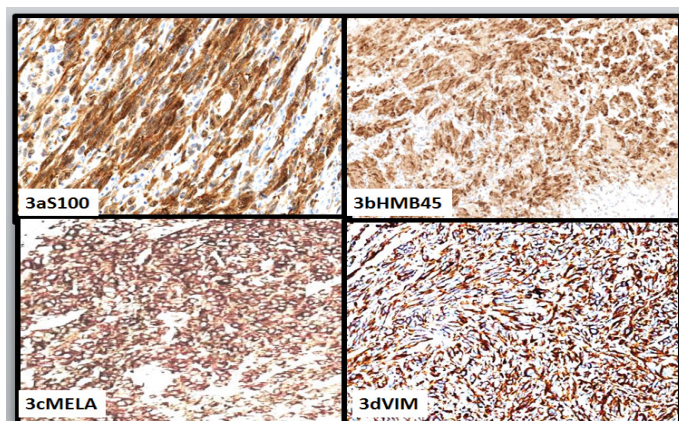


Figure 3. a: S100; b: HMB45; c: MELA; d: Vim; 150x.

Table 2. Markers presented intense and widespread reactivity.

Ab	Ck116	CKAE1-AE3	Vim	Smact	Desm	Cd68	Ckit	Dog1	Cd34	NSE	Crom	EMA	S100	HMB45	MELA
-	-	+	-	-	-	-	-	-	-	-	-	-	+	+	+
Figures		3d											3a	3b	3c

Table 3. Five were located in the cecum, six in the ascending colon, two in the transverse, three in the descending-sigma, in two the affected tract was not specified.

S. No.	Author	Sex	Age	Site	Follow Up	Ref
1	Yi NH	W	50	S	nd	9
2	Miliaras S	W	67	R	nd	10
3	Kaya E	nd	nd	Col	Met at surgery	11
4	Mori D	W	88	L	3 yrs l&w	12
5	Kenney B	M	54	T	nd	13
6	Raja J	nd	nd	T	nd	14
7	Avital S	Nd	nd	R	2 yrs l&w	15
8	Li WX	M	57	R	nd	16
9	Serin G.	M	30	C	1yr l&w	17
10	Poggi SH	M	/9	C	5yrs l&w	16
11	Sashiyama H	W	39	C	nd	19
12	Mester E,	nd	nd	col	nd	20
13	De Palma GD	W	56	R	2yrs l&w	21
14	McNicol FJ	M	84	C	30mth l with met	22
15	Takahashi-Monroy	W	51	C	nd	23
16	Mandot A	W	62	R	nd	24

R: Right; L: Left; C: Caecum; S: Sigmoid; Colon: NAS; nd: No done; l&w: Live & Well; met: Metastase

intestinal tract most affected by the metastatic process is the small bowel. Entering the Med Line "Primary Melanoma Colon" between the years 2000-2019, 16 items are reported regarding Reports of individual cases. Out of twelve evaluable cases, seven belonged to females, five to males. With ages ranging from 30 to 88 years Four was not indicated. Five were located in the cecum, six in the ascending colon, two in the transverse, and three in the descending-sigma, in two the affected tract was not specified (Table 3) [13-24].

Conclusion

The data currently available are provided by a modest number of reports concerning individual cases and the lack of consistent case series so far does not allow a concrete judgment to be made on the clinical behavior of these lesions. On such small series and with incomplete data, it is not possible to form a judgment regarding the prognosis of these tumors. The impression is that these are not particularly aggressive lesions even in the presence of metastases. The possibility of distinguishing as primary or secondary tumors of the gastrointestinal tract, expressing melanocytic markers, will hardly be achieved with clinical or purely morphological criteria, especially in the case of solitary lesions. Assuming that at least a part of them is really primary, I would remind myself that not all extra cutaneous tumors expressing melanocytic markers are melanomas (Clear Cell sarcoma, PeComa, Melanotic Schwannoma). The problem can be perhaps solved by comparing the bimolecular profiles of extra cutaneous lesions expressing melanocytic markers, with those expressed by cutaneous melanomas. At the moment there is a single report, concerning a colonic melanoma, stating that in the reported neoplasm the EWS-ATF-1 fusion transcript, which is usually detected in clear cell sarcoma, was not demonstrated on reverse transcriptase-polymerase chain reaction.

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