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Melanoma of the ciliary body revealed by uveitis

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Résumé :
Le mélanome malin du corps ciliaire représente 9% des tumeurs de l'uvée. Il constitue la tumeur du corps ciliaire la plus fréquente. Nous rapportons le cas d'un mélanome du corps ciliaire révéler par une baisse de l'acuité visuelle dont le comportement en imagerie par résonance magnétique était atypique.
Il s'agit d'une patiente de 55 ans, sans antécédents pathologiques particuliers. Elle s'est présentée à la consultation pour une baisse de l'acuité visuelle progressive au niveau de l'œil droit qui a débuté deux mois avant. L'acuité visuelle de l'œil droit était limitée à une perception lumineuse. L'examen clinique de l'œil droit a révélé une cataracte cortico-nucléaire. La tension oculaire était de 13 mmHg au Goldmann. Au fond d'œil, on observait une masse qui semblait être développée aux dépens du corps ciliaire(figure 1). L'échographie mode B(figure2) réalisée complétée par une IRM orbitaire (figure 3)a objectivé une lésion non compatible avec un mélanome du corps ciliaire. Un bilan en faveur d'une localisation secondaire a été lancé à la recherche d'une tumeur primitive qui s'est révélée négatif. La patiente a été programmée pour énucléation à visée thérapeutique et diagnostique. L'examen anatomopathologique de la pièce opératoire retrouve un mélanome fusocellulaire de la choroïde.
Les mélanomes sont les tumeurs les plus fréquentes au niveau du corps ciliaire. L'exploration repose sur l'ultrasonographie biomicroscopique (UBM). L'IRM est aussi d'un grand support. Notre cas a montré qu'un mélanome peut se comporter de façon différente par rapport à l'aspect habituelle décrit à l'IRM, mais la confirmation diagnostique reste histologique. L'énucléation est le traitement classique des tumeurs étendues.
Le mélanome du corps cilaire reste une pathologie grave puisque sa révélation est souvent tardive. Un examen clinique minutieux fait suspecter la tumeur, et le diagnostic précis va être aidé par l'imagerie et confirmé par l'histologie.

Abstract :
Malignant melanoma of the ciliary body represents 9% of all uveal tumors. It is the most frequent tumor of the ciliary body. We report the case of a ciliary body melanoma revealed by a decrease in visual acuity whose behavior on magnetic resonance imaging was atypical.
The patient was 55 years old and had no previous pathological history. She presented to the consultation for a progressive visual acuity decline in her right eye that started two months before. The visual acuity of the right eye was limited to light perception. Clinical examination of the right eye revealed a cortico-nuclear cataract. The eye pressure was 13 mmHg on the Goldmann. On the fundus, there was a mass that appeared to be developed at the expense of the ciliary body(figure 1). B-mode ultrasound(figure 2) and orbital MRI(figure 3) revealed a lesion that was not compatible with a melanoma of the ciliary body. A workup in favor of a secondary localization was initiated in search of a primary tumor, which proved negative. The patient was scheduled for enucleation for therapeutic and diagnostic purposes. Pathological examination of the surgical specimen revealed a fusocellular melanoma of the choroid.
Melanomas are the most frequent tumors of the ciliary body. The exploration is based on biomicroscopic ultrasonography (BMU). MRI is also of great help. Our case showed that a melanoma can behave differently from the usual appearance described on MRI, but the diagnostic confirmation remains histological. Enucleation is the classical treatment for large tumors.
Melanoma of the ciliary body remains a serious pathology since its revelation is often late. A careful clinical examination leads to the suspicion of the tumor, and the precise diagnosis will be helped by imaging and confirmed by histology.

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I. Introduction:

The incidence of malignant melanoma is increasing worldwide, posing a significant socioeconomic problem. Whereas it was a rare cancer a century ago, the average lifetime risk of melanoma is now 1 in 50 in many Western populations. From the 1960s onwards, the incidence of this cancer increased in Caucasian populations and, as a result, melanoma has become one of the most common cancers in light-skinned populations. (1)

Although uveal melanomas account for only 5% of all primary melanoma cases (90% being located in the skin), they are the most frequently diagnosed primary intraocular malignancy in adults. The incidence of uveal melanoma in all ethnic groups is estimated at 5.1 per million inhabitants per year. It remains stable: 9 per million inhabitants per year in the Strickland et al. study carried out between 1951 and 1975; 9 per million inhabitants per year in the Mork et al. study between 1953 and 1960 and 7.4 per million inhabitants per year in the European study by Swerdlow et al. between 1952 and 1978 (2). The incidence of new cases of uveal melanoma also remains stable in the recent Keenan study: one case per 100,000 population per year in England between 1999 and 2010. (3)

Uveal melanomas are uncommon but potentially fatal eye diseases. They develop from melanocytes located in the highly pigmented uveal tract, the main supplier of oxygen and nutrients to the retina. Anterior uveal melanomas originate in the iris while posterior uveal melanomas emerge from the choroid or ciliary body. Of these tumours, choroidal melanoma is the most frequently diagnosed tumour (nearly 90% of all uveal melanomas), followed by ciliary body melanoma (6% of cases) and iris melanoma (4% of cases). (4)

Approximately 170,000 new cases are recorded each year in the areas served by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) programme, with a case ascertainment rate of 98%. (2)

In Europe, the incidence of uveal melanoma is higher (up to 8 cases per million population per year) in Northern European origin Caucasians (Scandinavia and the Baltic States) and lower in Italy (3.3 cases per million population per year) and Spain (1.9 cases per million population per year). Hispanics and Asians have a lower incidence, and blacks have the lowest incidence. The relative risk of uveal melanoma has been estimated to be 1/1.2/5/19 in blacks/Asians/Hispanics/non-Hispanics, respectively. (4)

Malignant melanoma involving CC has a poor prognosis compared to other uveal melanomas.

To date, several risk factors have been identified in the development of uveal melanoma. Host susceptibility factors, such as light eyes, light skin colour, dysplastic nevus syndrome, ocular melanocytosis and xeroderma pigmentosum, have been established as predisposing factors. (5) (6)

Historically, uveal melanoma has been treated with enucleation, radiotherapy and other methods, with 5-year survival rates ranging from 25% to 66%. Recent advances in therapy have resulted in a reduction in the number of primary enucleations performed. With the development of new therapies and our evolving ability to guide treatment according to metastatic risk profile, it will be increasingly important to monitor treatment modalities and survival rates of patients with uveal melanoma. (2)

The aim of our work is to report an atypical presentation of ciliary body melanoma revealed by isolated hypertonia.

II. Observation :

A 55-year-old female patient with no previous pathological history presented with a progressive visual acuity decline in the right eye that started two months ago. The visual acuity of the right eye was limited to light perception and that of the left eye was 08/10. The intraocular pressure was 13 mmHg on the Goldmann. Clinical examination of the right eye revealed an incipient cortico-nuclear cataract, with no irregularity in the depth of the anterior chamber or alteration in the iris pattern. The fundus showed an anterior superior temporal sub-retinal mass from 10:30 to 1:00, with an irregular surface, pigmented in places, which appeared to have developed at the expense of the ciliary body, with vessels running through it, and an inferior nasal retinal serous detachment from 3:00 to 6:00. B-mode ultrasound showed a well-limited tissue formation at the expense of the ciliary body, with Doppler illumination, associated with a V-shaped retinal detachment and sub-retinal haemorrhage. An orbital MRI was also performed, showing a right anterior ocular process in FLAIR hypersignal and diffusion taking the contrast product of 12*8 mm without notable scleral effraction, with intra ocular hemorrhage. This lesion was not compatible with ciliary body melanoma on magnetic resonance imaging and a secondary location was suggested. A work-up was initiated to look for a primary tumour (general examination, mammography, thoracic CT scan, abdomino-pelvic ultrasound, endovaginal ultrasound, cervico-vaginal smear) which proved negative. Following a multidisciplinary consultation meeting, the patient was scheduled for enucleation for therapeutic and diagnostic purposes. The anatomopathological examination of the surgical specimen revealed a fusocellular melanoma of the choroid.

Histopathological examination of the enucleated right eye confirmed the presence of a 1×0.8×0.5 cm ciliary body melanoma with sheets of spindle to epithelioid cells with prominent nucleoli and abundant intracytoplasmic melanin pigment

III. Discussion:

The most common tumour of the ciliary body, ciliary body melanoma is extremely rare and, due to its hidden location, it usually presents at a more advanced stage. The most common symptoms are blurred vision, attributed to astigmatism due to displacement of the lens, iris or painless loss of the visual field when advanced in the visual axis or a painful decrease in vision due to a sudden increase in IOP. The tumour is also revealed by hyperpigmentation of the iris root. (7)

The haematogenous metastases seen at a rapid rate in ciliary body melanoma are attributed to the continuous contraction of the ciliary muscle, the rich vascularisation of their anatomical region and their access to the outflow channels, which predisposes these tumours to anterior or posterior extra scleral extension. (8) However, metastasis at first presentation is rare in ciliary body melanoma, but final metastasis often occurs in this condition, perhaps in part because it develops in an area of the eye that is difficult to examine. A diffuse growth pattern and large tumour size are important determinants of metastasis, and a histopathological mixed cell tumour comprising necrosis and epithelioid cells has the poorest prognosis. (9) Diagnosis of a large tumour before detection of any metastatic site, helps in its primary management, but despite the high accuracy of diagnosis and its primary treatment, histopathological evidence of the worst prognosis, the survival course remains unchanged. (10)

Uveal melanoma affects both men and women and the average age at diagnosis is 62 years, with extremes of 6 to 100 years. Risk factors for the development of uveal melanoma, which were absent in our patient, have been identified: neurocutaneous melanocytosis, neurofibromatosis type 1, a history of familial cutaneous melanoma and dysplastic nevi syndrome. In contrast to our observation, the mode of revelation of uveal melanoma is often noisy. In a group of 2586 patients with posterior uveal melanoma collected over a period of 14 years, ten patients were black: eight of them consulted for decreased visual acuity, only one was asymptomatic. (11) Four had tumours extending from the ciliary body to the Ora serrata, one melanoma was located between the Ora and the equator and five patients had tumours of the posterior pole, frequently associated with retinal serous detachment. In the prospective study by Damato et al, including 2384 patients, only one third were asymptomatic; 37.8% had decreased visual acuity, about 25% consulted equally for photopsies, floaters and visual field amputation. Pain was the reason for consultation in only 2.4% of cases. This reason was more frequent for tumours of the ciliary body, of large diameter, with extraocular invasion. (12) Among uveal tumours, ciliary body tumours are the most frequently missed at the first visit (27.3% of ciliary body tumours compared to 23.6% of choroidal tumours and 10.1% of iris tumours), thus exposing the risk of therapeutic management at a more advanced stage. Inflammation correlates with tumour volume, tumour necrosis, location of the anterior margin of the tumour. The prevalence of intraocular tumours revealed by hypertonia, as was initially the case in our patient, is low, estimated at 3-20%. (11) One of the causes of refractory glaucoma is the very rare annular melanoma of the ciliary body. (13) There was also a case of ciliary melanoma that went undetected in the form of chronic hypertensive panuveitis, which was only diagnosed after a second vitrectomy combined with an implant change.(14)

The suspicion of ciliary body melanoma was raised after various ophthalmological investigations such as biomicroscopy, ocular CT or MRI, and the diagnosis was confirmed histopathologically. After dilation of the pupils, the tumour can be observed as a dome-shaped mass with variable pigmentation that may extend to the iris or the posterior pole of the eye.(8) The dimensions of our tumour are comparable to the average dimensions of uveal melanomas (12 mm × 8 mm). (12)

B-ultrasound is a relevant examination for the diagnosis of uveal melanoma, especially in the case of the less clinically obvious ciliary body melanoma. The latter appears weakly or moderately reflexive on B-ultrasound, which helps to eliminate the differential diagnosis of areflexic choroidal detachment. (11) It specifies the dimensions and detects extraocular invasion. Biomicroscopic ultrasonography (BMU) is also used for exploration. MRI is also of great help, showing a T1 hyperintense and T2 hypointense mass which becomes impregnated after injection of Gadolinium. In our patient the mass was T1 isosignal and T2 hypersignal and homogeneously enhanced after injection of gadolinium. Our case showed that a melanoma can behave differently from the usual appearance described on MRI, but the diagnostic confirmation remains histological. (15)

The evolution of ciliary body melanoma is easily predictable. The tumour may grow and can be seen under the biomicroscope as a variable, diffuse, nodular or mixed pigmented mass located behind the pupil. (15) In addition, the tumour may invade the anterior chamber, affecting the iris, or grow in the posterior pole, affecting the choroid. Metastases occur after bloodstream dissemination because the eye has no lymphatic vessels. Furthermore, as suggested above, metastasis occurs earlier in patients with ciliary body melanoma than

in other types of uveal melanoma, partly because of the long and silent evolution and partly because of the rich vascularity of the ciliary body. (8)

Patients with a tumour larger than 7 mm on ultrasound have a high risk of metastasis and their morbidity rate is increased.(16) Approximately half of patients with primary uveal melanoma of any size will have distant metastases by haematological spread. These can occur up to 20 years after the diagnosis of the initial tumour. The location of the metastases determines survival. Ninety per cent of them occur in the liver, leaving a life expectancy of 4-5 months, and at most one year for 15% of patients. (11)

Ophthalmic oncologists now use a number of management options for uveal melanoma, including enucleation, local surgical resection of the tumour, photocoagulation and radiotherapy, and recently the use of adjunctive interferon therapy. However, enucleation remains the standard treatment for large tumours. Although irradiation alone gradually replaced enucleation from the 1980s, the 5-year survival rate remained stable at 81.6% between 1973 and 2008. Conservative treatment is thus favoured: plaque radiotherapy, proton beam radiotherapy. (11) (17)

Prognostic factors are classified into clinical, macroscopic and microscopic factors. Clinical factors include the occurrence of local and general signs, local extension, the presence of metastases, the age of the patient and the presence of dysplastic nevi. Macroscopically, the size of the tumour is the most important factor. Thus, if the largest diameter of the tumour does not exceed 11 mm, the tumour is considered "small" and has a 5-year survival rate of 86%. A diameter between 11 and 15 mm is considered "medium" and is associated with a 5-year survival rate of 66%. Large" tumours, with a diameter greater than 15 mm, have a survival rate of 56%. (15) Of all the microscopic factors, we have already discussed cell type and mitotic activity. In addition, the presence of necrosis, intense pigmentation and melanophagic and lymphocytic infiltrate correlate with the worst prognosis. (8)

IV. Conclusion:

Although melanoma of the ciliary body is a rare condition, it is a serious disease and raises many questions regarding early diagnosis, therapeutic management and subsequent evolution. It is often revealed late and paucisymptomatic. A careful clinical examination leads to the suspicion of a tumour. The precise diagnosis will be helped by imaging (UBM, MRI) and confirmed by histology. The most common treatment in the world today is radiotherapy, or brachytherapy with plates or proton therapy. External beam therapy or brachytherapy can be used for medium-sized tumours (less than 15 mm in diameter). In advanced cases, depending on the size of the tumour, local spread and cell type of the melanoma, treatment is surgical, with enucleation of the eye.

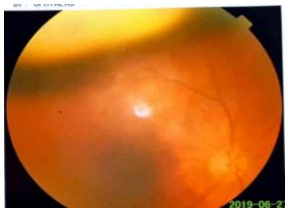

Figure 1: a single retro-crystalline superior temporal mass with an irregular pigmented surface

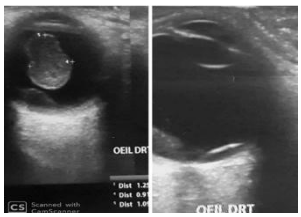

Figure 2: well-limited hyperechoic vascularized mass associated with an inferior retinal detachment

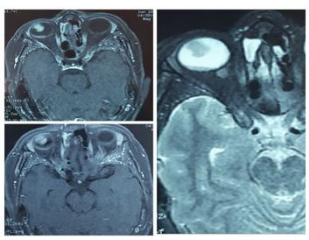

Figure 3: Single mass with regular contours in T1 isosignal and T2 hypersignal and was homogeneously enhanced after injection of gadolinium

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