Unusual sites of metastases from melanoma. US and CT findings.

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Learning objectives

To illustrate the spectrum of unusual possible locations of melanoma’s metastases.

To describe imaging findings for each uncommon lesion and to outline the insidious of a disease that can strike from a distance, even on sites usually unexpected for secondarism.
Background

Malignant melanoma is an aggressive neoplasm that can involve virtually every organ system.

The prognosis for melanoma is poor, since this tumor tends to metastatize early; the majority of metastases are seen within 2-5 years of initial diagnosis. Approximately 30% of patients develop metastatic disease that requires systemic therapy.

Melanoma can metastatize by direct extension, lymphatic spread, or hematogenous spread. The most common metastatic sites are the lungs, liver, brain, and bones.

More uncommon sites will be described and illustrated; these generally are expression of a very advanced disease.
Breast

Breast metastases from non-mammary primary tumors are uncommon, representing 0.5-2.0% of all breast malignancies. Melanoma is the most common extra-mammary cancer that metastatise to the breast, followed by carcinoma of the lung, stomach, ovaries and renal cells.

Metastatic lesions are much more likely to be multiple or bilateral than primary cancers, are more frequent in the subcutaneous fat of the upper outer quadrant of the breast and do not present skin changes and microcalcifications; the edges are generally rounded and sharp.

Spread is generally hematogenous, more rarely through the lymphatics [1-3].

US imaging of melanomas' metastases features hypoechoic nodules with irregular shape, inhomogeneous (Fig. 2 on page 9), fairly vascularized to the Color-Doppler US examination (Fig.3 on page 10, Fig. 4 on page 11).

CT features multiple nodular lesions, sharply marginated, or focal solitary abnormalities without specific characters and with variable enhancement (Fig.1 on page 9).

Heart and Pericardium

Metastases to the heart and pericardium are 30 times more common than primary cardiac tumors and are generally associated with a poor prognosis [4]; the highest percentage of cardiac and pericardial metastases has been found in patients with melanoma.

Generally a melanoma is disseminated by means of hematogenous spread to the myocardium and epicardium via the coronary arteries or less frequently from the vena cava [5]; even though all cardiac structures can be invaded, the metastases mainly involve the pericardium (Fig.5 on page 12).

Hematogenous metastases to the heart and pericardium are often associated with hematogenous metastases to other organs (lung metastases are usually present) [5, 6].

CT findings are represented by focal or diffuse wall thickening or intraluminal hypodense lesions (Fig.6 on page 13); frequent is the association with intra-pericardial effusion (Fig.7 on page 14).

Gastro-intestinal tract
Melanoma is the most common of the primary tumors that may spread hematogenously to the gastro-intestinal tract, followed by lung cancer and breast cancer [7, 9]. Small bowel and the mesentery are the most common (80%) site of GI disease. The haematogenous locations of the gastrointestinal tract (stomach, duodenum and small intestine, colon more rarely) are usually represented by multiple submucosal lesions of variable size, often located on the anti-mesenteric side [12].

Hematogenous metastases to the intestine typically appear as well-defined submucosal nodules or masses with or without a central area of ulceration [10]. Haemorrhagic aspects are common. Intraluminal growth realizes the high incidence of intussusception (Fig. 10 on page 17, Fig. 11 on page 18).

CT imaging can be extremely variable: lesions can appear like intraluminal vegetations, ulcerated mass, pseudonodular segmental or diffuse wall thickening (Fig. 8 on page 14) [11].

Bulky lesions, lobulated, exophytic in development, with central ulceration or necrosis can be detected on ultrasound (Fig. 9 on page 15); US has a role in detecting signs of intussusception: the sonographic hallmark of this pathological condition was first described as a "target", doughnut, or bull's eye sign (Fig. 10 on page 17, Fig. 11 on page 18).

**Gallbladder**

Melanoma accounts for more than 50% of gallbladder's metastases; these are usually clinically occult [13,14,18].

US features polypoid intraluminal lesions (Fig. 13 on page , Fig. 14 on page 21), often multiple, variable in size (generally> 10 mm.), with signs of vascularity on Color-Doppler US and CEUS (Fig. 13 on page 20).

The appearance is hyperechoic but the absence of acoustic shadow and the mobility at the decubitus changing let enable a simple differential diagnosis with the stones [16-17].

Moreover, CEUS is extremely useful for the differential diagnosis of metastatic lesions from small adenomyomas, which show a reduced contrast enhancement compared with metastases (Fig. 13 on page 20, Fig. 14 on page 21).

The findings of metastatic gallbladder's melanoma on CT scans are similar to those on US images: CT demonstrates a thickened gallbladder's wall or the presence of multiple polypoid lesions that extend into the lumen and can completely fill it, simulating a primary tumor [16]. The wall nodules are relatively hyperattenuating after contrast medium administration, a finding suggestive of enhancement, which raised concern about the possibility of malignancy (Fig. 12 on page 19) [12-13].
**Pancreas**

Metastatic lesions from malignant melanoma are rarely found in the pancreas.

Metastatic pancreatic involvement is manifested as either circumscribed lesions (single or multifocal) or diffuse gland's enlargement.

At CT circumscribed lesions appear isodense or, more often, slightly hypodense on unenhanced scans with an occasionally bulging of the gland's contour; the diffusely enlarged type of metastasis is manifest as an increase in size of pancreas, with contour smooth or lobulated (Fig.15 on page 22).

After injection of contrast medium, the larger lesions enhance inhomogeneously, leaving a central hypodense necrosis area whereas smaller lesions enhance more homogeneously [19-20].

On US examination, pancreatic metastases from melanoma appear as solid hypoechoic intraparenchimal space occupying masses.

**Skeletal Muscles**

The distribution of muscle metastases reflects the distribution of muscle mass with the lower limbs predominating as the site of disease spread.

US shows intensely hypoechoic nodular lesions in the context of an unstructured muscle (Fig.16 on page 23, a,b).

The CT appearance is characterized by an increase in volume of the muscle and the lesion's feature on contrast-enhanced helical CT is that of a rim-enhancing mass with central hypoattenuation or of an homogeneous enhanced mass (Fig.16 on page 23 c-e) [21-22].

**Kidney**

Secondary tumours to the kidney usually occur as part of a widespread dissemination; renal involvement is frequently bilateral and multinodular [23, 25]. Renal lesions can be localized within the parenchyma, widening the cortico-medullar thickening, or have a peripheral location or can see in the perirenal fat which can also be the only location of disease.

In typical cases the ultrasound examination shows multiple small cortical lesions, hypoechoic and inhomogeneous (Fig.17).
The appearance of renal metastases on CT scans is variable: generally show low and homogeneous enhancement. The metastatic melanoma have a tendency to infiltrate into the perirenal space: we could find curvilinear hyperdense streaks with or without micronodular lesions and thickening of renal fascia (Fig.17 on page 24) [24].

**Urinary Bladder**

Bladder metastatic disease is unusual and rarely clinically evident; nevertheless, 40% of metastatic neoplasms of the bladder originate from melanoma [27-29].

US shows a thickening of the bladder’s wall, an echogenicity generally higher than the remaining wall, an interruption of the echogenic mucosa line and an obtuse angle of connection with the mucosal surface itself.

In the evaluation of the bladder, CEUS can be useful for differential diagnosis of a malignant polypoid lesion and a blood clot, when it is not mobile and undissociable from the bladder’s wall; the polyp will show contrast enhancement, the clot not (Fig.19 on page 26).

CT features a polypoid pattern appearance, made of multiple vegetating lesions from the bladder wall (Fig.18 on page 25) [26].

**Thyroid**

Clinically significant metastases to the thyroid gland are very rare; even less common is a case of malignant melanoma metastatic to the thyroid. Indeed the most common metastatic tumors involving the gland are mainly those with hematogenous spreading such as melanoma, breast cancer and cancer of the kidney and of the lung.

US examination will generally feature homogeneous hypoechoic lesions, well bounded, with a preference for the lower lobe, but lesions can also be multiple, heterogeneous, overthrowing the thyroid tissue (Fig.20 on page 27) [30-31].

CT features of metastatic nodules are not specific, characterized by heterogeneous hypodensity, related to necrotic and haemorrhagic components inside the lesion, and a moderate peripheral contrast enhancement [30].

**Salivary glands**

Salivary glands are very uncommonly sites of metastases; among primary tumors metastasizing to salivary glands, melanoma is the most frequent, as well as in more distant parts of the body [32].
At US, metastases may be well defined and oval or more frequently nodular, with irregular infiltrating borders; the echostructure is hypoechoic and heterogeneous for the presence of calcifications and necrotic-hemorrhagic areas [33].

At CT, lesions generally have an infiltrating appearance and can present necrotic areas inside (Fig. 21 on page 28).

**Lacrimal gland**

The orbital metastasis may involve the lacrimal gland, adipose tissue local-regional or extra-ocular muscles; at CT these lesions can appear as thickening or small masses with irregular margins, heterogeneous density, sometimes with infiltration of the bony structures (Fig. 22 on page 29) [34].
Fig. 0: Breast metastases - (a,b,c) CT scans show three different location of nodular melanoma metastases, sharply marginated, with diffuse contrast enhancement. Dimension can be variable as well as the location within the breast: deep (a,b) or subcutaneous (c)

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**Fig. 0:** Fig. 2: Breast metastases - US. B-mode US findings of melanoma’s secondary lesion: multiple little hypoechoic nodules (a) or coarse and disomogeneous hypoechoic mass with irregular shape (b).

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**Fig. 0**: Fig.3: Breast metastases - (a) B-mode US and (b) Color-Doppler US show a disomogeneous hypoechoic mass with some vascular spots inside.

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**Fig. 0**: Fig.4: Breast metastases - (a) B-mode US and (b) ColourDoppler US show nodular well-defined metastatic lesions of the breast, fairly vascularized at US Color-Doppler.

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Fig. 0: Pericardial metastases - (a,c) Transverse and (b)coronal CT shows inhomogeneous nodular involving pericardium on left ventricle surface (red arrows); another lesion under the right atrium.

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Fig. 0: Fig. 6: Cardiac metastases - (a) CT: infiltrative secondary lesion of the inter-atrial septum and partial involvement of the right atrial cavity (arrow); (b) CT: another nodular metastasis at a papillary muscle (arrow).

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**Fig. 0:** Cardiac metastases - (a,b) transverse, (c) coronal and (d) sagittal enhanced CT: pericardial metastasis with pericardial effusion; coexist lack of opacification of right heart's chambers (atrium and ventricle) to refer to repetitive lesions protuding in the visceral lumen.

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Fig. 0: Fig.8 - Gastric metastases - CT : (a,b) two cases of gastric localization of melanoma's metastases. A productive intraluminal vegetation of the gastric fundus (a) and a productive lesion developing from the posterior wall of the gastric antrum (b) (arrows).

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**Fig. 9:** Small bowel metastases - (a,b) B-mode US showing coarse inhomogeneous hypoechoic mass involving small bowel's loops.

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Fig. 0: Fig. 10: Intestinal metastases - (a,b) B-mode US shows intestinal lesions consistent of irregular bowel loops for the presence of secondary hypoechoic inhomogeneous deposits inside.(c) Intussusception with an hypoechoic lesion that is the lead-point for the development of the intussusception.

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Fig. 0: Fig.11 : Intestinal metastases - (a,b) B-Mode US and Color-Doppler US show a hypoechoic nodular lesion of an intestinal loop, which makes head-point of intussusception;(c) Transverse and (d) Sagittal enhanced CT show a small bowel loop intussusception with an intraluminal vegetation.

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Fig. 0: Fig. 12: Gallbladder metastases - CT (a,b): thickening of gallbladder's walls with multiple nodular lesions, enhanced after contrast medium administration.

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Fig. 0: Fig.13: Gallbladder metastases - (a) B-mode US shows polypoid lesions protruding in the lumen of the gallbladder. (b) Colour-Doppler US demonstrates intraluminal vascular spots. (c) CEUS shows intense vascularity of the lesion, suggestive for secondarism. (d) CT shows multiple polypoid lesions of the gallbladder's wall, intensely enhancing after contrast medium injection.

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**Fig. 0:** Fig.14: Gallbladder metastases - (a) B-mode ultrasound shows a coarse mass inside the lumen of the gallbladder. (b) CEUS shows the intense vascularization of the lesion of the gallbladder's wall, suggestive for a secondary lesion.

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Fig. 0: Fig.15 : Pancreas metastases - CT. Pancreatic involvement by secondary lesions. A) Nodular appearance(a,) that marks the edge of the gland's head.B,C,D)Inhomogenous and lobulated lesion which increases globally pancreas' head with compression of the duodenum.

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Fig. 0: Fig.16 : Muscular metastases : (a,b)US and colourDoppler US show oval hypoechoic lesions inside muscle bundle; the lesion is intensely vascularized at the colourDoppler examination (b) and distorts regular contours of the muscle. (c,d,e) CT: muscular lesions from melanoma consistent of nodular, well-marginated, intensely enhanced masses in the context of muscular bounds ; the lesions may involve only the muscle (intrafascial mass)(c,d) or extend beyond the fascia with involvement of adjacent tissues (extrafascial extending mass)(e).

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**Fig. 0**: Fig.17 : Kidney metastases - (a,c) B-mode US shows two cases of nodular hypoechoic lesions of the kidney, with bulging of the renal contour. (b) Coronal enhanced CT shows an hyperdense, quite enhanced, little round lesion of the inferior pole of the left kidney.

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**Fig. 0:** Fig.18 : Urinary bladder metastases - (a) Sagittal, (b) Transverse and (c) Coronal enhanced CT showing bladder's lesions as multiple little polypoid well-enhanced lesions, protruding in the bladder lumen, not yet filled by contrast medium in early phase of acquisition.

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**Fig. 0:** Fig.19 : Urinary bladder metastases - (a) Contrast enhanced CT shows a hyperdense lesion in the lumen of a filled bladder: the findings could be consistent with an intra-bladder clot. (b) US show an echogenic area inside the bladder lumen while CEUS shows that the clot does not enhance after contrast medium administration, while is visible a polypoid enhancing lesion suggestive for metastasis.

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Fig. 0: Fig. 20: Thyroid metastases - (a) B-mode US and (b) ColorDoppler US show a widespread structural disorganization of the thyroid parenchyma due to the presence of multiple scattered nodules with vasculature inside.

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**Fig. 0:** Fig.21 : Salivary gland metastases - (a) Transverse,(b) sagittal and (c) coronal enhanced CT of a patient with increase in volume and inhomogeneous hypodensity of the left submandibular salivary gland related to secondarism from melanoma.

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Fig. 0: Fig. 22: Lacrimal gland metastasis -(a) Transverse and (b) coronal enhanced CT shows a nodular inhomogeneous lesion localized at the lateral side of the right orbital cavity, giving compression on the lateral rectus muscle of the eye and a slight inferomedial dislocation of the eye globus.

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Conclusion

We have presented the spectrum of uncommon sites of melanoma's metastases; by paying careful attention to these less known aspect of metastatic melanoma, radiologist will be able to provide the referring physician for a more accurate staging of disease, thereby helping guide therapy management.
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