

A rare case of bone marrow infiltration by medulloblastoma in a child

Journal:	<i>British Journal of Haematology</i>
Manuscript ID	BJH-2019-00607.R1
Manuscript Type:	Images
Date Submitted by the Author:	n/a
Complete List of Authors:	Santarsieri, Anna; Cambridge University Hospitals NHS Foundation Trust, Department of Haematology Dickens, Emmy; Cambridge University Hospitals NHS Foundation Trust, Department of Paediatric Haematology Hook, Catherine; Cambridge University Hospitals NHS Foundation Trust, Department of Histopathology Allinson, Kieren; Cambridge University Hospitals NHS Foundation Trust, Department of Neuropathology Matys, Tomasz; Cambridge University Hospitals NHS Foundation Trust, Department of Radiology Murray, Matthew; Cambridge University Hospitals NHS Foundation Trust, Department of Paediatric Haematology and Oncology
Key Words:	BONE MARROW PATHOLOGY, medulloblastoma extracranial, medulloblastoma 'bone marrow' metastases

Images in Haematology

A rare case of bone marrow infiltration by medulloblastoma in a child

Anna Santarsieri¹, Emmy Dickens², C. Elizabeth Hook³, Kieren Allinson⁴, Tomasz Matys⁵,
Matthew J. Murray^{6,7*}

¹ Department of Haematology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

² Department of Paediatric Haematology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

³ Department of Histopathology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

⁴ Department of Neuropathology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

⁵ Department of Radiology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

⁶ Department of Paediatric Oncology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

⁷ Department of Pathology, University of Cambridge, Tennis Court Road, Cambridge, CB2 1QP

***Correspondence:** Dr. Matthew Murray, Department of Paediatric Oncology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ; Email: Telephone 0044 (0)1223 256298; Fax: 0044 (0)1223 586794; Email: mjm16@cam.ac.uk.

Article

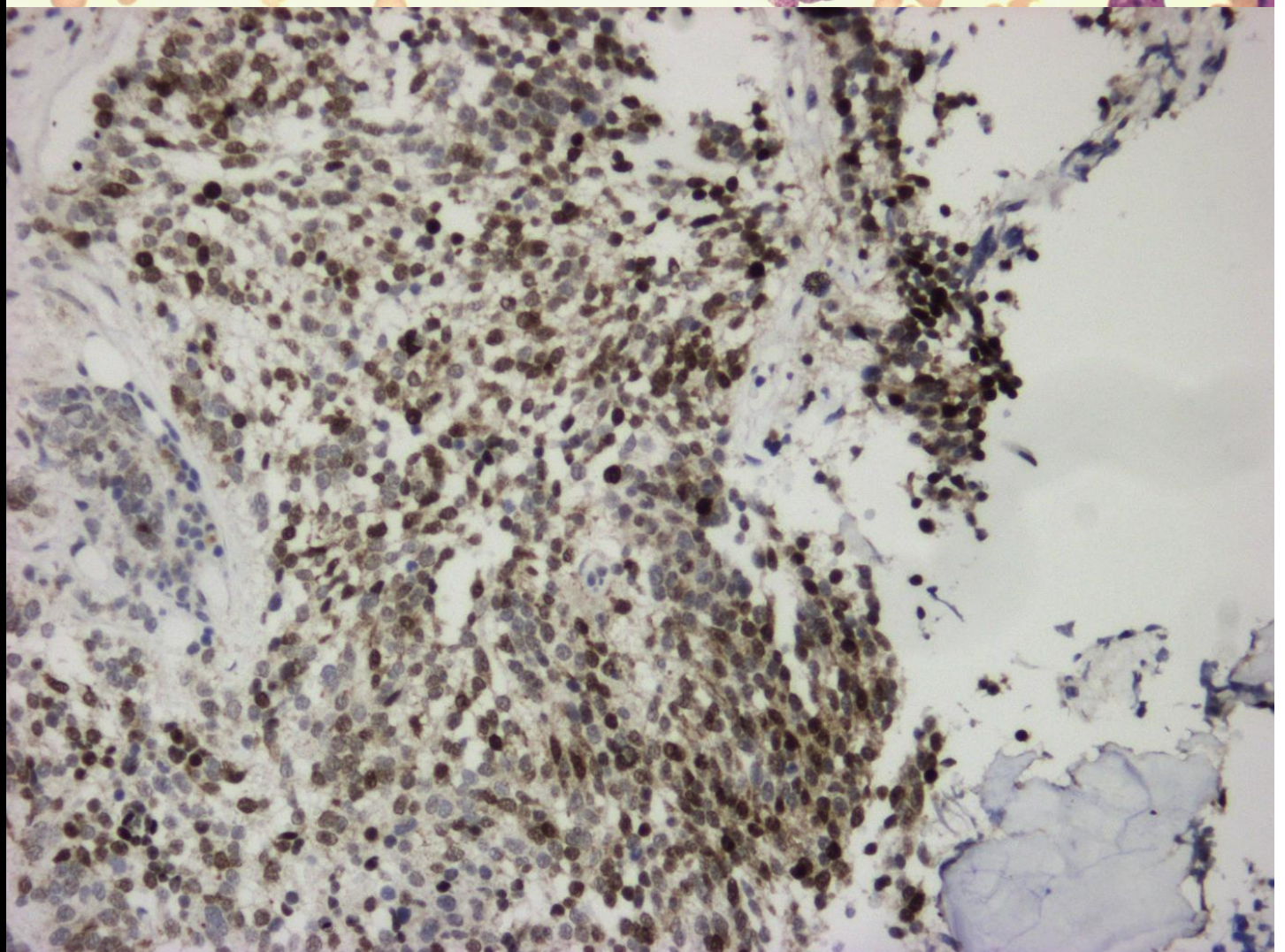
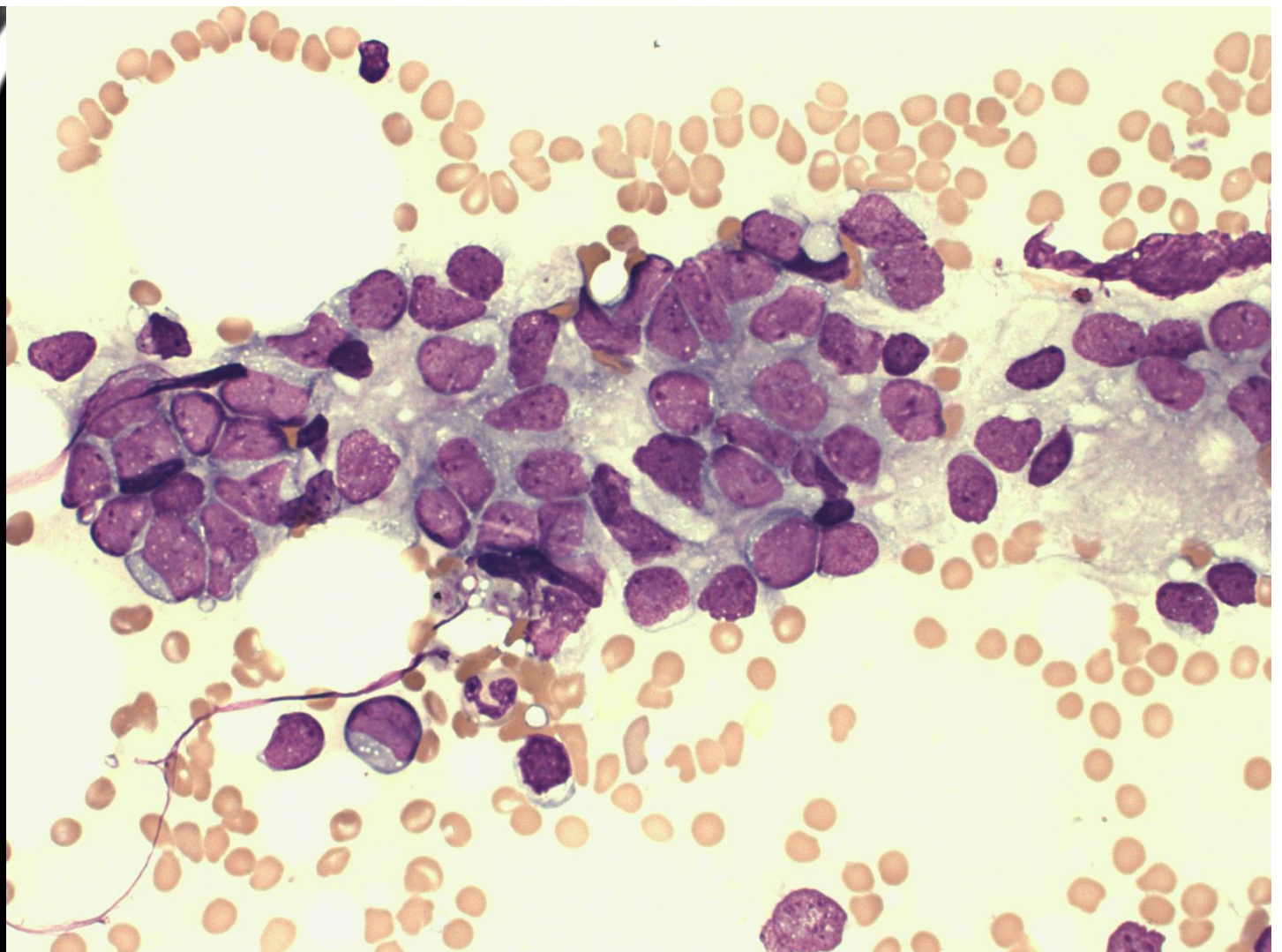
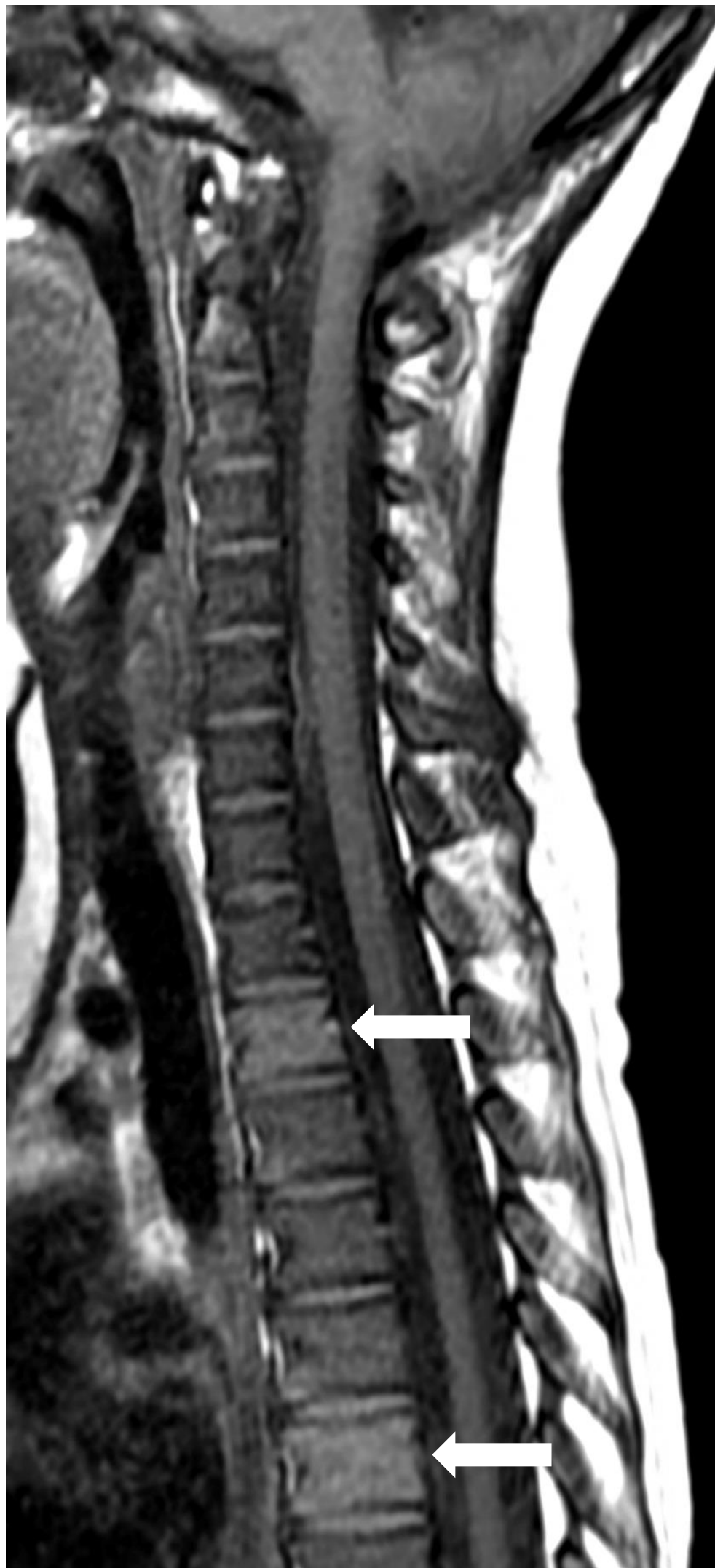
A seven-year-old boy had previously been treated for a posterior fossa medulloblastoma, with extensive central nervous system metastases. At initial presentation a chemotherapy approach was preferred, due to both his young age and extent of disease; this achieved complete radiological and cytological remission prior to consolidation with high-dose chemotherapy and autologous stem cell rescue. He then experienced an asymptomatic localised posterior fossa relapse on surveillance imaging, treated by complete surgical resection, craniospinal irradiation and maintenance chemotherapy. Unfortunately, end-of-treatment magnetic resonance imaging (MRI) of the neuro-axis revealed an asymptomatic new small enhancing intracranial lesion. Repeat MRI performed six weeks later showed minor progression of the intracranial disease and no intrathecal metastases, but new low T1 signals in multiple vertebral bodies with sparing of T3 and T7 vertebrae (arrows; left image). A full blood count showed Hb 97 g/l, WBC $7.7 \times 10^9/l$, neutrophils $5.4 \times 10^9/l$ and platelets $204 \times 10^9/l$. In view of the radiological appearances, bone marrow aspiration and trephine biopsy were performed from the posterior iliac crest. The aspirate revealed heavy infiltration with clusters of non-haematopoietic cells, characterized by high nuclear:cytoplasmic ratio, open chromatin and agranular, weakly basophilic cytoplasm with vacuolation (right upper image). Trephine biopsy immunohistochemistry demonstrated positive staining for synaptophysin, CD56, Neu-N (right lower image), retained INI1 expression and negative CD99 and desmin, confirming medulloblastoma. Spread of medulloblastoma to the bone marrow is a very rare event. In this case, despite an unremarkable full blood count, radiological changes in the spinal column suggesting widespread marrow infiltration were confirmed by bone marrow examination. Early identification of extracranial metastasis afforded the family and clinicians the opportunity to make informed choices regarding ongoing management.

Acknowledgements

Specific contributions to the work described in the manuscript: AS and ED reported the bone marrow aspirate, obtained images, contributed to the manuscript and agreed the final version. CEH and KA reported the bone marrow trephine and obtained images, contributed to the manuscript and agreed the final version. TM reported the MRI spine and obtained images, contributed to the manuscript and agreed the final version. MJM was the clinician responsible for patient care, coordinated the work, wrote the manuscript and agreed the final version.

For Peer Review

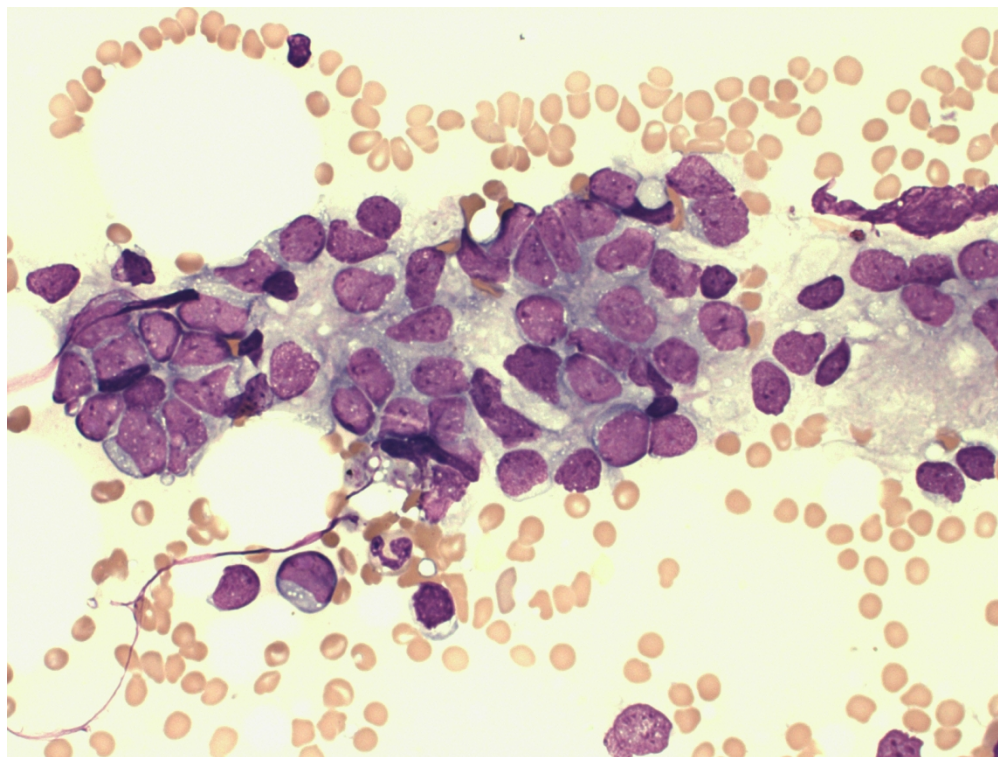
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



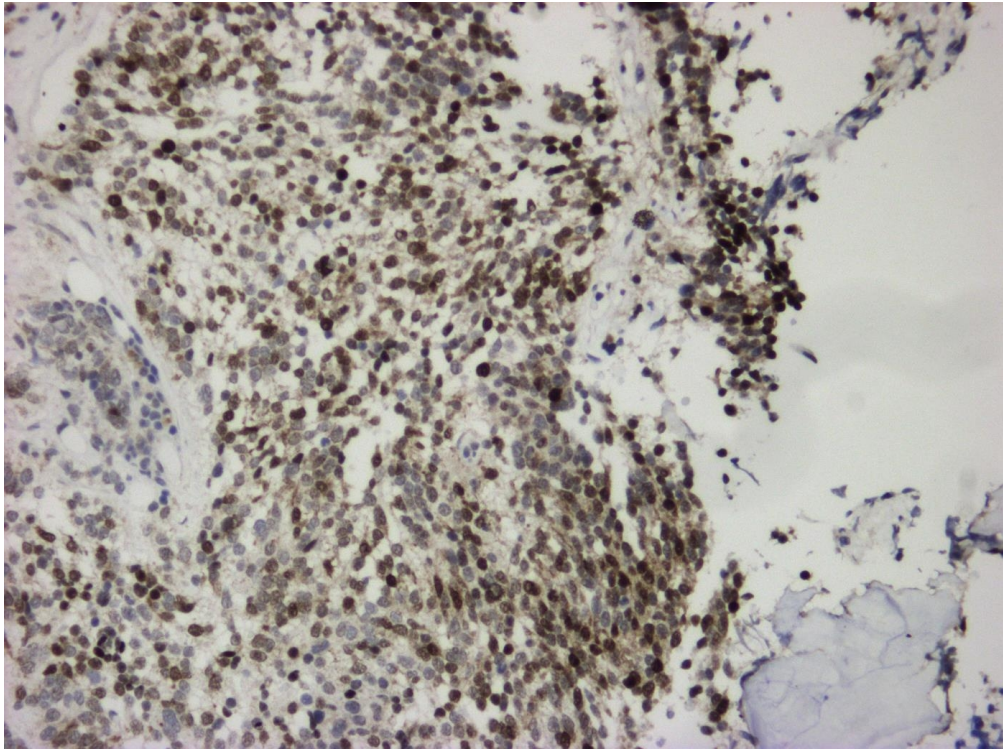
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



368x275mm (96 x 96 DPI)

Images in Haematology

A rare cause of bone marrow infiltration [by medulloblastoma](#) in a child

Anna Santarsieri¹, Emmy Dickens², C. Elizabeth Hook³, Kieren Allinson⁴, Tomasz Matys⁵,
Matthew J. Murray^{6,7*}

¹ Department of Haematology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

² Department of Paediatric Haematology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

³ Department of Histopathology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

⁴ Department of Neuropathology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

⁵ Department of Radiology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

⁶ Department of Paediatric Oncology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ

⁷ Department of Pathology, University of Cambridge, Tennis Court Road, Cambridge, CB2 1QP

***Correspondence:** Dr. Matthew Murray, Department of Paediatric Oncology, [Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, CB2 0QQ](#); Email: mjm16@cam.ac.uk.
Telephone 0044 (0)1223 256298; Fax: 0044 (0)1223 586794; Email: mjm16@cam.ac.uk.

Article

A seven-year-old boy ~~had~~ ~~was~~ previously ~~been~~ treated for ~~the primary~~ posterior fossa ~~tumour~~, medulloblastoma, with extensive central nervous system metastases ~~including leptomeningeal and intrathecal spinal disease; methylation profiling confirmed a Group 4 tumour~~. At initial presentation a chemotherapy approach was preferred, due to both his young age and extent of disease; this achieved complete radiological and cytological remission prior to consolidation with high-dose chemotherapy and autologous stem cell rescue. He then experienced an asymptomatic localised posterior fossa relapse on surveillance imaging, treated ~~by~~ ~~with~~ complete surgical resection, craniospinal irradiation and maintenance chemotherapy. ~~This chemotherapy was interrupted due to poor count recovery following irradiation, and a bone marrow aspirate and trephine were performed which excluded metastatic medulloblastoma or secondary leukaemia. Alternative maintenance with temozolomide was well tolerated.~~ Unfortunately, end-of-treatment ~~magnetic resonance imaging (MRI) imaging~~ of the neuro-axis revealed an asymptomatic new small enhancing intracranial lesion. ~~An early repeat MRI was performed six weeks later which~~ showed minor progression of the intracranial disease and no intrathecal metastases, but new low T1 signals in multiple vertebral bodies with sparing of T3 and T7 vertebrae (arrows; left image) ~~compared with the imaging performed just six weeks previously~~. A full blood count ~~showed~~ ~~revealed~~ Hb 97 g/l, WBC 7.7 $\times 10^9/l$, neutrophils 5.4 $\times 10^9/l$ and platelets 204 $\times 10^9/l$. In view of the radiological appearances, bone marrow aspiration and trephine biopsy were performed from the posterior iliac crest. ~~The~~ ~~a~~ Aspirate revealed heavy infiltration with clusters of non-haematopoietic cells, characterized by high nuclear:cytoplasmic ratio, open chromatin and agranular, ~~weakly~~ ~~pale~~ basophilic cytoplasm with vacuolation (right upper image). Trephine biopsy immunohistochemistry demonstrated positive staining for synaptophysin, CD56, Neu-N (right lower image), retained INI1 ~~expression~~ and negative CD99 and desmin, confirming medulloblastoma. Spread of

1
2
3 medulloblastoma to the bone marrow is a very rare event. In this case, despite an unremarkable
4 full blood count, radiological changes in the spinal column ~~correlated with easily identified~~
5 ~~disease in aspirate and trephine samples taken from the posterior iliac crest~~ suggesting
6 widespread marrow infiltration were confirmed by bone marrow examination. Early
7 identification of extracranial metastasis afforded the family and clinicians the opportunity to
8 make informed choices regarding ongoing management.
9
10
11
12
13
14
15
16
17
18
19
20

21 **Acknowledgements**

22
23
24 Specific contributions to the work described in the manuscript: AS and ED reported the bone
25 marrow aspirate, obtained images, contributed to the manuscript and agreed the final version.
26
27 CEH and KA reported the bone marrow trephine and obtained images, contributed to the
28 manuscript and agreed the final version. TM reported the MRI spine and obtained images,
29 contributed to the manuscript and agreed the final version. MJM was the clinician responsible
30 for patient care, coordinated the work, wrote the manuscript and agreed the final version.
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60