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Gallbladder polyps in association with metachromatic leukodystrophy

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1. Introduction

Polypoid lesions of the gallbladder (PLG) are rare in the paediatric population. Growth in technology with the availability of high-quality ultrasonography and in the experience of radiologists in detecting such lesions, has led to an increase in incidental detection of PLG. In children, the occur either as a primary disorder or in association with other conditions, including metachromatic leukodystrophy, Peutz-Jeghers syndrome, or pancreatobiliary malunion [1].

Due the rarity of these lesions in the paediatric age group, accurate management algorithms are inherited from the adult population. In these, PLG is a more common pathology, occurring in 4–7% of patients undergoing ultrasonography, with clinical significance relating largely to their malignant potential [2,3].

2. Case report

A boy, aged 4 years old, affected by metachromatic leukodystrophy was referred to our operative unit because of a gallbladder polyp causing episodic abdominal pain in the right upper quadrant. Patient's history was characterized by regular psychomotor development until 16 months of age. He was then admitted at 22 months with fever accompanied by vomit, diarrhoea and horizontal saccadic eye movement. After that episode, he developed gradual regression of motor skills acquisitions. These led him to spastic tetraparesis and dysphagia, for which he underwent a procedure of open gastrostomy in 2017. Diagnosis of metachromatic leukodystrophy was later made, in October 2017, thanks to elevated values of leukocyte arylsulfatase A.

During this recent recovery haematological investigations and liver function tests were normal. An ultrasonography (USG) of the abdomen was negative for gallbladder polyps but revealed thickened and hyperechoic walls [Fig. 1]. There was no evidence of calculus in the gallbladder. The common bile duct was normal. Contrast-enhanced computed tomogram (CECT) confirmed the presence of markedly thickened walls and the absence of PLGs and calculi [Fig. 2]. There was no evidence PLG on magnetic resonance cholangio-pancreatography (MRCP) neither.

Open laparotomic cholecystectomy was performed. On gross examination, the gallbladder, 7 cm long, demonstrated a mucosal polypoid mass of 2 cm with other minor polyps [Fig. 3]. There was no stone.

The patient had a smooth recovery and was discharged on the eighth day symptom-free. Histopathology report revealed multiple polyps with arborizing growth arising from the body of the gallbladder with areas of oedema and myofibroblasts proliferation. Such polyps present specific characteristics which are typical of this pathology, both in the architecture of the fibres and in the metaplastic and cytopathic events. No section of the gallbladder showed inflammation neither dysplastic nor neoplastic aspects [Fig. 4].

3. Discussion

Gallbladder polyps are defined as outgrowths of the gallbladder mucosa [4]. As a rule, they can be categorized as benign or malignant. Benign lesions have been further subdivided into neoplastic or non-neoplastic. The most common benign lesions are cholesterol polyps, followed by hyperplastic and adenomatous polyps. Adenomas of the gallbladder are benign epithelial tumours composed of cells resembling biliary tract epithelium and are classified into tubular, papillary and mixed. The most common malignant lesion is adenocarcinoma, which is much more common than gallbladder adenoma. The most predictive feature for malignancy is the size of the polyp. Polyps larger than 2 cm are almost always malignant and, in many cases, the cancer is advanced. Polyps 1–2 cm in size should be regarded as possibly malignant.

PLGs are identified on ultrasonography as single or multiple echogenic foci attached to the gallbladder wall and protruding into the lumen. They can be easily differentiated from gall stones because they are fixed and do not move when the patient is rolled from one side to another. In addition to this, they lack acoustic shadow. Computed tomography and MRI represent second level examination with a crucial role in studying the anatomy pre-operatively and staging the disease.

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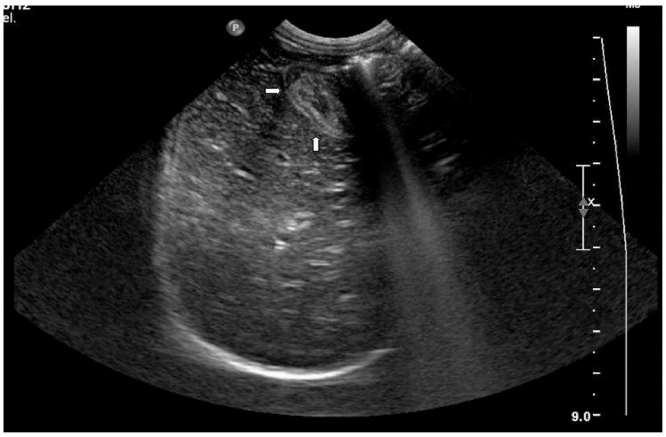

Fig. 1. Ultrasonography reveals thickened and hyperechoic gallbladder walls (white arrows).

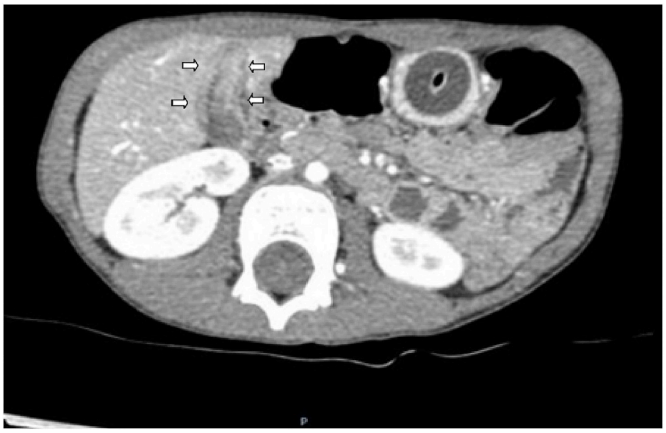

Fig. 2. CT scan shows thickened gallbladder walls (white arrows) ad absence of gallbladder polyps.

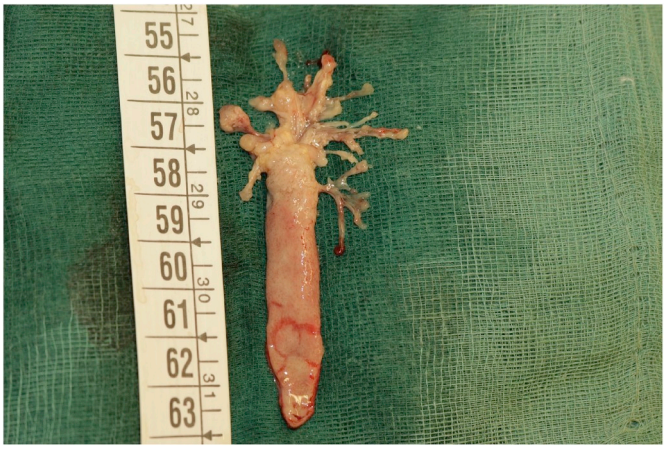

Fig. 3. Macroscopic examination reveals a mucosal polypoid mass of 2 cm with other minor polyps with arborizing growth.

Endoscopic ultrasonography is regarded as the most sensitive test for gallbladder imaging, but its role in establishing a strategy for the management of gallbladder polyps is not well defined.

Metachromatic leukodystrophy (MLD) is an autosomal recessive lysosomal storage disease [1]. The disease has a spectrum of clinical presentations. Symptoms usually develop in late infancy or adolescence or in adult age. The late infantile form typically appears at six months to two years of life with regression of motor skills, gait difficulties, seizures, ataxia, hypotonia, extensor plantar responses, and optic atrophy. The prognosis is worse than later onset forms of MLD as progression to death typically occurs within five to six years of life. Adult age onset is usually heralded by dementia and behavioural difficulties, while the juvenile onset form of MLD is heterogenous in presentation. The disease is caused by a deficiency in the enzyme arylsulfatase A [5]. The accumulation of undigested sulfatides in oligodendrocytes and Schwann cells leads to central and peripheral nervous system demyelination. Sulfatides accumulate in the macrophages of various organs including gallbladder [6].

The only effective treatment for gallbladder polyps is cholecystectomy, which should be considered in symptomatic patients or as prophylaxis to prevent malignant transformation. Optimal follow-up of patients who do not undergo surgery has not yet been properly standardized.

Heitz et al. examined the progression of PLGs in the adult population, reassessing 27 patients 11 years after their first diagnosis. Fourteen of these subjects (51.9%) still had polyps, while 13 subjects (48.1%) no longer had any evidence of gallbladder polyps on ultrasound scanning. Observation of the gallbladder polyps with respects to echogenicity, shape and contours, showed very little change with time. Echogenicity changes from hyperechoic to hypoechoic in only one subject, and the previously regular contours became irregular in two subjects [7].

Beck et al. claimed that the risk factors (obesity, glucose intolerance, male gender, cholelithiasis, and hereditary polyposis syndromes) shown for the adult age group can be used for children as well [8], plus in the presence of accompanying metachromatic leukodystrophy, pancreaticobiliary duct abnormalities (maljunction), achondroplasia, Peutz-Jeghers syndrome, operation should be the method of choice, as these conditions seem related to a higher risk of developing malignancy [6]. Likewise, Stringer et al. recommended follow-up in patients who are asymptomatic, without co– morbidities as mentioned above, and with polyps less than 10 mm in size. At least 2 separate examination are required for the confirmation of the diagnosis, according to Stringer, due to the inter-operator variability [9].

Ballouhey et al. presented the largest series of PLGs in children, as a result of a multicentre study conducted over 10 centres of paediatric surgery. Of the 18 patients met the inclusion criteria, 9 (50%) were managed surgically and another 9 (50%) were managed by follow-up. In the first group, the main rationale in undertaking a radical excision seemed to be the presence of symptoms [10].

At the current state of art, there are only 61 child age cases between 1 and 17 years of age reported in the literature (M/F = 41/20) in case reports [1,8–17]. Four of them were with Peutz- Jeghers syndrome, 8 had metachromatic leukodystrophy, 14 were adenomas, 3 were hyperplastic polyps (2 with pancreaticobiliary maljunction and 1 with MLD), 2 were gastric heterotrophy, 4 had cholesterol polyps and at last, only one case presented an hamartomatous lesion. Most of the cases were admitted to the hospital with complaints of abdominal pain, nausea, and vomiting. They were either followed conservatively or operated (26 were operated and 35 were followed-up), considering the cut-off size in the adult age group, i.e. 10 mm and presence of symptoms.

Owing to the benign nature of these lesions with the potential of a spontaneous regression for smaller lesions, and the low risk of malignant transformation, in asymptomatic lesions smaller than 1 cm in size, the proper choice should be conservative management relying on annual medical examination and ultrasound monitoring. Surgical resection is warranted for lesions larger than 10 mm in size or when associated with rapid growth or associated symptoms. Laparoscopic cholecystectomy should be the chosen approach in centres with adequate experience in minimally invasive surgery (MIS) and patients fit for MIS.

As regards to the frequency of gallbladder polyposis and carcinoma in MLD, Van Rappard et al. assessed 34 patients with MLD screened by ultrasound for gallbladder abnormalities [18]. Only 8 of 34 (23%) had a normal gallbladder, while gallbladder polyps were visible in 8 patients

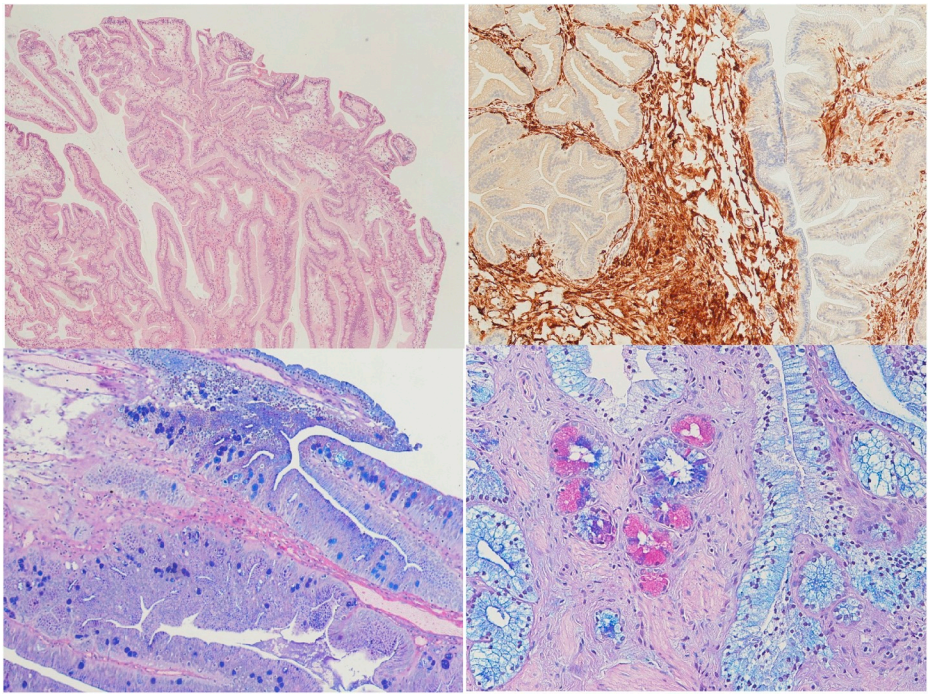

Fig. 4. Histopathology (A. EE stain highlights complex arborizing structure of polyps; B. Immunohistochemical stain for SMOOTH MUSCLE MYOSIN highlights muscular cells more suggestive of an hamartomatous polyp rather than of an hyperplastic one; C-D. ALCIAN BLU PAS-DIASTASE stain highlights goblet cells of intestinal metaplasia (in blue) and pyloric metaplasia (in red), typical vacuolisation of surface cells is recognizable). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

(23%). Cholecystectomy was performed in 11 patients (32%), Pathology reports showed various abnormalities, including hyperplastic polyps and intestinal metaplasia. 1 of these 34 patients died at young age because of gallbladder carcinoma. They therefore concluded that gallbladder involvement in the rule rather than an exception in MLD and advocate prompt screening of the gallbladder by ultrasound.

4. Conclusion

We presented a very rare case of PLG in a boy with MLD, the management of which seems to agree with what reported in literature. In our case, the decision of a radical excision was based on the presence of symptoms combined with the underlying disease. Up to date, from a lack of experience of childhood PLGs, their management is limited to the algorithms of the adult age group. Ultrasonography plays a key role in diagnosis and follow-up in the paediatric age group. We hope that the reporting of new cases will help build enough experience and improve follow-up and treatment strategies.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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