



Case Report

A rare case report of an adult with down syndrome and gallbladder cancer



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ABSTRACT

Introduction: The most frequent malignancies observed on adult with Down syndrome are lymphoblastic and myeloblastic leukemia. The incidence and the relationship between gallbladder cancer and Down syndrome is unknown.

Case presentation: We report a rare case of a 25-year-old male with Down syndrome who consulted to the emergency because of deterioration in overall health associated with post-meal food vomiting, abdominal distension and diffuse abdominal pain. CECT scan reveal suspicious locally advanced parietal tissue thickening of the gallbladder, associated with peritoneal carcinosis, and a bilateral massive pulmonary embolism, in addition to a large bilateral pleurisy and moderate pericardial effusion. The patient died three weeks later.

Discussion: Solid tumors are rare among population with Down syndrome, especially gallbladder cancer.

Main risk factors are: cholelithiasis and gallbladder abnormalities, which are frequent in these patients. Management of this lethal disease depends on precocity of diagnosis. For this we suggest an abdominal ultrasound in children with DS to screen previously cholelithiasis and prevent this fatal cancer.

Conclusion: Some Authors found that the rate of gallbladder disease especially cholelithiasis, was 25% among Down syndrome group, compared to 4.5% among the control group ($p = 0.002$). We suggest that cholelithiasis is the main risk factor of gallbladder cancer in this population. However, other prospective studies should be accomplished so as to confirm this outcome.

1. Introduction

Down syndrome (DS) is a worldwide disorder that has a huge medical and social cost. It's frequently associated with a high risk of malignancies especially lymphoblastic and myeloblastic leukemia in childhood. Population with DS has a globally decreased incidence of solid tumors as compared to non-DS [1].

The most gallbladder (GB) disease related in several series is cholelithiasis and other GB abnormalities in pediatric patients with Down syndrome [2], but the link and frequency of GB cancer among adult with trisomy 21 is less developed in literature.

We report a rare case of a 25-year-old male patient with DS diagnosed of locally advanced parietal tissue thickening of the GB associated with peritoneal carcinosis and complicated with pulmonary embolism. The case report has been reported in line with the SCARE criteria [3].

2. Case presentation

A 25-year-old male with no personal medical history, presented to the emergency in a general state deterioration. He had lost 13% of his weight in 2 months. The patient also presented post-meal food vomiting, abdominal distension and diffuse abdominal pain, that had appeared a month and a half before. Clinical examination found a patient who had physical characteristics of DS such as small chin, slanted eye, poor muscle tone, flat nasal bridge, a single crease of the palm and disabilities. He was conscious; his respiratory and hemodynamic parameters were stable, without jaundice, his performance status (PS) was about 2. We noted an epigastric tenderness and ascites on abdominal examination. CECT-scan showed a suspicious locally advanced parietal tissue thickening of the GB (Fig. 1), associated with high abundance ascites and densification of peritoneal fat suggesting peritoneal carcinosis

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Fig. 1. Abdominal CT scan show locally advanced parietal tissue thickening of the gallbladder.



Fig. 3. Abdominal CT scan showing focal hypodense hepatic lesions.

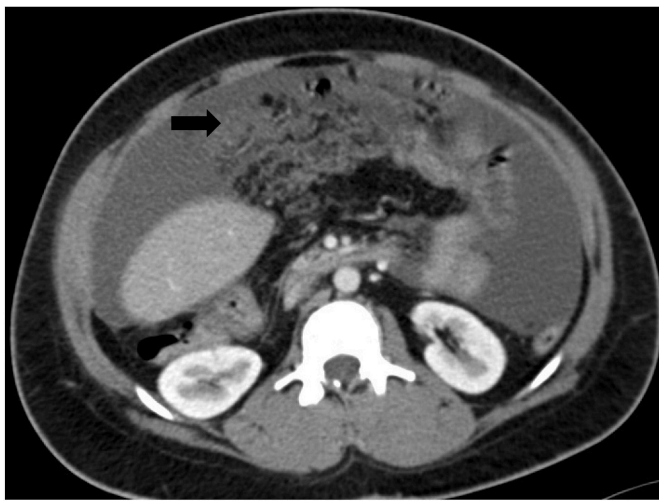


Fig. 2. Abdominal CT scan with high abundance ascites and densification of peritoneal fat.

(Fig. 2).

On imaging, the process was infiltrating the liver, which contained secondary lesions: on segments IV and V measuring respectively 25mm and 30mm, between segments VII and VIII measured 20mm of long axis and a lesion localized in segment VI, sub-capsular, of 6mm long axis (Fig. 3). Furthermore, the chest CT scan showed a bilateral massive pulmonary embolism (Fig. 4) associated with large bilateral pleurisy and moderate pericardial effusion (Fig. 5). Liver blood tests were normal, the level of CA 19-9 reached 5835,02 U/ml and ACE level was >1000 ng/ml.

Pleural and peritoneal fluid were macroscopically hematic and exudative on biochemical analysis. Peritoneal fluid cytology didn't reveal any malignant cells. The patient received immediately subcutaneous injection of Tinzaparine 175UI/kg as a treatment of pulmonary embolism.

After a multidisciplinary team meeting composed by hepatogastroenterologists, surgical oncologist, radiologists, oncologist and pathologists; we decided to execute a puncture pleural biopsy under local anesthesia, which the patient didn't tolerate. Diagnostic laparoscopy was indicated as an alternative in order to explore abdominal cavity and achieve a biopsy of peritoneal carcinomatosis nodule before

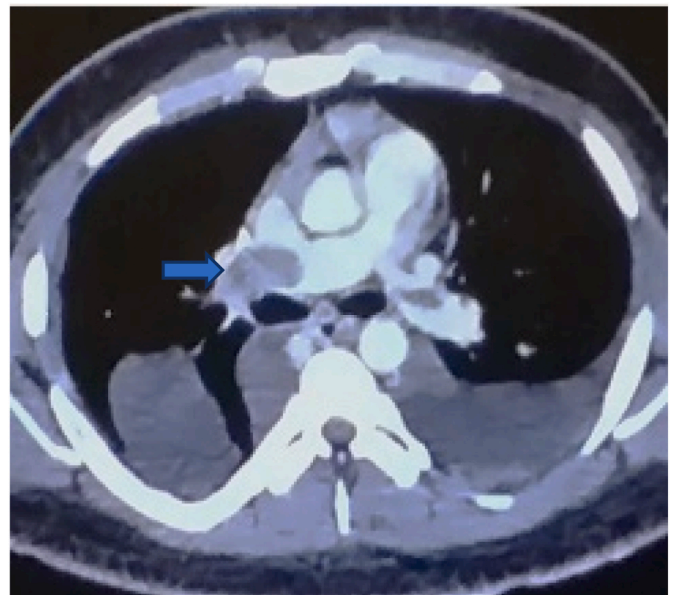


Fig. 4. Thoracic CT scan showing pulmonary embolism.

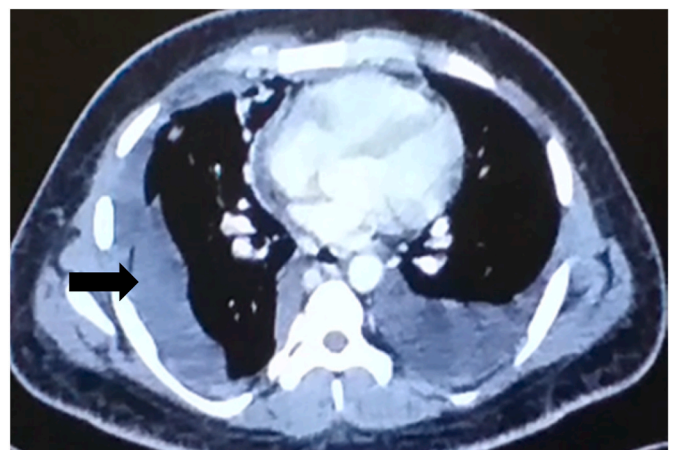


Fig. 5. Thoracic CT scan with a large pericardial and pleural effusion.

starting chemotherapy, following the standard therapy of metastatic GB cancer mentioned in National Comprehensive Cancer Network (NCCN) guidelines [4]. Two weeks later, the patient had dyspnea, his respiratory parameters were instable: oxygen saturation was 60%, he had a tachypnea with a respiratory rate evaluated at 30cpm, he couldn't benefit from laparoscopy under general anesthesia. Right pleural effusion and Ascites were drained twice, in vain. He died because of a severe hypoxia 3 weeks after diagnosis. Nevertheless, his parents refuse to perform an autopsy to confirm the diagnosis.

3. Discussion

Down syndrome (DS) is the most common human aneuploid abnormality in children, occurring about 1 in 800 live births [5].

Children with DS have a 10- to 20-fold increased risk of developing acute leukemia [6]. However, basing on some epidemiologic studies, DS may provide overall low risk development of solid tumors except testicular cancer [7].

The few papers dealing with gastrointestinal diseases in DS focus mainly on malformations, gastrointestinal reflux, Hirschsprung disease, and malabsorption. No publication talking about digestive neoplasms has been available [8].

There are few cases and series which mentioned the incidence of GB cancer among adult with trisomy 21 (Table 1).

In fact, Patja et al. observed an elevated risk of cancer of the GB and thyroid gland in the intellectual disability population [9]. Hermon et al. discovered that deaths from cancer in DS population, were attributed to cancer of the GB, esophagus, liver, nasal cavity, bladder and myeloma [10]. Oster et al. mentioned that the main causes of mortality among patient with DS were respiratory diseases, heart diseases, also malignant conditions included two cases of childhood leukemia and pancreatic cancer. The other causes of death from malignancy were cancer of the GB, rectum, stomach, ovary and one case of seminoma [11].

Currently, the GB cancer is a lethal disease. Overall; its prognosis is poor with a 5-years survival of approximately 5% [12].

Relating to our experience during the last 6 years, this is the only case of an adult with trisomy 21 who had a suspicious locally advanced parietal tissue thickening of the GB, associated with peritoneal carcinosis, and a bilateral massive pulmonary embolism. Unfortunately, the patient died three weeks later, before completing the investigations that would confirm the diagnosis.

There is a high risk of GB cancer among adult with trisomy 21, because pediatric patients with DS had an increased prevalence of asymptomatic cholelithiasis and other GB abnormalities. Indeed, Tyler et al. found that the rate of GB disease was 25% among DS group, compared to 4.5% among control group ($p = 0.002$) [2].

Many several conditions are considered to be risk factors for biliary lithiasis in neonates, infants and children with DS such as: hemolytic disease, cystic fibrosis, ileal resection, hypercholesterolemia, congenital hepatobiliary anomalies, congenital heart disease, prematurity, phototherapy, sepsis, parenteral nutrition, diuretics and antibiotics, particularly ceftriaxone [13].

In addition to whatever factors promote lithogenesis in infancy and childhood, adults with DS have significant rates of co-morbid obesity, diabetes mellitus and gluten-sensitive enteropathy; each of these has also been independently associated with risk for GB disease [2].

The main cholelithiasis complications are acute cholecystitis, cholangitis, biliary or gallbladder perforation, obstructive jaundice, biliary cirrhosis, and GB carcinoma.

Actually, the presence of gallstone, duration of gallstone disease, number and size of gallstones are various factors which are directly associated with chronic insult to GB mucosa. Consequently, the chronic irritation to mucosa coupled with bacterial infection lead to metaplasia followed by dysplasia and invasive carcinoma [12].

This case report is limited by the lack of similar cases in literature, and by the unavailability in our case of histological features that prove the malignancy.

4. Conclusion

Available data on the prevalence of GB cancer among adults with DS is still limited, due to rare series and case reports published until now. Children with DS are predisposed to cholelithiasis, from which we suggest this is the main risk factor of GB cancer among adult with this disease.

Other clinical trials and research about the relationship between DS and GB cancer are needed, to identify risk factors of GB cancer in this population. Finally, early screening abdominal ultrasound in children with DS is recommended in order to screen previously cholelithiasis and prevent this fatal cancer.

Consent for publication

After explaining to the family the benefits from this publication, the patient's mother give us the consent to publish this case. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

The ethical committee approval was not required give the article type (case report). However, the written consent to publish the clinical data of patients was given and is available to check by the handling editor if needed.

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Author contribution

KAOUTHAR RAIS: study concept or design, data collection, data analysis or interpretation, writing the paper, NAJOUA EL MOUTAOU-KIL: Data collection, data analysis, OUMAYMA EL EULJ: Data collection,

Table 1

Observed and expected numbers of gallbladder cancer among patients with DS and SIR, SMR with their CI 95%.

Authors	Setting	Years	Number of all patients	Number of patient observed with gallbladder cancer	patient expected to have gallbladder cancer	SIR	CI 95%	SMR	CI 95%
Hasle et al. [4]	Denmark	1968–2012	3530	0	0,44	0	0,00–8,38		
Patja et al. [14]	Finland	1978–1986	3581	2	0,3	6	0.7–21.6		
Hill et al. [15]	Sweden	1965–1993	3359	2				10,6	1,2–38,1
Ehara et al. [16]	Denmark	1977–1989	1513	0					0-68,3%
	Japan	1974–2000	1514	2					

Abbreviations: SIR = standardized incidence ratios, SMR = standardized mortality ratios.

data analysis, ABDELKRIM ZAZOUR: Data collection, data analysis, GHIZLANE KHARRASSE: Data collection, data analysis, IMANE KAMAOU: Data collection, data analysis, WAFAA KHANNOUSSI: Data collection, data analysis, MOULAY ZAHI ISMAIL: supervision and data validation.

Consent

Written informed Consent was obtained from patients for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

This is not an original research project involving human participants in an interventional or an observational study but a case report. This registration is was not required.

Guarantor

KAOUTHAR RAIS.

Provenance and peer review

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Declaration of competing interest

None.

References

- [1] D. Satgé, M.G. Seidel, The pattern of malignancies in Down syndrome and its potential context with the immune system unique cancer distribution in DS, *Front. Immunol.* 9 (2018) 1–6, <https://doi.org/10.3389/fimmu.2018.03058>.
- [2] C.V.T. Jr, S.J. Zyzanski, L. Runser, Increased risk of symptomatic gallbladder disease in adults with Down syndrome, *Am. J. Med. Genet.* 353 (2004) 351–353, <https://doi.org/10.1002/ajmg.a.30243>.
- [3] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, A. Thoma, A.J. Beamish, A. Noureldin, A. Rao, B. Vasudevan, B. Challacombe, B. Perakath, B. Kirshtein, B. Eksler, C.S. Pramesh, D.M. Laskin, D. Machado-Aranda, D. Miguel, D. Pagano, F. H. Millham, G. Roy, H. Kadioglu, L.J. Nixon, I. Mukhejee, J.A. McCaul, J. Chi-Yong Ngu, J. Albrecht, J.G. Rivas, K. Raveendran, L. Derbyshire, M.H. Ather, M. A. Thorat, M. Valmasoni, M. Bashashati, M. Chalkoo, N.Z. Teo, N. Raison, O. J. Muensterer, P.J. Bradley, P. Goel, P.S. Pai, R.Y. Affi, R.D. Rosin, R. Coppola, R. Klappenbach, R. Wynn, R.L. De Wilde, S. Surani, S. Giordano, S. Massarut, S. G. Raja, S. Basu, S.A. Enam, T.G. Manning, T. Cross, V.K. Karanth, V. Kasivisvanathan, Z. Mei, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, *Int. J. Surg.* 84 (2020) 226–230, <https://doi.org/10.1016/j.ijsu.2020.10.034>.
- [4] N.E. Blocks, *Hepatobiliary Cancers*, *Natl. Compr. Cancer Netw. NCCN.*, 2020.
- [5] H. Hasle, J.M. Friedman, J.H. Olsen, S.A. Rasmussen, Original Research Article Low risk of solid tumors in persons with Down syndrome, *Am. Coll. Med. Genet. Genomics.* 18 (2016) 1151–1157, <https://doi.org/10.1038/gim.2016.23>.
- [6] Y. Matloub, K.R. Rabin, L. Ji, M. Devidas, J. Hitzler, X. Xu, B.C. Bostrom, L.C. Stork, N. Winick, J.M. Gastier-foster, N.A. Heerema, E. Stonerock, W.L. Carroll, S. P. Hunger, P.S. Gaynon, Excellent long-term survival of children with Down syndrome and standard-risk ALL : a report from the Children ' s Oncology Group, *Blood Adv* 3 (2019) 10–12, <https://doi.org/10.1182/bloodadvances.2019032094>.
- [7] M.D. Allan H. Ropper, Down syndrome, *N. Engl. J. Med.* (2020) 2344–2352, <https://doi.org/10.1056/NEJMra1706537>.
- [8] D. Satg, J.S. Michel, M.P. Jean-franc, Aspects of Digestive Tract Tumors in Down Syndrome : A Literature Review, Springer, 2006, pp. 2053–2061, <https://doi.org/10.1007/s10620-006-9131-3>.
- [9] K. Patja, P. Eero, M. Iivanainen, Cancer incidence among people with intellectual disability, *J. Intellect. Disabil. Res.* (2001) 300–307.
- [10] C. Hermon, E. Alberman, V.B.A.J. Swerdlow, Mortality and cancer incidence in persons with Down ' s syndrome , their, *Ann. Hum. Genet.* (2017) 167–176.
- [11] M. Mikkelsen, A. Nielsen, Mortality and life-table in down's syndrome, *Acta Paediatr Scand* (1975) 322–326.
- [12] B.P. Singh, W.F. Khan, Y.S. Rathore, M.M. Pol, Incidental carcinoma gallbladder : incidence , risk factors , and factors affecting survival — 5-year experience from a tertiary, *J. Gastrointest. Cancer* (2019).
- [13] F. Figueira, Cholelithiasis and biliary sludge in Down ' s syndrome patients, *Sao Paulo Med. J.* 125 (2007) 329–332.
- [14] K. Patja, E. Pukkala, R. Sund, M. Iivanainen, M. Kaski, Cancer incidence of persons with Down syndrome in Finland : a population-based study, *Int. J. Cancer* 1772 (2006) 1769–1772, <https://doi.org/10.1002/ijc.21518>.
- [15] S.C. Deirde, A. Hill, Gloria gridley, mortality and cancer incidence among individuals with Down syndrome, *Am. Med. Assoc.* 163 (2003) 705–711.
- [16] H. Ehara, K. Ohno, H. Ito, Benign and malignant tumors in Down syndrome : analysis of the 1514 autopsied cases in Japan, *Pediatr. Int.* (2011) 72–77, <https://doi.org/10.1111/j.1442-200X.2010.03189.x>.